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Scientific appraisal of plant origin *Emmenagogue* and its therapeutics in unani medicine: A review

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Abstract
Unani system have holistic approach to deals many gynecological disorders in a systematic manner as evident from classification of diseases available in ancient Unani literature and the number of plant drugs thereby available and have greater significance for their treatment. One of the categories of these herbs is of emmenagogue (Mudir-e-Tams) drugs. Prevalence of pathological amenorrhoea is one of the most common gynecological problem has been reported to be 3-4% worldwide. Hormonal therapy based on estrogen and progesterone is the mainstay of treatment present in contemporary system which is associated with a number of side effects. This situation produces a dire need to search a safe, alternate, effective therapy of natural origin. In Unani literature several herbs have been mentioned and practiced by ancient Unani physicians till now having Mudir-e-Haiz property *viz*: Abhal, Hilteet, Darchini, Tarmas, Hasha, Pudina etc, which stimulate the flow of blood towards uterus and dilate its blood vessels, liquefy blood and removes sudda (obstruction) and rectify the functional defects of the uterus. Among them many have been scientifically validate their safety and efficacy. In this appraisal an attempt is done to explore information regarding herbal emmenagogue and their therapeutic potential present in Unani literature and PubMed, Science Direct, Google Scholar researches.

Keywords: Unani medicine, emmenagogue, Mudir-e-Haiz, Hormonal therapy

1. Introduction
Tibb e Unani which also acknowledge as Greco-Arab Medicine is a comprehensive medical system aimed with prevention and cure of diseases as well as promotion of quality of life. Much therapeutics is described in various classical texts of Unani for the management of different diseases. It provides promotive, preventive, curative and rehabilitative healthcare. The Unani medicine primarily based on the Hippocratic doctrine of four humors-bloods, phlegm, yellow bile, black bile with four fundamental qualities- hot and moist, cold and moist, hot and dry and cold and dry respectively. When these humors are imbalance, it threatens the very existence of life and derangement of which results in disease [1]. The demand of Unani Medicine is increasing exponentially because of people's faith in its safety and efficacy. Women's health is of utmost importance since ancient time. Regarding this, menstrual irregularities are the most common gynecological problems encountered worldwide. Emmenagogue in Unani Medicine are called "Mudir-e-Haiz" or "Mudir-e Tams" and are prescribed for the treatment of some cases of menstrual bleeding cessation. In Unani literature a spectrum of gynecological conditions are treated with Mudir-e-Haiz (Emmenagogue) drugs. Such drugs stimulate the flow of blood towards uterus and dilate its blood vessels, liquefy blood and removes *sudda* (obstruction) and rectify the functional defects of the uterus [2]. Emmenogauge drugs are used in menstrual abnormalities like oligomenorrhoea, amenorrhoea, hypomenorrhoea which comes under the heading of Ehtabas-e-tams in Unani literature. These emmenagogue drugs have abortifacient activity as well [3]. Amenorrhoea *(Ehtebas-e-Tams)* means absence of menstruation [4]. Primary amenorrhoea is the absence of menstruation by sixteen years of age in the presence of normal secondary sexual characteristics or by fourteen years of age if secondary sexual characters have not developed [5].Secondary amenorrhea is defined as amenorrhea for three normal cycles or for six months in the absence of pregnancy and lactation [5, 6]. Overall prevalence of pathologic amenorrhea is about 3-4% [4]. The causes of amenorrhea are diverse. The cause of primary amenorrhea is pregnancy, hypogonadotropic hypogonadism, endocrine lesions, congenital abnormalities, tumors. Causes of secondary amenorrhea are weight loss, chronic ovulation, pituitary tumor, cushing syndrome, ovarian tumors [7]. Oligomenorrhoea is defined as the length of menstrual cycle greater than 35 days. Causes of oligomenrrhoea include polycystic ovarian disease, androgen secreting tumor of

ovary and adrenal gland, cushing syndrome, hyperthyroidism, prolactinomas, asherman syndrome, pelvic inflammatory disease. The prevalence of oligomenorrhoea is 13.5% out of which polycystic ovarian disease accounts for 4-10% [8].

Ehtebas-e-Tams means absence of menses for two months or more. According to *Sahib-e-Kamil*, *Tabai-Haiz* commence by the age of 10-14 years and ceases by the age of 36-60 years. *Ibne Sina* has mentioned that when menstrual blood is unable to exit through uterus, it returns back to the body and leads to various diseases. Causes related to this condition are *ghalba-e-hararat* and *yaboosat* in uterus, *warm-e-rahem*, *sudda-e-rahem*, *ghilzat-e-dam*, *qillat-e-dam*, injury to the uterus, excessive stress, narrowing of uterine vasculature, inversion of uterus and obesity [9-11]. In contemporary practices management of amenorrhea include treatment of the underlying etiology, dietary modification, physical activities, use of nom steroid anti-inflammatories and hormonal therapy based on estrogen and progesterone compounds like oral contraceptives. Unfortunately, this treatment would present a certain number of disadvantages to know of the gastro-intestinal disorders, renal insufficiency, hepatic toxicity, cardiovascular diseases and infertility [12], therefore, the general population is turning toward complementary and alternative medicine as the first line of defense to battle illnesses. One of the most important consideration for accepting Unani and other traditional medicine is the area which lacks effective and safe allopathic drugs. Inspite of tremendous scientific advancement in the field of gynaecology in recent years, such type of menstrual irregularities are highly responsible for unovulatory or oligoovulation and the efficacy of available treatment in conventional medicine is under consideration due to high cost and adverse effects. On the other hand Tibb-e-Unani (Unani Medicine) claims to possess a number of effective and safe drugs useful in the treatment of oligo and Amenorrhea or scanty menses. In Unani literature the treatment modalities mentioned are lifestyle modification, wet and dry cupping, venesection and use of *Mudir-e-Tams* (emmenagogue) drugs. A number of Unani drugs has been describe under the heading of *mudir-e-tams* to be effective in different forms of *ehtebas-e-tams* and Unani physicians are using them since ages successfully in which a lot of plant origin *viz*: *Abhal*, *karafs*, *arand*, *harmal*, *Afsanteen*, *Baboona*, *Turmus*, *Murr*, *Suddab*, *Ajwain desi*, *Heeng*, *Mashkatramashee*, *Majeth*, *Jaosheer*, *Hulba* etc. (Table 1). These drugs are cost effective and considered to be safe and efficient in managing ehtabas-e-tams. Only few of these herbs have been experimentally studied for their emmenagogue property. Age-old practice with all these Unani drugs in it is the testimony of their efficacy however many technical and ethical considerations require that a systemic study on these drugs should be conducted to produce data in support of the claimed efficacy.

Fig 1: Certain *Mufrad* drugs with *Emmenagogue* activity.

2. Material and Methods

Literature was searched in the Unani texts like *Al-Hawi*, *Ghina Muna*, *Al-Akseer*, *Kāmil aṣ-Ṣinā Jamia al-Hikmat* ʿ *Bustanul Mufradat* to collect information on drugs having *mudir-e-tams* (Emmenagogue) property. Famous scientific search engines *viz*., PubMed, Medline, Google Scholar, and Science Direct Researchgate were used to retrieve online literature and experimental and clinical studies on Emmenagogue property of various herbs. All referenced studies published in indexed journals were included. About 31 review papers, 9 clinical trial research, 13 classical Unani books and 3 English books with the relevant matter were search. Glossary of Indian Medicinal plants and different indexed journals were consulted for botanical names and family. Standard Unani Medical Terminology published by CCRUM was used to describe the appropriate Unani terminologies.

Table 1: List of plants in Unani text with Emmenagogue property

Unani Name	Botanical Name	Family	Part used	Pharmacological Action	Pharmacological studies	References
Abhal	*Juniperus communis*	Coniferae	Berry cone, psuedo fruit	Diuretics, anti-inflammatory, emmenagogue	Emmenagogue, antioxidant, antibacterial activities	Afsahul Kalam *et al.* [13]
Darcheeni	*Cinnamomum zeylanicum*	Lauraceae	Bark	Cardio-protective, anti-bacterial, anti-inflammatory, emmenagogue	Antidiabetic, cardioprotective, antibacterial, antioxidant, anti-inflammatory, emmenagogue activity	Reesha Ahmad *et al.* [14]
Hanzal	*Citrullus colocynthis*	Cucurbitaceae	Fruit	Anti-inflammatory, emmenagogue, emetic, purgative	Antimicrobial, anti-inflammatory & analgesic, antihyperglycemic, antiobesity activity	Qin-Yuan Li, *et al.* [15]
Jundbedastar	*Castoreum*		Secretion	Desiccant, demulcent, nerve tonic, nerve stimulant, emmenagogue	Anticonvulsant, antioxidant, metal chelating activity	Afsahul Kalam, *et al.* [16]
Methi	*Trigonella foenum graecum*	Papilionaceae	Seed	Anti-inflammatory, concoctive, emmenagogue, analgesic	Antiarthritic, estrogenic, anti-inflammatory, analgesic, antifertility activity	Shamim Ansari *et al.* [17]
Karafs	*Apium graveolens*	Apiaceae	Fruit, stem, root	Deobstruent, carminative, emmenagogue, diuretic, antihelminthic	Antihelminthic, antibacterial, antifungal, anti-inflammatory, gastro intestinal activity	Mohd Tabarak Hussain, *et al.* [18]
Qust	*Saussurea lappa*	Compositae	Rhizome	Hepatoprotective, anti-inflammatory, emmenagogue, analgesic, immune-modulator	Antiviral, hepatoprotective, immunemodulator, anti-inflammatory, anticancer activity	Shabnam Ansari, *et al.* [19]
Majeth	*Rubia cordifolia*	Rubiaceae	Root	Anti-inflammatory, emmenagogue, hepatoprotective, neuroprotective	Anti-inflammatory, antioxidant, antinephrotoxicity, hepatoprotective, neuroprotective activity	Khaled F El-Massry, *et al.* [20]
Shoneez	*Nigella sativa*	Ranunculaceae	Seed	Diuretic, emmenagogue, abortifacient	Antibacterial, anti-inflammatory, immunomodulator, antiallergic activity	Zehra Zaidi, *et al.* [21]
Nankhwah	*Trachyspermum ammi*	Umbelliferae	Fruit	Emmenagogue, abortifacient, antidiarrheal, anti-spasmodic, galactopoetic	Estrogenic, hypolipidemic, antidiarrheal, antiasthmatic, anti-spasmodic activity	Hamiduddin *et al.* [22]
Jaosheer	*Opopanax chironium*	Apiaceae	Gum	Deobstruent, nerve tonic, resolvant, antidote, emmenagogue	Anticancer activity	Giovanni Appendino *et al.* [23]
Satar	*Satureja hortensis*	Lamiaceae	Whole plant	Antiflatulent, aphrodisiac, hepatic and gastric depurative	Antioxidant, antimicrobial, hepatoprotective, anticancer activity	Irina Fierascu *et al.* [24]
Turmus	*Lupinus albus*	Leguminosae	Seed	Antihelminthic, diuretic, emmenagogue, anti-inflammatory, analgesic	Antimicrobial, antihelminthic, anti hyperlipidemic, antioxidant, anticonvulsant activity	Mohamed *et al.* [25]
Ushnan	*Seidlitzia rosmarinus*	Amaranthaceae	Leaf, stem, ash	Emmenagogue, abortifacient, detergent	A study showed that it is effective against Recurrent cystitis	Mahin Kmaliford *et al.* [26]
Foodanj	*Mentha arvensis*	Melastomaceae	Aerial, leaf	Carminative, diuretic, emmenagogue	Antimicrobial, anti-spasmodic, antioxidant, emmenagogue activity	Peyman Mikaili *et al.* [27]
Hilteet	*Ferula asafoetida*	Umbelliferae	Oleo-gum resin	Emmenagogue, anti-spasmodic, expectorant, stimulant	Anti dysmenorrhic, anti-hypertensive, chemoprotective, hepatoprotective, antioxidant activity	Poonam *et al.* [28]
Kunjad	*Sesamum indicum*	Pedaliaceae	Seed	Demulcent, lactogogue, emmenagogue, diuretic	Anti-inflammatory, antioxidant, antimicrobial, antiatherosclerotic activity	Shamim *et al.* [29]
Mur	*Commiphora myrrh*	Burseraceae	Gum	Diuretic, emmenagogue, brain depurative, dehiscent	Cytotoxic, emmenagogue, antioxidant, antimicrobial activity	Ismath shameem *et al.* [30]
Suddab	*Ruta graveolens*	Rutaceae	Leaf, seed	Abortifacient, antiepileptic, anti-inflammatory, emmenagogue, emetic, carminative	Anti-inflammatory, antilipidemic, antiatherosclerotic activity	Shams Raza *et al.* [31]
Irsa	*Iris ensata*	Iridaceae	Rhizome, root	Emmenagogue, anti-inflammatory	Anticervicitc, antiprotozoic, antiasthmatic activity	Diksha Jat *et al.* [32]
Haasha	*Thymus serpyllum*	Labiatae	Aerial, leaf	Antimicrobial, antihypertensive, diuretic, emmenagogue	Antimicrobial acitivity, anticancer activity	L Galovicova *et al.* [33]
Anisoon	*Pimpinella anisum*	Umbelliferae	Fruit	Expectorant, stimulant, carminative, emmenagogue diuretic, diaphoretic	Antimicrobial, antifungal, antidiabetic, anticonvusant, antidysmenorrhic activity	Khadija Zahid *et al.* [34]
Saleekha	*Cinnamomum cassia*	Lauracae	Bark	Anti-inflammatory, hepato tonic,expectorant, astringent, abortifacient, emmenagogue	Anti-inflammatory, hepatoprotective, antioxidant, anti-ulcer activity	Shabnam bano *et al.* [35]
Zarawand	*Aristolochia rotunda*	Aristolochiaceae	Aerial, root	Deostruent, demulsent, detergent, emmenagogue, antipyretic, anti-inflammatory	Hepatoprotective, anti-inflammatory activity	Ansari AP *et al.* [36]
Afsanteen	*Artemisia absinthium*	Compositae	Leaf, flower	Hepatoprotective, carminative, antihelminthic, antipyretic, analgesic, emmenagogue	Analgesic, antipyretic, diuretic activity	Ayesha Hashim *et al.* [37]

Branjasif	*Achillea millefolium*	Compositae	Whole plant, leaf, flower	Anti-inflammatory, analgesic, antipyretic, diuretic, emmenagogue, blood purifier	Antioxidant, antimicrobial, anti-inflammatory, antifertility, estrogenic activity	Atiya Sayed *et al.* [38]
Bekh-e-Soosan	*Lilium candidum*	Liliaceae	Bulb	Aphrodisiac, emmenagogue, detergent, dehiscent	Hepatoprotective, anti-inflammatory, antitumor activity	Jiri Patecka *et al.* [39]
Sakbeenaj	*Ferula persica*	Apiaceae	Resin	Stimulant, emmenagogue detergent, carminative, antispasmodic	Antimicrobial, anti-inflammatory, chemoprotective activity	Zohra Sattar *et al.* [40]
Baboona	*Matricaria chamomilla*	Asteraceae	Flower, root	Analgesic, anti-inflammatory, antispasmodic, emmmenagogue, hepatoprotective, immunomodulator	Antibacterial, antifungal, antidiabetic, anti-inflammatory, antitumor activity	Amina *et al.* [41]
Jitiyana	*Gentiana lutea*	Gentiaceae	Root	Astringent, deobstruent, detergent, resolvent, emmenagogue	Anti-inflammatory, antibacterial, gastroprotective, cytotoxic activity	Fatemah *et al.* [42]
Unsul	*Allium cepa*	Liliaceae	Bulb	Aphrodisiac, depurent, deobstruent, carminative	Antiobesity, antiplatelet, antimicrobial, antidiabetic, anticancer activity	Arka Jyoti *et al.* [43]
Dooqou	*Daucus carota*	Apiaceae	Root	Emmenagogue, diuretic, gastrotonic	Spermatogenic, steroidogenic, anticholesterolemic, gastroprotective activity	Rosita *et al.*[44]
Aslaq	*Vitex agnus castus*	Lamiaceae	Fruit, leaf	Emmenagogue, astringent, deobstruent, resolvent	Postmenopausal syndrome, emmenagogue, activity	M. Shahnazi *et al.* [45]
Fawania	*Paeonia lactiflora*	Paeoniaceae	Seed, root	Astringent, emmenagogue, dehiscent,anti-inflammatory	Emmenagogue, antiviral, anti-inflammatory, antioxidant activity	T. Ushiroyama, *et al.* [46], Shefton Parker, *et al.* [47]
Anjorah	*Urtica dioica*	Urticaceae	Flowering plant, root	Anti-inflammatory, emmenagogue, diuretic, galactogogue	Antiendometriosis, antioxidant, emmenagogue,anti-inflammatory activity	Yasaman Taheri, *et al.* [48], F. Najafipour *et al.* [49]

3. Pharmacological studies

3.1 Badyan (*Foeniculum vulgare*)

In a double blind randomized placebo-controlled trial, performed by E. Mohebbi-Kian *et al.*, married women(n=78) of age 15-45 years using depot medroxyprogesterone acetate(DMPA) and with amenorrhoea for 45-140 days were divided into three groups as test group, control group and placebo group and these groups were treated with a capsule made up of essential oil from fennel twice a day, low-dose combined oral contraceptive(LD-COC) pills and placebo pills respectively for 21 days. 73% women in test group and 81% women in control group experienced menstrual bleeding which was markedly higher than the placebo group (19%) [50].

3.2 Aslaq (*Vitex agnus castus*)

M Shahnazi *et al.* performed a randomized triple-blind clinical trial with a placebo controlled with the aim to induce menstrual bleeding, 70 women in age group of 18-45 years with polycystic ovarian syndrome(PCOS) and oligomenorrhea or amenorrhea in two equal group, a test group and a placebo control group were enrolled. Test group was given fruit extract of aslaq in capsule form for the 3months. The effects of placebo control with low dose estrogen (68.6%) and *Vitex agnus castus* (60%) on the normalization of menstrual cycle and the serum levels of prolactin and free testosterone were found to be similar [45].

3.3 Darcheeni (*Cinnamomum verum*)

One propective, placebo controlled, double-blinded randomized clinical trial was conducted by D.H. Kort *et al.* to evaluate the effect of darcheeni on induction of menstrual bleeding in PCOS women within the age group of 18-38 years. Four cinnamomum capsules of 125mg thrice a day were given for 6 months to the treatment group. Results showed significant improvement in regulation of menstrual cycle in cinnamomum group compared with placebo group. It was observed that menstruation resulted from increase in luteal phase progesterone level >3ng/ml [51].

3.4 Hulba (*Trigonella foenum-graecum*)

A propective, placebo controlled, double-blinded randomized clinical trial done by M.H.Bashtian *et al.* showed that Hulba is effective in regulating menstrual cycle, improving fertility decreasing LH to FSH ratio thereby reversing clinical signs of PCOS as well as its sonographic findings in 20-35 year old women with PCOS, menstrual irregularities and infertility. The women were treated with 2 capsules of 500mg extract twice daily and metformin thrice daily for 3 months. With decrease in LH/FSH ratio (3.16 to 1.61), decrease in cyst size in 47 subjects, no cyst in 36 subjects and regular cycles in 71% of subjects were observed [52].

3.5 Foodanj (*Mentha longifolia*)

A double blind randomized placebo controlled study were conducted by R. Mokaberinejad *et al.* on 18-35 years old women with secondary amenorrhea and oligomenorrhea with 45ml of syrup prepared with plant extract, thrice a day for three months. 68.3% patients in the treatment group experience menstrual bleeding with regulation of cycle in 33.3% patient as compared to the placebo group. There is also decrease in LH levels in test group compared to placebo. Another study was done on 30-40 years old amenorrheic women in a pilot study with 250 ml cup of herbal tea made up of mentha dried leaves. The herbal tea was given for three times a day. There was decrease in FSH level and occurrence of menstrual bleeding in all 27 patients except four after taking medication [53].

3.6 Fawania (*Paeonia lactiflora*)

In a randomized controlled clinical trial performed by T Ushiroyama *et al.*, 100 anovulatory women with increased plasma LH level in two groups control and treatment were treated with *Paeonia lactiflora* with *Cinnamomum cassia* for 8 weeks. It was reported that plasma LH levels were decreased and estradiol levels were increase with improvement in menstrual cyclicity in treatment group [46].

3.7 Kunjad (*Sesamum indicum*)

A pilot study was conducted by M. Yavari *et al.* on 21 women aged 20-40 years with oligomenorrhea. Women were given 60gm of powdered drug with a tea spoon of honey once a day before breakfast for 7 days. 85% women underwent menstrual bleeding with two weeks of receiving treatment. In another single blind randomized controlled clinical trial, 56 oligomenorrhic women were treated with medroxyprogesterone (n=29) and 60gm sesame powder once

daily (n=27) for 7 days. 93.10% women in progesterone group and 72% women in sesame group experienced menstruation without prominent side effects [54].

3.8 Anjora (*Urtica dioica*)

One randomized controlled clinical trial was conducted by Najafipour F *et al.* to evaluate the effect of dried root extract of *Urtica dioica* on females with hyperandrogenism. 20 females were taken in both treatment and standard control group. 300-600mg of plant dried extract were given to treatment group and cyproterone and spironolactone to standard group for 4 months. Decrease in total, free testosterone and DHEAS (Dihydroepiandrosterone sulfate) after treatment was noted in the experimental group although improvement in menstrual irregularities was lower as compared to the control group [49].

4. Result & Discussion

Menstrual irregularities represent one of the most common gynecological disorders that can adversely affect the various aspects of woman's health. Amenorrhoea & oligomenorrhea can leads to various complications such as infertility, increase risk of cardiovascular diseases, hypertension, osteoporosis, anxiety and depression, thereby hampering the women's quality of life. Hormonal therapy is the mainstay of treatment; however, it has its own complications. Therefore, there is a need for an alternative system of medicine. In ancient civilizations, physicians were familiar with various gynecological disorders, including dysmenorrhoea, amenorrhea, prolapse of uterus, cancer, and leucorrhoea. There are a number of herbal medicines mentioned in Unani literature for the treatment of amenorrhea under the heading of *mudir-e-tams* such as *abhal, badyan, darchini, irsa, suddab* etc. Thus Unani system of medicine contains many effective and safe emmenagogue drugs several of which are yet to be prove its *mudir-e-haiz* property scientifically.

5. Conclusion

Unani manuscripts are very much enriched with information related to menstruation and its management with diet therapy, *hijamah bila shart* (dry cupping), *takmeed* (hot fomentation), nutool therapy, and medicinal herbs with emmenagogue property such as *abhal, badyan, darchini, irsa, suddab* and so on.This review of Unani literature provides a number of herbal drugs having emmenagogue property. These reports are although of preliminary nature but showing great potential of Unani Medicine to deliver promising agents that can be used to treat various urinary and gynecological problems. Scientific validation of few of them has proved their efficacy as emmenagogue justify upto some extent the claim of mudir-e-tams property of these drugs by Unani physicians. Therefore, the study of Unani emmenagogue drugs gain importance as one of the means of characterizing and identifying a better group of drugs that can be used as therapeutic. Further investigations on various herbs are necessary to provide evidence for the same. Thus, traditional knowledge validation and protection is mandatory and prerequisite for prospective research and valuable for use in the modern-day era.

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