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An Overview of Polycystic Ovarian Disease Associated Secondary Amenorrhoea in Unani System of Medicine

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Abstract: ***Polycystic ovarian syndrome (PCOS) is a heterogeneous disorder, with multiple reproductive, cosmetic and metabolic complexities which is characterized by dysfunction in ovulation and clinical or biochemical hyperandrogenism and the presence of polycystic ovarian morphology. Women with PCOS have increased rate of insulin resistance and hyperandrogenism which have been implicated in the dysfunction of HPO-Axis, leading to anovulation and menstrual irregularities. In classical Unani text, it is mentioned that ihtibas-i-tams usually occurs in women with balghami mizaj and fair complexion, and is mainly caused by dominance of khilt-i-balgham, which increases the viscosity of khun-i-hayd and form sudda, as a result menstrual blood fails to expelled out of the uterus. The treatment available in conventional medicine is oral use of hormone therapy and insulin sensitizing agents, but this treatment has got its own side effects and complications. Several medicines are available in Unani system of medicine, which act as insulin sensitizer, uterotonics and causes withdrawal bleeding in patients with PCOS associated amenorrhoea. This review article gives a detailed description of PCOS associated secondary amenorrhoea including its etiopathogenesis, diagnosis, principle of treatment in Unani system of medicine.***

Keywords: PCOS, Secondary amenorrhoea, Herbal insulin sensitizer, Unani system of medicine.

1. Introduction

PCOS is the most common gynecological endocrinopathy [1,2,3] of child bearing aged women characterize by hyperandrogenism, ovarian dysfunction, and polycystic ovarian morphology, which affects approximately 4 to 12%,[3,4,5] of whole female population. Secondary amenorrhoea occurs in 10-20% of patients complaining of infertility and is one of the commonest reasons for referral to a gynecological endocrine clinic.[6,7] It has been estimated that secondary amenorrhoea, has a prevalence ranging from 3 to 4% in reproductive age group women.[8,9] Adams *et al.* (1986), found PCOs in 26- 30% of patients with amenorrhoea, and in 87% with oligomenorrhoea.[10] The prognosis depends on the cause of amenorrhoea. Secondary amenorrhoea associated with PCOD will respond to treatment.[6] The available treatment in conventional medicine is hormone therapy (for withdrawal bleeding and menstrual regulation) and also use of insulin sensitizing agents (to reduce insulin resistance and androgen levels as well as to improve ovulatory function) in women with PCOS.[11] Metformin, the most widely used drug in PCOS is often poorly tolerated because of gastrointestinal side effects,[11,12] and hormonal therapy though effective in menstrual cyclicity, has got its own complications like venous thrombo-embolism, stroke, breast, endometrial and ovarian cancer[13] and are contraindicated in patients with hypertension, cardiac diseases, liver diseases, DVT etc.[6] Conventional pharmaceutical management is limited by the prevalence of contraindications in women with PCOS, non-effectiveness in some circumstances, side effects and by preferences of women with PCOS for alternatives to pharmaceutical management.[14] Hence, there is an increase demand for herbal therapy which is to be safe, effective and easily available. The treatment plan in Unani system of medicine for secondary amenorrhoea in PCOD patients is based on the concept that, treat the cause of amenorrhoea i,e. PCOD with life style modification through *tadbir, ghiza* and *dawa*,[15,16] use of *qawi mudirr-i-hayd advia*[17] to induce menstruation,[16] use of *munzij wa mushil-i-balgham advia* for *tanqia-i-badan* [15,16,18,19]and finally use of Unani medicines which act as insulin sensitizers in PCOD patients.[20]

2. Material & methods

For Unani concept of disease, available authentic text of Unani Medicine was searched. Literature was also searched on PubMed, Google Scholar, Medline, Science Direct with the keywords; PCOS, secondary amenorrhoea, herbal insulin sensitizer, Unani system of medicine etc.

Unani Concept: Unani physicians mentioned the description of PCOD under the headings of amenorrhoea, obesity, phlegmatic diseases and liver disorders. [15,17,18]

***Ihtibas-i-tams* (Amenorrhoea):** In classical Unani text, it is defined as cessation of menstruation,[16,21,22] either it varies from scanty flow to complete cessation or it occurs at interval of ≥2 months. Duration of inter menstrual period ranges from 20 to 60 days and if it exceeds, above this level then, it is considered as abnormal and called as *ihtibas-i-tams.*[23] It usually occurs in women having *balghami mizaj* and fair complexion[15] and such women generally suffer from *usr-i-tams*,[16, 24] as heavy menstrual bleeding may occur after a long period of amenorrhoea. [19]

Etiopathogenesis:

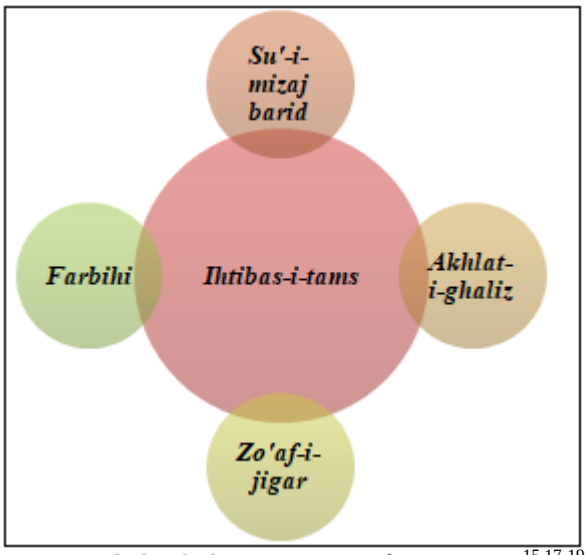

Figure 1: *Asbabe Ihtibas-i-tams* specific to PCOD [15,17-19,25]

a) *Su'-i-mizaj barid* [17] causes *sudda* formation in uterine blood vessels due to excessive intake of fluids, which in turn [15,18,23] leads to amenorrhoea and infertility. [17,18]
b) *Akhlat-i-ghaliz* [15,17,23] mainly *balgham* increases the viscosity of blood due to *lazujat*.[17,18] This *ghaliz madda* gets accumulates in the blood after intake of *ghaliz* and *sakhil ghiza* and forms *sudda*, which blocks the uterine vessels and results in amenorrhoea.[15,18]
c) *Zo'af-i-jigar* causes amenorrhoea via three factors:[15,17-19, 23]
   - Blood flow to distant organs fails as liver is unable to differentiate the blood from other body fluids.
   - Improper *tawlid-i-khun* (defective haemopoesis).[17,19]
   - Formation of *sudda* within the liver,[17,19,23] causes obstruction in blood flow towards the uterus.[17]
d) *Farbihi* causes amenorrhoea in three ways:[15,17,23]
   - Excessive fat deposition on the uterus compresses the uterine blood vessels.
   - *Sudda* formation due to excess accumulation of *balgham* in uterine vessels.[17,18]
   - Alteration in the ovarian function due to dominance of *rutubat* and *burudat* in the body,[17,23] causes *tul ihtibas-i-mani* (chronic anovulation);[19,25] which results in menstrual irregularities and infertility.[15,17,18]

Diagnosis: It is based on clinical presentation of the patient-

General symptoms: Headache,[15,18,19,23] dyspnoea and chest pain on exertion,[15,18] palpitation, fainting,[19] indigestion,[17,18,23] loss of appetite,[15,17,18,23] nausea,[17,18,19,23] excessive thirst,[18,19] constipation,[15] heaviness in the body,[15,17,19,23] restlessness,[15,17,23] dysuria,[15,17,18,23] low urine output,[15,17] high coloured urine,[15,19] excessive sleep,[17] salivation,[23] tiredness,[19] obesity[15] etc.

Specific symptoms:

Ghalba-i-balgham: Patient is obese, puffy and flabby body, cold skin,[15,17] pale face,[15,17,23] prominent vessels, *nabz- bati* and *mutafawit, bawl- sufaid, ghaliz* and *kasir, baraz-balghami*,[17,23] menstrual blood is red in colour and thin in consistency,[21] and scanty pubic hair.[17,21]

Zo'af-i-jigar: Patient present with h/o liver diseases[18] and c/o heaviness in right hypochondium, whitish coloured urine seldom mixed with blood and change in skin colour. On examination- hardness felt in right hypochondric region.

***Sudda*:** Menses stops gradually, feeling of heaviness in the body, abdominal distension due to flatulence, and change in skin colour.[19]

Sometimes amenorrhoea results in marked changes in the body structure such as, appearance of excessive hair growth on the body mainly on face, hoarseness of voice, and change in temperament of the organs as well as the body. These changes mainly occur in those women who are multiparous; having musculine features, prominent vessels and such women resembles men.(*Jalinoos*) [15,19,23]

Complications: *Ibn Sina* states that when blood goes towards the uterus (which is a natural passage for excretion of menstrual blood) and if it does not find the way to escape out from the body; it will return back to the body, and when this process is repeated several times, it results in complications such as [23] *ikhtinaq al-rahim* (hysteria), *sayalan al-rahim* (leucorrhoea), *waram al-sulb sawdawi wa saqirus* of *rahim* (uterine tumours and malignancy), *uqr* (infertility),[15,17,23] *waram al-jigar* (hepatitis)[19] *istisqa* (ascitis)[15,17-19,23] *awram-i-ahsha* (visceral inflammation) [15,17,23] *malankholia*, generalised anasarca etc.[17,23]

Ibn Sina states that amenorrhoea is associated with *tul ihtibas-i-mani, farbihi*,[17] and *uqr*[15,23]and such type of women resembles men. Thus, a well established association exists between anovulation, amenorrhoea, obesity, and infertility which correlate with polycystic ovarian disease.

PCOD: It is mainly based on the dominance of *khilt-i-balgham*. It has been mentioned in Unani encyclopaedia's that *su'i mizaj barid* (abnormal cold temperament) of the liver may leads to abnormal production of *balgham*,[26] as liver is unable to convert chyme into blood, instead it converts it into *balgham-i-lazuj*. One of the abnormal form of *balgham* is *ma'i balgham,* which is thinner in consistency and can accumulate in sacs to form cysts.[27]Also the other predominant symptoms of PCOD like amenorrhoea, oligomenorrhoea and obesity have been attributed to rise of *balgham.*[17,18] Hence, it is claimed that PCOD arises due to dominance of *khilt-i-balgham* in the body which leads to cyst formation in ovaries, amenorrhoea, obesity and infertility.[20]

Hirsutism: It is mentioned as a complication of prolonged amenorrhoea associated with other masculine features like hoarseness of voice, male body contour, acne etc.[17,18] *Ibn Sina* and *Ismail Jurjani* explained the basic pathophysiology of hirsutism as variation in normal temperament of women. If amenorrhoea persists for a long duration, it causes alterations in internal environment of the body and disturbed the equilibrium status of women, leading to growth of excessive hair over the body.[17,18,26] The normal temperament of women gets transformed towards that of men due to prolonged amenorrhoea, which is mainly due to *ihtiraq* of *balgham* to *sawda* which leads to hirsutism, hyper pigmentation (acanthosis nigricans) and formation of some

unwanted material which is being excreted through skin pores in the form of *busur-i-labaniyya* (acne).[15] It was observed by *Ibn Sina, Ismail Jurjani* and *Al-Razi* that development of masculine features is more common in obese women with robust body and prominent blood vessels, as these women have almost similar temperament as that of men.[17,18]

Acne Vulgaris *(Busur-i-labaniyya):* These are small white eruptions on the face, which resemble condensed drop of milk, thus named as *muhasa* (*Ibn Sina*).[23] These eruptions are caused by *madda-i-ṣadidiya* (infected matter) which comes towards skin surface due to *bukharat-i-badan*.[19,28]Generally, it appears in young girls between 16-25 years of age due to menstrual disturbances or amenorrhoea.[29]

Usul-i-ilaj:

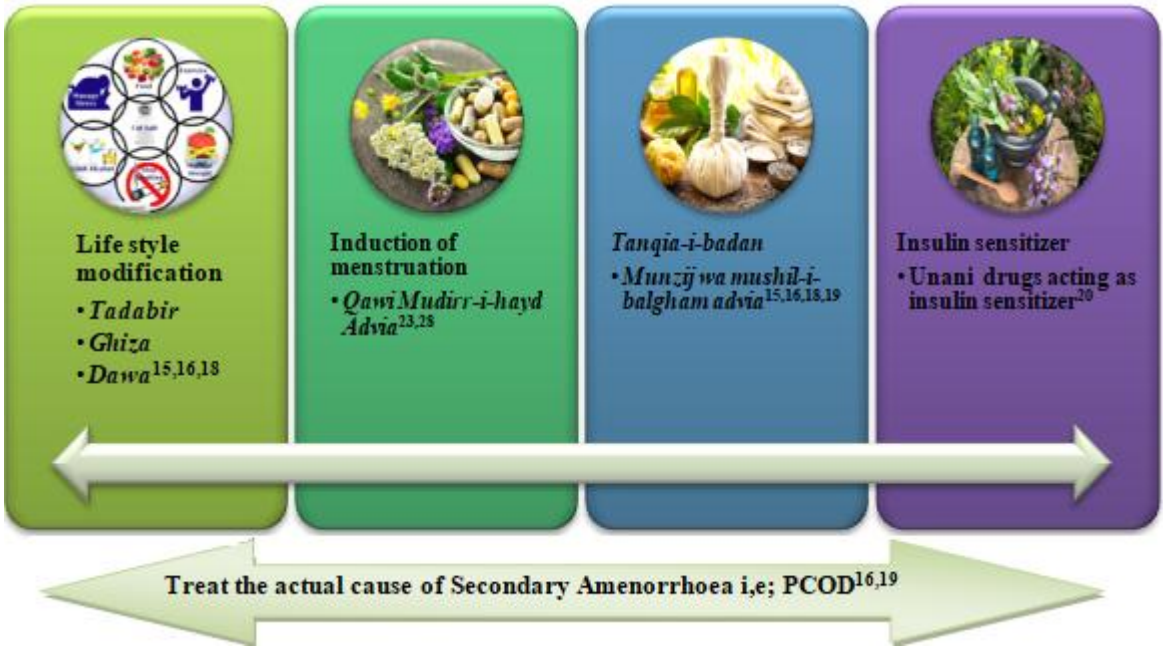

Figure 2: Principles of treatment in Unani medicine

1. Life style modification:

***Ilaj bi'l ghiza*:**

- *Taqlil-i-ghiza*[15,17]
- Use *mulattif aghzia* like[15,23]luke warm water or *sirka*/*kanji* in empty stomach.[30]

Diet allowed

- Use *qalil al-taghziya wa kasir al-kamiya't ghiza*[17,31]like vegetables & fruits etc which fills the stomach.[16,26]
- Add spices such as *filfil, raai, zeera, lehsan* to the vegetables;[18] use plain soup, vegetables with dry chapatti.[15]

Diet restricted

- Avoid cold water,[17,18] milk, butter, mutton, fish,[32] oily and fried food.[33]

***Ilaj-bil-tadbir*:**

- ***Riyazat****: Riyazat-i-qawi* [15,17,23] to reduce body weight.[18]
- ***Dalak***: *Natrun* or *zift balut* followed by *hammam* can reduce fat accumulation.[15]
- ***Abzan***: *Joshanda* of *mulattif* drugs such as *shibbat, marzanjosh, pudina, sudab, babuna, aqleelul malik, sa'atar, qardmana, kalonji, heeng, asaroon, tagar, doqu*.[18,23]
- ***Takmid***: *Takmid* at lower abdomen with *har advia* mainly *advia-i-muhammira* as it stimulates blood flow towards the uterus.[18]
- ***Zimad****: Joshanda* of *har* and *mulattif* advia[18,23]over lower abdomen.[18]
- ***Huqna****: Sheham hanzal, ro'ghan zaitoon, namak, boriq*.[15,23]
- ***Humul:*** *Shehad, ro'ghan sosan, mur, samagh kankaz, asal musaffa, sakbeenaj, muqil, ro'ghan sosan,* and *mur*.
- ***Firzaja:*** *Ma'al-asal, ro'ghan sosan* and *murmakki*.[15]
- ***Hammam-i-yabis*:** It is recommended in obese women before taking meals,[31] and after the procedure, advice her to sleep for some time, then use small quantity of food.[34]
- ***Fasd:*** *Fasd* of *rag-i-safin*[17] and *rag-i-mabiz* as it diverts the flow of blood towards the uterus to induce menstruation.[15,23]
- ***Hijama:*** Application of *hijama* over the calf muscles is more beneficial in comparison to *fasd* of *rag-i-safin* to induce menstruation, in obese and robust women having narrow uterine vessels and whose blood is thin; as venesection fails to evacuate the sufficient amount of blood from the narrow uterine vessels but the cupping does, as it purifies the blood.[15,35] *Hijama* at *sa'aq* forcefully absorb morbid matter from the upper part of the body[19] and divert it towards the uterus.[23] It is applied 2 or 3 days prior to the expected menstruation, one day on one calf followed by its application on next day on second calf to induce menstruation.[15,17,18] *Hijama* works on the principle of *tanqia-i-mawad* and

removes the toxic blood from the body, thus it detoxify the body.[35]

Ilaj bi'l dawa:

- Use *ma'al-usul* with *mulattif* and *har mudirrat* like *joshanda post-i-khyarshamber, mushktaramashi, parsiyaushan, qand siyah kohna* etc.[23]
- *Mudirrat-i-harra advia* like *parsiyaushan, badiyan, khubazi, zoofa, tukhm sudab, anisoon, biranjasif, qust sheerin, hab balsan, kalonji, ajmood, pudina, ajwain desi* etc.[26]
- Use *ma'jun* having demulcent property e.g: *tiryaq-i-kabeer, ma'jun-i-kamooni,*[18] *ma'jun-i-biladuri.*[30]

2- Use of *qawi mudirr-i-hayd advia*:

Oral use:

- *Ayarij* and *loghaziya*;[16] *afawiya, fuwwah*.[15]
- *Joshanda turmus* and *surkh lobiya* with *shehad* or *joshanda turmus* with *mur* and *sudab*.
- *Mushktatamashi, abhal, majeeth* each 1 part, *tukhm-i-karafs, soanf, elaichi khurd, behroza, sakbeenaj, jausheer, mastagi*, each ½ part; all ingredients are finely powdered and used in a dose of 5 g with *joshanda turmus* and *lobiya surkh* after adding *shehad*.
- *Sikanjabeen-i-usuli* with *habb-ul-ghar* 4 g and *behroza* 2 g.[19]
- Prepare tablet of *muqil, mur, abhal* in equal quantity and used in a dose of 10.5 g.[23]
- Prepare tablet from the extract of *majeeth, mushkatramashi, kardmana, sudab, abhal* and *heeng*, each 2 g and used in a dose of 35 g.[15]

- **Single Drugs:** *Darchini, ayarij feeqra, sakbeenaj, jausheer, junbedastar, kardmana, tukhm marzanjosh, mushkatramashi, abhal, majeeth, pudina nehri, pudina kohi, afsanteen, soanf, kibr, karafs, anisoon, sudab, zarawand, irsa, bakhur maryam, ashnan, asaroon, izkhar, qust, habb-ul-ghar, javitri, o'od balsan, ushq, murmakki, indrain, farfiyoon, kalonji, turmus, lobiya* etc.[15,17,19,23]
- **Compound formulations:** *Qurs abhal, ma'jun abhal, sharbat buzuri, sharbat kasoos, sharbat ja'ada, sharbat biranjasif, sharbat saleekha, naqu'buzur,*[17,23] *dhamarsa, ayarij feeqra, loghazia, aqras mur, sharbat afsanteen.* [19]

Local use:

Humul:

- *Farbiyun*[15] or *farfiyun*[18,30] or *bikh-i-badam talkh, usara brinjasif* with *mur, zarawand, ro'ghan aqehwan.*[17]
- *Ashnan farsi, aaqarqarha, kalonji, sudab taza, farfiyun* in equal quantity, mixed with *ganda behroza* and used with *ro'ghan zanbaq*.[15,17]
- *Muqil* 35 g, *jausheer, asal labni, harf, kardmana, tukhm jarjeer, jundbedaster* and *ro'ghan sosan*.

***Dhuni*:**

- *Nankhwah,*[15] *hanzal, jausheer, kardmana, hilteet, sakbeenaj*[17] *tukhm karafs, heeng.*[18] *Karam kalla or behroza, jausheer, gandhak* daughed in *zehra gau.*[19]
- *Methi,*[15] *jundbedaster, nakchhikni, izfarutteeb, o'od, miy'a saila*.

Abzan:

- *Sudab, abhal, karafs, karnab, raziyana,*[16] *mushktaramashi.*[17]
- *Tukhm karafs, karnab, raziyana, sudab, biranjasif, abhal, footnaj*.[16]

Zimad

Apply paste of *biranjasif* over suprapubic region[15] or *tukhm bedanjeer* over umbilical region.[23]

***Takmid*:** *Mudir* and aromatic drugs

- *Afawiya* (over umbilical and suprapubic region).[15,17,23]
- Prepare *joshanda* with coarse powder of *balcharh, darchini, jawitri, jaiphal, elaichi qust, aqaqia* over the umbilical region.[19]
- *Sumbul, saleekha, darchini, o'od balsan, hab balsan, jawitri, jauzbuwa, elaichi khurd wa kalan, qust, hamama, shagufa izkhar*.[15,16]

***Huqna*:**

- *Ro'ghan yasmeen* with *ro'ghan nardeen,*[16] or *ro'ghan sumbul* or *qust* or *chambeli.*
- *Abhal, turmus, lobiya surkh* each 35 g, *majeeth, afsanteen, pudina, balcharh, sudab khushk, izkhar* each 7 g, *shoneez, kundus, behroza, jausheer* each 4 gm, boil in water and mix *ro'ghan yasmeen.* Use 100 ml decoction after adding *jundbedaster* 1 g and sprinkle *za'fran* over it.[19]

3-Use of *munzij wa mushil-i-balgham advia:*[15,32]

Oral:

- *Tanqia-i-balgham* with *hab ayarij* or *hab sakbeenaj* and expel out *ghaliz madda* via *qa'i*.[18,23] If *balgham-i-lazuj* fails to get evacuated, same can be expelled out via *ishal*.[17]
- *Ma'al-usul* with *ro'ghan bedanjeer* 7 g, *ayarij feeqrah* 1.047 g and use every morning for 7-9 days.[18]
- *Ma'al-usul, ro'ghan arand* with *hab muntin.*[15]
- *Joshanda aftimoon* [25] or *post-i-khayarshamber, parsiyaushan, qand siyah kohna.*[23]
- Powder of *mastagi, zanjabeel, zeera siyah*, each 1 g with *jawarish jalinoos* 7 g.
- *Joshanda pudina khushk, elaichi khurd wa kalan*, each 5 g; *zanjabeel, zeera siyah, anisoon* each 3 g, mixed with *khameera banafsha* 50 g and used in the morning. *Sheera* prepared from *badiyan* 5 g, *zeera siyah, zanjabeel, anisoon* 3 g, *arq elaichi* 120 g, with *khameera banafsha* 4 g and used in evening. [24]
- *Mashruditus, sanjareena, dawa'al-misk har, tiryaq-i-farooq, ma'jun filasifa,* and other *har ma'jun* and *jawarishat.*[23]

Local:

Zimad: *Karnab* and *methi,*[18] *tukhm bedanjeer.*[23]

***Huqna*:** *Joshanda babuna, soya, marzanjosh, methi, anjeer khushk* mixed with *ro'ghan kunjud.*

Humul:

- *Ro'ghan bedanjeer* or *ro'ghan naardeen* or *gazardashti.*[18]
- *Za'fran, sumbulutteeb, shib yamani, o'od, sazij hindi, anzarut, charbi murghabi* and *zardi-i-baize murgh*.
- *Jauzbuwa, kazmazish, phitkari biryan, post anar* each 4.5 g finely powdered.[23]

Abzan:

- *Joshanda methi, marzanjosh, babuna, soya.*[18]
- *Joshanda shibbat, pudina, marzanjosh, sudab, babuna, akleelul malik, sa'tar.*[23]

Dhuni:

- *Zarneekh surkh, mur, jauzsar, miy'a, qinna, habbul-ghar*; used after menses.
- *Muqil, ushq, ilakulambat, shoneez.*[15]

Use of *munzij wa mushil-i-sawda advia* for hirsutism & acne vulgaris:

Usul-i-Ilaj: Oral use of *tanqia-i-badan* with *munzij-mushil* therapy followed by topical application of *mujaffif* and *muhallil advia* for acne & *haliq* and *mukhaddir advia* for hirsutism.[19,29]

Hirsutism:

- First apply, lime with lead corbonate[26] for removal of hair, followed by application of *nagarmotha, amba haldi, methi, pudina, soya, neem, kalonji* to prevent further hair growth.[20]
- *Tukhm utangan* with *ro'ghan* or *asapgol* with *sirka* or *jundbedaster* with *shehad.*[19]

Acne vulgaris:

- ***Nuskha Matbukh***: *Post halela zard* 7 g, *post halela kabli* 17 g, *aftimoon* 20 g, *ustukhuddus* and *gul-i-banafsha* each 14 g, *bisfaij fustuqi* 10.5 g*;* first boil *halejat* and *bisfaij* in 3 litre of water till 750 ml water remains, afterwards add *ustukhuddus* and *gul-i-banafsha* and boil till 500 ml water remains, then add *aftimoon* after rapping in a cloth and boil for 2 or 3 times and put off the fire, allow it to cool down by itself and filtrate it.
- *Elwa* 3.5 g, *ghariqoon, maghz bil* each 2 g, *namak hindi* 1.75 g, *kharbaq siyah* 860 mg, all ingredients are grinded to make fine powder, then doughed in sugar syrup and used followed intake of *nuskha matbukh* 2 to 3 hours later.

Local use:

- ***Tila-i-Muhasa***: *Irsa, post-i-saroos, barg shibbat, aard-i-jau, safaida kashagiri*, all in equal quantity grinded in goat's milk.[29]
- *Shoneez, naushadar* and *bura armani* mixed with *sirka.*[28]
- *Murdar sang, bura armini*, with *ro'ghan gul or kalongi* with *sirka.*
- *Gil-i- armani, bura ushnan sabz* and *tukhm kharbuza.*[19]

4- Use of Unani medicines which act as insulin sensitizers:[20,36]

Mechanism of action of herbal insulin sensitizers: These medicinal plants act on insulin sensitivity via various cellular and metabolic targets and the principle sites of target are the liver, adipocytes and muscles. These potential plants targeted insulin action via several pathways: inhibition of hepatic glucose production or potentiating the peripheral glucose utilization in the muscles and adipocytes by regulating the activity and expression of key enzymes and glucose transporters. In addition, a lot of medicinal plants improve insulin sensitivity through the stimulation of insulin-signaling pathways. Herbal insulin sensitizers are *methi,*[37,38]*karela,*[39] *jamun,*[40]*haldi,*[41]*zaitoon,*[42]*darchini,*[43,44]*kalonji,*[45]*zanjabeel,*[46,47]*gurmar,*[48]*zaffran,*[49]*elwa* [50] etc.

3. Conclusion

Polycystic ovary syndrome (PCOS) is a complex, reproductive and endocrine disorder affecting up to 17.8% of reproductive aged women characterized by polycystic ovaries, chronic anovulation and hyperandrogenism leading to symptoms of oligo/amenorrhoea, hirsutism, acne, and infertility. Conventional pharmaceutical management is limited due to contraindications in women with PCOS, non-effectiveness in some circumstances, side effects and by preferences of women for alternative management. In USM effective treatment is available with fewer side effects and recurrence rate; but experimental studies were conducted on few Unani medicines, that too on small number of patients with variations in dosage & duration of treatment. Hence, future trials are recommended on large sample size for longer duration to prove the efficacy and safety of Unani drugs in the management of secondary amenorrhoea in PCOD patients.

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5. Conflict of Interest

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