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HERBAL CARE FOR WOMEN: A GUIDE TO PHYTOTHERAPEUTIC AGENTS IN GYNAECOLOGY AND REPRODUCTIVE HEALTH

CHAPTER 3: HERBAL AGENTS FOR MENTRUAL DISORDER

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ABSTRACT

Many uncomfortable symptoms are frequently brought on by menstruation. The most prevalent problems, like mild cramps and tiredness, are included in premenstrual syndrome (PMS), however these symptoms normally disappear once your period starts. Menstrual disorders including dysmenorrhea and amenorrhea can be effectively managed with the help of medicinal plants.

Despite interrupting women's daily activities, menstrual disorders are typically not considered major health concerns by global health organizations. Access to safe and effective medication is necessary to improve menstruation health, yet many women in Latin America, Africa, or Asia prefer traditional medicine over contemporary treatments (such contraceptives) because allopathic medicines can result in physical symptoms linked to infertility.

Google Scholar, PubMed, ScienceDirect, and Web of Science, as well as secondary sources like books and conference proceedings, were used to methodically gather the data on herbal remedies for women. Fifty different plants were employed to treat various menstruation diseases. The greatest significant therapeutic value was discovered to be found in seeds





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(43.8%), followed by leaves (20.8%) and fruits (16.7%). Menstrual disorders are treated with *Ruta graveolens* L, *Diels* (*Angelica sinensis*), *Zingiber officinale* Roscoe, *Catharanthus roseus*, *Angelica sinensis*, *Foeniculum vulgare* Mill, and other medications with clear benefits and long-term use. *Triticum aestivum*, *Taraxacum officinale*, *Citrus limon*, *Allium cepa*, *Cicer arietinum*, *Trigonella foenum-graecum*, *Rubia manjith*, *Ocimum tenuiflorum*, and *Oryza sativa* were the plants with high use value. The most popular families of medicinal plants utilized for these kinds of therapies include Asteraceae, Lamiaceae, Apiaceae, Fabaceae, and Zingiberaceae. The primary method of medication intake was found to be oral administration.

Keywords: menstruation; PMS; amenorrhea; dysmenorrhea; menstrual disorders.

1.Introduction

Medicinal plants have been utilized for centuries in traditional systems of medicine, and diverse healthcare practices, for the management of gynecological and menstrual problems.

In terms of the menstruation, menstrual health is a condition of complete well being in terms of social, mental and physical state rather (1). Menarche is an important biological landmark in the life of a woman as it marks the beginning of the reproductive phase. Hormones control menstruation, which results in bleeding that typically lasts three to five days as the the lining of the uterus, endometrium gradually thickens and sheds (38).

Serious medical ramifications may emerge from menstruation abnormalities characterized by frequent and unpredictable bleeding, extended bleeding, or profuse bleeding (2).

1.1 Overview of the Female Reproductive Cycle: Endocrine Regulation and the Hypothalamic–Pituitary–Ovarian (HPO) Axis

This chapter provides an overview of the hypothalamic-pituitary-ovarian (HPO) axis, also known as the female reproductive axis. The main hormone that plays a role are estrogen and progesterone. During adolescence, the brain secretes GnRH which gives signal to the pituitary





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to release FSH and LH. Progesterone and estrogen are released in response to FSH and LH. During the menstrual cycle, variable levels of progesterone and estrogen are released, leading to the luteal phase and the follicular phase (3).

The primary neuroendocrine system via which human females adjust reproductive functioning in response to shifting environmental conditions is the HPO axis. Determining the proximate and distant factors of human reproductive patterns requires an understanding of the degree and reasons of adaptive and non-adapted variation in ovarian functioning (4). Through coordinated cyclic changes in the ovaries, uterus, and endocrine system, the female reproductive cycle is a complicated physiological process that primes the body for fertilization and pregnancy. Although cycles ranging from 21 to 35 days are regarded as typical in healthy women, the average menstrual cycle lasts about 28 days. It is made up of two interconnected cycles: the menstrual, proliferative, and secretory phases of the uterine cycle and the follicular, ovulation, and luteal phases of the ovarian cycle. Precise hormonal interactions control follicular maturation, ovulation, endometrial growth, and, in the absence of fertilization, menstruation.

In mammals, the female reproductive system is responsible for producing female gametes, permitting sperm fertilization, encouraging the growth and development of the embryo and fetus, and aiding in the delivery and feeding of the offspring. Consequently, hormones that are generally characterized by their metabolic functions are also critical for managing reproduction (5). Additionally, poor nutrition, severe exercise, or lifestyle stressors may cause menstruation loss in previously normal-ovulatory women (6).

1.2 Pathophysiology of common menstrual disorders

Heavy and painful menstrual cycles have long been linked (7). According to one study, there was a substantial correlation between the length of bleeding and dysmenorrhea, and girls who experienced bleeding for longer than five days were nearly twice as likely to experience pain. Additionally, those who had clots were more than twice as likely to experience dysmenorrhea.





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Similar to dysmenorrhea, about 30% of teenage and young women experience heavy menstrual bleeding (8).

Menstrual blood loss beyond 80 milliliters every cycle is known as menorrhagia or heavy bleeding. This figure derives from research revealing that when blood loss above this level, anemia is typically the result (9). Menorrhagia leads to hamper women's life in all the ways (10). The majority of endoscopic endometrial destructive surgery are performed due to menorrhagia, which is the primary presenting complaint for women referred to gynecologists. fibrinolytic system and PG abnormalities have been linked to this condition (39).

The abnormal or absence stopping of menstruation is known as amenorrhea. Amenorrhea that occurs prior to menarche is referred to as primary amenorrhea, while amenorrhea that occurs after menarche is referred to as secondary amenorrhea. Primary and secondary amenorrhea have so many common causes (40). The main cause of primary amenorrhea is due to abnormalities in the chromosomes that results in basic ovarian insufficiency, Androgen insensitivity, led;-1Breast development, Imperforate hymen, Prolactinomas, Kallman syndrome, Congenital adrenal hyperplasia, Prolactinomas and. secondary amenorrhea occur when regular menses stops for 3 months and irregular menses stops for 6 months. Most common causes for secondary amenorrhoe are PCOD, Low or normal FSH, Cushing's syndrome, Sheehan syndrome, Asherman syndrome, Ovarian tumor and primary ovarian insufficiency (29, 40).

2. Symptoms and risk factors

The word "dysmenorrhea" refers to lower abdomen pain and swelling prior to, during and following menses, as well as back pain or other discomfort (17). Colic discomfort in the suprapubic area that radiates to the lumbar and thighs before or during menstruation without pelvic disease is called primary dysmenorrhea (18). On the other hand, pathology or underlying pelvic problems are the cause of secondary dysmenorrhea (17).





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2.1 Primary dysmenorrhea

Lower abdominal pains are the most common sign of dysmenorrhea, although many teens and young adults also have headaches, nausea, and vomiting. In a recent cross-sectional study of teenage girls with this in the United States, menstrual cramps were associated with vomiting and nausea in approx 24% and 55% of participants respectively. Symptoms typically coincide with the start of menstrual flow or manifest a few hours prior to or following menstruation throughout the first 2 days (11).

2.2 Secondary dysmenorrhea

Secondary dysmenorrhea is more commonly associated with metrorrhagia, dyspareunia, midcycle pain, and persistent pelvic pain. Compared to either cyclic or acyclic pain alone, adolescents with endometriosis are more likely to experience both types of pain.

Patients who have a first-degree relative with endometriosis are five to ten times more likely to have the condition than the general population. Studies on monozygotic twins reveal a 75% endometriosis concordance rate. The path of inheritance is probably a polygenic, multifactorial pattern, and the expression is probably linked to interactions with environmental factors. Furthermore, an increased risk of fibroids, ovarian cysts, and endometriosis has been associated with bleeding problems.

3. Treatment

3.1 Primary dysmenorrhea

3.1.1. Non-pharmacological approach

- **Effect of physiotherapy-** Every electrical nerve stimulation, yoga and heat study showed a significant reduction in pain intensity.





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- **Effect of acupuncture-** Five minutes after acupuncture treatment at the Sanyinjiao point, menstruation pain levels significantly decreased.
- **Effect of reflexology-** This method is also effective in reduction of pain intensity.
- **Effect of aromatherapy massage-** Intensity of pain is reduced by the usage of lavender oil (45).

3.1.2. Pharmacologic approach

The main objectives of treatment include preventing hyperplasia of endometrium, maintaining bone density and maintaining heart(12).It is treated with hormone replacement therapy (HRT) and human growth hormone treatment (41).This HRT therapy will improve the above mentioned symptoms if continued till menopause (42).

A) Non-steroidal anti-inflammatory drugs

Prostaglandin synthetase inhibitor or NSAIDs has some advantages over other medication. It does not significantly suppress pituitary-ovarian axis and it is taken for only initial 2-3 days of menstruation cycle. It does not have any serious metabolic effect like oral contraceptives. Ibuprofen is effective for dysmenorrhoea. The recommended dose is 0.4 mcg every 6 hour (43). Naproxen is also effective in relieving severe cramps and also prevent symptoms like dizziness and vomiting (44).

B) Hormonal treatment

Combined estrogen and progestin oral contraceptive pills

Combined oral contraceptive pills (OCPs) are a common treatment for women with primary dysmenorrhea. Adolescent dysmenorrhea may be best treated with OCPs:

They provide major health benefits for teenagers like lowering acne and preventing pregnancies. OCPs directly prevent or alleviate dysmenorrhea by inhibiting synthesis of prostaglandin in endometrium and preventing growth of endometrium. They accomplish this





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indirectly by stopping ovulation and the subsequent release of progesterone (13). The regimen which is generally used is 625 mcg and 200 mg of oral estrogen and oral progestrone per day for twelve days every month (42).

3.1.3. Injectable long-acting hormonal contraceptives

Depot medroxyprogesterone acetate (DMPA), an injectable contraceptive, is a progestin-only having longer duration of action, efficient, and practical means of birth control. It comes in two different formulations: The FDA approved the intramuscular formulation (Depo-Provera and Depo-subQ Provera both of which are given every 12 weeks. DMPA can be used to treat dysmenorrhea symptoms since it inhibits ovulation for up to seven to nine months following a single intramuscular injection (13).

3.1.4. Other long-acting progestin-only hormonal contraceptives

The Levonorgestrel-releasing IUD (LNG-IUS, Mirena ®) releases 20 µg of levonorgestrel daily into the uterus for five years. Women (ages 25 to 47) reported that the main advantages of using Mirena were the reduction of menstrual pain and the eradication or diminution of menstruation. The etonogestrel subdermal implant (Implanon ®), which provides effective contraception was also authorized by the FDA in 2006 (14).

3.2. Secondary dysmenorrhea

A) Combined regimen of Progestrone and estrogen for extended period

Ongoing combined hormone therapy is the first line of treatment for teens and young adults with endometriosis, particularly for girls less than sixteen. The Cochrane Database review results show that further study is required to demonstrate long-term advantages, even if this strategy may deliver effective treatment.

B) Agonists of GnRH





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Gonadotropin-releasing hormone (GnRH) agonists cause a hypestrogenic state and alleviate endometriosis symptoms by downregulating the hypothalamic-pituitary axis. However, because of the negative effects of the hypoestrogenic condition on bone mineralization, this medication is not recommended as a first choice of medication. Adolescents and young adults using GnRH agonists must intake adequate calciferol and Ca^{2+} , as well as participate in sufficient physical exercise, in order to maintain optimal bone health. This therapy is supplemented with steroids to maintain bone density when long-term GnRH agonist treatment is being used.

C) Aromatase inhibitors

The enzyme that limits the pace at which oestrogen is produced from C19 androgens is aromatase. Aromatase inhibitors (AIs) have been proposed as the next generation of medications for the treatment of endometriosis since they can successfully prevent the local manufacture of oestrogen in the endometriotic lesions [85–87]. The triazole compounds letrozole (Femara ®) and anastrozole (Arimidex ®) are reversible, competitive AIs that decrease aromatase levels by 97–99% at dosages of 1–5 mg/day [88]. Irreversible AI exemestane (Aromasin ®) effectively inactivates the aromatase enzyme by binding to its active site.

D) Other investigational drugs

Dysmenorrhoea can also be treated by the modulation of only progesterone receptor (14). Immune modulators, oestrogen receptor beta-agonists, angiogenesis inhibitors, and matrix metalloprotease inhibitors are presently being studied as prospective endometriosis therapies (15).

4. Classification of medicinal plants used in menstrual disorder

(1) *Zingiber officinale* (Ginger)





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Ginger may be a useful remedy for premenstrual syndrome symptoms. A prostaglandin system alteration is one of the hypothesized causes of premenstrual syndrome. Ginger inhibits the metabolism of lipoxygenase and cyclooxygenase, which stops prostaglandins from being produced. Headaches and migraine symptoms are two symptoms associated with PMS. Ginger was proven to be useful in treating headaches (25).

(2) *Rubus idaeus* (raspberry)

Rubus idaeus or raspberry, is a member of the Rosaceae family. The raspberry leaf is mostly thought to be beneficial during pregnancy and menstruation. The leaves of raspberries are rich in protective antioxidants.

Raspberry leaves include antioxidizing polyphenols including tannins, bioflavonoids, and alkaloids that help tone and relax the uterine and pelvic muscles. These drugs help to tighten and tone the pelvic muscles.

(3) Chamomile (*Matricaria chamomilla*)

Because of its anti-spasmodic qualities, chamomile can ease the severe cramps that come with menstruation. Additionally, its tea helps balance or at least lessen the effects of depression symptoms by modulating the actions of serotonin and dopamine. However, the antispasmodic properties give relief in the pain associated with dysmenorrhoea (30).

(4) Aloe vera (*Aloe barbadensis* Mill.)

It contains a variety of bioactive substances, such as phytosterols, many vitamins, polysaccharides, amino acids, etc., which are in charge of its various pharmacological actions, including the treatment of PCOS. Androgen levels have been observed to rise dramatically in PCOS, which results in hyperglycemia and resistance to insulin action, leading to obesity and diabetes. FSH levels also drop concurrently with an increase in testosterone, a healthy hormonal imbalance that causes PCOS. Aloe vera inhibits PCOS phenotypes (32).





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(5) Turmeric (*Curcuma longa*)

They reduce pain and inflammation by blocking prostaglandin synthesis and cyclooxygenase-2 (COX-2) activity. It has analgesic benefits, and alleviates PMS and dysmenorrhea symptoms, while curcumin's antioxidant qualities guard against oxidative stress. Additionally, it will modulate the function of NTM, such as elevated dopamine and 5-HT concentration, which is responsible for CNS depressant action (33).

(6) Ginger (*Zingiber officinale*)

Ginger may be a useful remedy for premenstrual syndrome symptoms. A prostaglandin system alteration is one of the causes of premenstrual syndrome. Ginger stops prostaglandin synthesis by inhibiting the metabolism of COX and LOX (34).

(7) *Glycyrrhiza glabra* (Licorice)

Ibuprofen tablets and *G. glabra* root extract both exhibited beneficial action in primary dysmenorrhea discomfort. By blocking the Cyclo-oxygenase and Lipo-oxygenase pathways, glabridin and isoliquiritigenin, which are extracted from *G. glabra* root, reduce prostaglandin generation. The results of the experiments verifying the components' anti-inflammatory, anti-spasmodic, and analgesic properties are consistent with the phytochemical investigation of *G. glabra* roots (36).

(8) *Paeonia lactiflora* Pall (Chinese peony)

For 1200 years, the medicinal plant *Paeonia lactiflora* Pall has been utilised in China, Korea, Japan, and Iran. Hepatitis, dysmenorrhea, headaches, stomachaches, and irregular menstrual cycles have all been treated with it. A combination of extracts from *Glycyrrhiza glabra* and *Paeonia lactiflora* has previously been shown to be successful in restoring menstruation and hormonal balance in people with PCOD (16).

(9) *Foeniculum vulgare* (Fennel)





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Fennel which is a member of Apiaceae family helps in promoting menstrual blood flow. It also relieve the inflammation and has estrogen like properties (26). When compared to the control group, it shows positive results in inducing menstruation following the administration of medroxyprogesterone acetate. (16).

(10) *Mentha longifolia* (Horse Mint)

Mentha longifolia is one of numerous plants in the Lamiaceae family that are employed in industrial and pharmacological settings. For many years, this medicinal herb has been utilised to treat gynaecologic and gastrointestinal issues. *Mentha longifolia* extracts have been demonstrated to induce menstruation. Additionally, it shows that in patients with primary ovarian failure, this extract reduces FSH and causes menstruation (16).

(11) *Sesamum indicum* (Sesame)

The flowering plant *Sesamum indicum* belongs to the Pedaliaceae family and genus *Sesamum*. This medicinal plant has been used in TPM to treat lung and renal conditions, induce menstrual bleeding, and boost libido. Additionally, sesame has been demonstrated to have good action against oxidation in the body and cholestrol deposition. It has been shown to cause menses in women with severe oligomenorrhea without causing any negative effects.

(12) *Urtica dioica* (Common Nettle)

A herbaceous perennial blooming plant of Urticaceae family. *Urtica dioica* have diuretic action and it also give relief in rheumatoid and arthritis. According to a study, *Urtica dioica* extract improved the clinical and paraclinical symptoms of hyperandrogenism in women, but improvement of menstrual irregularities was lower in the intervention group compared to the control group. Ancient Iranian physicians used this plant to increase libido, induce menstruation, and treat renal and pulmonary diseases (16)

(13) *Cimicifuga racemosa* (Black Cohosh)





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There are roughly fifteen species of *Cimicifuga* found in the world's northern temperate zones. The widespread use of this plant is found in traditional medicine in Asian nations like China, Japan, India, Bhutan, and Myanmar. *Cimicifuga racemosa* is commonly used to treat dysmenorrhea, premenstrual symptoms, and menopausal symptoms. Its effects are comparable to those of hormones.

(14) *Trigonella foenum-graecum* (Fenugreek)

Iran and the Mediterranean region are home to the annual plant *Trigonella foenum-graecum*, which is a member of the Fabaceae family. It has long been used to treat gynaecologic, lung, and gastrointestinal disorders. Research indicates it can improve fertility, regulate menstrual cycles, and improve the ultrasonographic features of PCOD by reducing the hormone ratio. (16).

(15) *Cinnamomum verum* (True Cinnamon)

Cinnamon is an evergreen shrub with aromatic properties that belongs to the Lauraceae family. It has the potency to heal lung and brain disorders, regulate menstruation, and increase sexual desire. By increasing blood progesterone levels during the luteal phase, cinnamon is thought to help control the menstrual cycle (16). The cinnamon group experienced significantly less menstrual bleeding. At different intervals, the cinnamon group's mean pain severity score was lesser than the placebo group's. At different intervals, the cinnamon group's mean nausea severity and vomiting frequency were considerably lower than those of the placebo group (31).

(16) *Angelica sinensis* (Female Ginseng)

Traditional Chinese medicine uses *Angelica sinensis* as a tonic, hematopoietic, and anti-inflammatory for a variety of conditions, including gynecological issues (27). It increase blood circulation to control menstrual cycles and reduce period pain. Common name of *Angelica sinensis* is female ginseng and main constituents of the plant responsible for the activity is ferulic acid, cyanocobalamin, iron, choline, Vitamin B9 and ligustilide (28).





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(17) *Vitex agnus-castus* (chasetree)

Since 2000 years ago, *Vitex agnus-castus*, also known as chasetree, belong to Lamiaceae family has been used as a common medicine to cure infertility and irregular menstruation. This plant and Low-dose oestrogen had comparable effects on the menstruation return to normal as well as maintain normal level of hormone in the serum of women with PCOD (16). The efficacy of a dried extract on the four symptoms of PMS—depressive symptoms, anxiety and hyperhydration during three menstrual cycles—was examined in an open-label, multicenter study which involve 1634 PMS patients. Reduction in the symptoms was noted by nearly 93% of individuals (22).

Table 1. Herbal drugs recommended to treat menstrual diseases

S.no	Scientific name	Family	Common Name	Part used	Menstrual Diseases	Reference
1.	<i>Sambucus nigra</i>	Adoxaceae	Elderberry	Root	treat amenorrhea	Mazzei R et al. (2024)
2.	<i>Cinnamomum cassia</i>	Lauraceae	Chinese cinnamon	Bark	treating premenstrual syndrome.	Jiao M et al. (2022)
3.	<i>Ziziphus jujuba</i> Mill.	Rhamnaceae	Chinese Date	Fruit	treating premenstrual syndrome.	Jiao M et al. (2022)





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4.	<i>Apium graveolens L.</i>	Apiaceae	celery	leaves	menorrhagia	Mazzei R et al. (2024)
5.	<i>Hydrastis Canadensis L</i>	Ranunculaceae	Golden seal	Rhizomes	Dysmenorrhea	Begum M, et al. (2016)
6.	<i>Ocimum basilicum L;</i>	Lamiaceae	Basil	leaves	Dysmenorrhea	Begum M, et al. (2016)
7.	<i>Cinnamomum zeylanicum</i>	Lauraceae	cinnamon	Bark		Begum M, et al. (2016)
8.	<i>Vitex agnus-castus</i>	Verbenaceae	monk's pepper	Fruit	premenstrual syndrome (PMS)	Loch EG et al. (2000)
9.	<i>Ruta graveolens L.</i>	Rutaceae	Rue		irregular menstruation	Luo P et al. (2024)
10.	<i>Pimpinella anisum L.</i>	Apiaceae	Anise	seeds	treat amenorrhea	Mazzei R et al. (2024)





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11.	<i>Hedera helix L.</i>	Apocynaceae	Common Ivy	leaves	Regulate menstruation	Mazzei R et al. (2024)
12.	<i>Nerium oleander L.</i>	Apocynaceae	Oleander	leaves	treat amenorrhea	Mazzei R et al. (2024)
13.	<i>Petroselinum crispum L.</i>	Apiaceae	Parsley	leaves	Dysmenorrhea	Begum M, et al. (2016)
14.	<i>Valeriana officinalis L.</i>	Valerianaceae	Valerian	Leaves	Dysmenorrhea	Begum M, et al. (2016)
15.	<i>Alchemilla vulgaris L.</i>	Rosaceae	Ladies' mantle	Roots	reduce menorrhagia	Begum M, et al. (2016)
16.	<i>Matricaria chamomilla L.</i>	Asteraceae	Chamomile	flowers	treat dysmenorrhea and amenorrhea	Mazzei R et al. (2024)
17.	<i>Petasites albus Gaertn.</i>	Asteraceae	White butterbur)		treat metrorrhagia	Mazzei R et al. (2024)





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18.	<i>Borago officinalis L.</i>	Boraginaceae	Starflower	Leaves	treat amenorrhea	Mazzei R et al. (2024)
19.	<i>Boswellia spp.</i>	Burseraceae	Incense	flower	treat amenorrhea	Mazzei R et al. (2024)
20.	<i>Bryonia dioica Jacq.</i>	Cucurbitaceae	White bryony	root	treat amenorrhea	Mazzei R et al. (2024)
21.	<i>Juniperus sabina L.</i>	Cupressaceae	Savin juniper	flower	treat amenorrhea	Mazzei R et al. (2024)
22.	<i>Acacia senegal</i>	Fabaceae	Gum arabic tree)	gum	to treat metrorrhagia and menorrhagia	Mazzei R et al. (2024)
23.	<i>Hypericum perforatum L.</i>	Hypericaceae	St John's wort	leaves	treat dysmenorrhea	Mazzei R et al. (2024)
24.	<i>Crocus sativus L.</i>	Iridaceae	Saffron	flowers	treat amenorrhea	Mazzei R et al. (2024)





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25.	<i>Juglans regia L.</i>	Juglandaceae	Walnut	leaves	treat menorrhagia	Mazzei R et al. (2024)
26.	<i>Lavandula angustifolia Mill.</i>	Lamiaceae	Spanish lavender		regulate menstruation	Mazzei R et al. (2024)
27.	<i>Salvia officinalis L.</i>	Lamiaceae	Sage	leaves	block menstrual flux	Mazzei R et al. (2024)
28.	<i>Malva sylvestris L.</i>	Malvaceae	Common mallow	leaves	treat amenorrhea	Mazzei R et al. (2024)
29.	<i>Cimicifuga racemosa</i>	Ranunculacea e	black cohosh	roots	Cimicifuga racemosa	Rahal A et al. (2013)
30.	<i>Zingiber officinale</i>	Zingiberaceae	Ginger	rhizom e	Improve premenstrual syndrome	Khayat S et al. (2014)
31.	<i>Viburnum lentago L.</i>	Adoxaceae	nannyberry	Root	Improve Irregular menstruation	Jiao M et al. (2022)





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32.	<i>Adiantum pedatum L.</i>	Pteridaceae	maidenhair fern	Root	Menorrhagia	Jiao M et al. (2022)
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5. Safety, Toxicology, and Drug Interactions

Herbal products are not subject to purity and potency regulations, in contrast to conventional pharmaceuticals. Herbal remedies contain substances that can either increase or decrease the activity of enzyme involved in the biotransformation of medications. Therefore, taking some therapeutic plants and drugs at the same time could have serious side effects and lessen the efficacy of the treatment. Unpredictable side effects may occur when medications with a restricted therapeutic index are combined with plants that can alter drug metabolizing enzymes. The most prevalent misconduct in the trade of herbal raw materials is the presence of impurities, contaminants, and adulterants in herbal goods (35).

The main route for herbal drug interaction is by the cytochrome P450 mechanism, P glycoprotein and UDP- glucuronyl transferase. Most common interaction results in pharmacokinetic interaction.

6. Preventive measure to reduce toxicity of herbal products

- The label and expiration date of the herbal products should be checked for the regulatory authority's seal.
- If the herbal cure is used in conjunction with allopathic medications, the doctor should be informed.
- Drugs including warfarin, digoxin, cyclosporin, and theophylline that have a limited therapeutic window should not be administered with herbal products.





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- Steer clear of herbal products that contain heavy metals including arsenic, lead, and mercury (37).

References

1. Hennegan J, Winkler IT, Bobel C, Keiser D, Hampton J, Larsson G, Chandra-Mouli V, Plesons M, Mahon T. Menstrual health: a definition for policy, practice, and research. *Sexual and reproductive health matters*. 2021 Jan 1;29(1):31-8.
2. Harlow SD, Campbell OM. Menstrual dysfunction: a missed opportunity for improving reproductive health in developing countries. *Reproductive health matters*. 2000 Jan 1;8(15):142-7.
3. Davis HC, Hackney AC. The hypothalamic–pituitary–ovarian axis and oral contraceptives: regulation and function. In *Sex hormones, exercise and women: scientific and clinical aspects* 2016 Nov 11 (pp. 1-17). Cham: Springer International Publishing.
4. Vitzthum VJ. The ecology and evolutionary endocrinology of reproduction in the human female. *American journal of physical anthropology*. 2009;140(S49):95-136.
5. Athar F, Karmani M, Templeman NM. Metabolic hormones are integral regulators of female reproductive health and function. *Bioscience reports*. 2024 Jan;44(1):BSR20231916.
6. Golden, N.H. and Shenker, I.R. (1994), Amenorrhea in anorexia nervosa neuroendocrine control of hypothalamic dysfunction. *Int. J. Eat. Disord.*, 16: 53-60.
7. Hoppenbrouwers K, Roelants M, Meuleman C, et al. Characteristics of the menstrual cycle in 13-year-old Flemish girls and the impact of menstrual symptoms on social life. *Eur J Pediatr*. 2016;175(5):623–30.
8. Kural M, Noor NN, Pandit D, Joshi T, Patil A. Menstrual characteristics and prevalence of dysmenorrhea in college going girls. *J Family Med Prim Care*. 2015;4(3):426–31.





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9. Hallberg L, Hogdahl AM, Nilsson L, Rybo G. Menstrual blood loss – a population study. *Acta Obstet Gynaecol Scand.* 1966;45:320–51.
10. Munro MG, Critchley HO, Fraser IS. The FIGO systems for nomenclature and classification of causes of abnormal uterine bleeding in the reproductive years: who needs them? *Am J Obstet Gynecol.* 2012;207:259–65.
11. O'Connell K, Davis AR, Westhoff C. Self-treatment patterns among adolescent girls with dysmenorrhea. *J Pediatr Adolesc Gynecol* 2006 ; 19 : 285 -9.
12. Master-Hunter T, Heiman DL. Amenorrhea: evaluation and treatment. *American family physician.* 2006 Apr 15;73(8):1374-82.
13. Baldashti E, Wimmer-Puchinger B, Loschke K. Acceptability of the long-term contraceptive levonorgestrel-releasing intrauterine system (Mirena ®): a 3-year follow-up study. *Contraception* 2003 ; 67 : 87
14. Chwalisz K, Perez MC, Demanno D, et al. Selective progesterone receptor modulator development and use in the treatment of leiomyomata and endometriosis. *Endocr Rev* 2005 ; 26 : 423 -3.
15. Zeev Harel Warren Alpert Medical School of Brown University, Hasbro Children's Hospital/Rhode Island Hospital, Division of Adolescent Medicine, Department of Pediatrics, Providence, RI 02903, USA.
16. Moini Jazani A, Hamdi K, Tansaz M, Nazemiyeh H, Sadeghi Bazargani H, Fazljou SM, Nasimi Doost Azgomi R. Herbal medicine for oligomenorrhea and amenorrhea: a systematic review of ancient and conventional medicine. *BioMed research international.* 2018;2018(1):3052768.
17. Jiao M, Liu X, Ren Y, Wang Y, Cheng L, Liang Y, Li Y, Zhang T, Wang W, Mei Z. Comparison of herbal medicines used for women's menstruation diseases in different areas of the world. *Frontiers in Pharmacology.* 2022 Feb 4;12:751207.
18. Guimarães I, Póvoa AM. Primary dysmenorrhea: assessment and treatment. *Revista Brasileira de Ginecologia e Obstetrícia/RBGO Gynecology and Obstetrics.* 2020 Aug;42(08):501-7.





WISELEAF SCIENTIFIC VENTURES

19. Mazzei R, Genovese C, Magariello A, Patitucci A, Russo G, Tagarelli G. Plants in menstrual diseases: a systematic study from Italian folk medicine on current approaches. *Plants*. 2024 Feb 22;13(5):589.
20. Jiao M, Liu X, Ren Y, Wang Y, Cheng L, Liang Y, Li Y, Zhang T, Wang W, Mei Z. Comparison of herbal medicines used for women's menstruation diseases in different areas of the world. *Frontiers in Pharmacology*. 2022 Feb 4;12:751207.
21. Begum M, Das S, Sharma HK. Menstrual disorders: causes and natural remedies. *J Pharm Chem Biol Sci*. 2016 Aug;4(2):307-20.
22. Loch EG, Selle H, Boblitz N. Treatment of premenstrual syndrome with a phytopharmaceutical formulation containing *Vitex agnus castus*. *Journal of women's health & gender-based medicine*. 2000 May;9(3):315-20.
23. Luo P, Feng X, Liu S, Jiang Y. Traditional uses, phytochemistry, pharmacology and toxicology of *Ruta graveolens* L.: a critical review and future perspectives. *Drug Design, Development and Therapy*. 2024 Dec 31:6459-85.
24. Rahal A, Kumar A, Chakraborty S, Tiwari R, Latheef SK, Dhama K. *Cimicifuga*: a revisiting indigenous herb with multi-utility benefits for safeguarding human health—a review. *International Journal of Agronomy Plant Production*. 2013;4:1590-601.
25. Khayat S, Kheirkhah M, Behboodi Moghadam Z, Fanaei H, Kasaeian A, Javadimehr M. Effect of treatment with ginger on the severity of premenstrual syndrome symptoms. *International scholarly research notices*. 2014;2014(1):792708.
26. Jiao M, Liu X, Ren Y, Wang Y, Cheng L, Liang Y, Li Y, Zhang T, Wang W, Mei Z. Comparison of herbal medicines used for women's menstruation diseases in different areas of the world. *Frontiers in Pharmacology*. 2022 Feb 4;12:751207.
27. S. Kataki M, B. Kakoti B. Women's Ginseng (*Angelica sinensis*): an ethnopharmacological dossier. *Current Traditional Medicine*. 2015 Apr 1;1(1):26-40.
28. Shah N, Kumari M, Sadhu P, Talele C, Aundhia C. Herbal solutions for menopausal problems: a comprehensive literature review.





WISELEAF SCIENTIFIC VENTURES

29. Klein DA, Poth MA. Amenorrhea: an approach to diagnosis and management. *American family physician*. 2013 Jun 1;87(11):781-8.
30. Khalesi ZB, Beiranvand SP, Bokaie M. Efficacy of chamomile in the treatment of premenstrual syndrome: a systematic review. *Journal of Pharmacopuncture*. 2019 Dec 31;22(4):204.
31. Jaafarpour M, Hatefi M, Najafi F, Khajavikhan J, Khani A. The effect of cinnamon on menstrual bleeding and systemic symptoms with primary dysmenorrhea. *Iranian Red Crescent Medical Journal*. 2015 Apr 22;17(4):e27032.
32. Chakraborty K. Therapeutic implication of *Aloe barbadensis* Mill.(aloe vera) for the management of polycystic ovarian syndrome (PCOS): a systematic review. *Journal of Biochemistry International*. 2022 Jan 20;9(1):22-6.
33. Shabanian Boroujeni Z, Heidari-Soureshjani S, Sherwin CM. Effects of *Curcuma longa* (turmeric) and curcumin on the premenstrual syndrome and dysmenorrhea: a systematic review. *Journal of Endometriosis and Pelvic Pain Disorders*. 2024 Mar;16(1):33-44.
34. Khayat S, Kheirkhah M, Behboodi Moghadam Z, Fanaei H, Kasaeian A, Javadimehr M. Effect of treatment with ginger on the severity of premenstrual syndrome symptoms. *International scholarly research notices*. 2014;2014(1):792708.
35. Başaran N, Pash D, Başaran AA. Unpredictable adverse effects of herbal products. *Food and Chemical Toxicology*. 2022 Jan 1;159:112762.
36. Jafari Z, Emtiazy M, Sohrabvand F, Talei D, Oveidzadeh L, Abrishamkar M, Meyssami M, Kamalinejad M. The effect of *Glycyrrhiza glabra* L. on primary dysmenorrhea compared with ibuprofen: a randomized, triple-blind controlled trial. *Iranian Journal of Pharmaceutical Research: IJPR*. 2019;18(Suppl1):291.
37. Kahraman C, Arituluk ZC, Cankaya II. The Clinical Importance of Herb-Drug Interactions and Toxicological Risks of Plants and. *Medical Toxicology*. 2021 Feb 3:245.
38. Kaur R, Kaur K, Kaur R. Menstrual hygiene, management, and waste disposal: practices and challenges faced by girls/women of developing countries. *Journal of environmental and public health*. 2018;2018(1):1730964.





WISELEAF SCIENTIFIC VENTURES

39. Oehler MK, Rees MC. Menorrhagia: an update. *Acta obstetricia et gynecologica Scandinavica*. 2003 Jan 1;82(5):405-22.
40. Practice Committee of the American Society for Reproductive Medicine. Current evaluation of amenorrhea. *Fertility and sterility*. 2004 Sep 1;82:33-9.
41. Klein DA, Poth MA. Amenorrhea: an approach to diagnosis and management. *American family physician*. 2013 Jun 1;87(11):781-8.
42. Klein DA, Paradise SL, Reeder RM. Amenorrhea: a systematic approach to diagnosis and management. *American family physician*. 2019 Jul 1;100(1):39-48.
43. Dawood MY. Ibuprofen and dysmenorrhea. *The American journal of medicine*. 1984 Jul 13;77(1):87-94.
44. Chan WY, FUCHS F, POWELL AM. Effects of naproxen sodium on menstrual prostaglandins and primary dysmenorrhea. *Obstetrics & Gynecology*. 1983 Mar;61(3):285-91.
45. Aboualsoltani F, Bastani P, Khodaie L, Fazljou SM. Non-pharmacological treatments of primary dysmenorrhea: a systematic review. *Archives of Pharmacy Practice*. 2020;11(1-2020):136-42.

