



A REVIEW ON EFFECTIVE SINGLE DRUGS (*MUFRAD DAWA*) USED IN THE UNANI SYSTEM FOR THE MANAGEMENT OF POLYCYSTIC OVARIAN SYNDROME (*MARZ E AGHZIYA E KHUSSIYATUR REHAM*) SYNDROME: A REVIEW

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INTRODUCTION

The modern civilization has given rise to various lifestyle diseases. The sedentary lifestyle, craving towards the junk food, emotional and behavioural disturbances (like highly competitive attitude and social insecurities; all these factors disturb the hypothalamic-pituitary-ovarian (HPO) axis and perpetuate life style diseases like PCOS (Lujan,2008). Polycystic ovarian syndrome (PCOS) is the most common endocrine disorder that affects up to 18% of the women of reproductive age and is the commonest cause of infertility due to anovulation. It was originally described by Stein and Leventhal in 1935 (Begum, 2001). PCOS results in the production of high amounts of androgen particularly testosterone and chronic anovulation. Clinical manifestations of hyper androgenism are as hirsutism, acne, alopecia and virilization. PCOS accounts for most cases of oligomenorrhoea and about a third of those of amenorrhoea. History, examination, and first line investigations usually establish the diagnosis (Lujan, 2008). A more recent joint consensus statement between the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM) has revised the criteria for diagnosis of PCOS to include two from three of the following criteria Oligomenorrhoea/anovulation; Clinical or biochemical evidence of hyperandrogenism; Polycystic ovaries, with the exclusion of other etiologies. The hallmark clinical features of PCOS are menstrual irregularities (amenorrhoea, oligomenorrhoea, or other signs of irregular uterine bleeding), signs of androgen excess, and obesity. This disease is complex and it further gives rise to serious complications like infertility, cardiovascular ailments, type-2 diabetes mellitus and carcinoma of breast and endometrium. (PG,2010). The onset of this disease is peri-menarcheal, as during this stage major endocrinological and emotional change takes place and this probably could explain the reason behind its onset at this stage (SD 2007). Conventionally, PCOS treatment is directed to the ovary for normalizing its functions. Medications are used to regulate the menstrual cycles and to stimulate ovulation. As different drugs used in the treatment of PCOS cater to different symptoms, effective treatment to manage PCOS is a challenge. In conventional medicine, the best-known treatment of PCOS is clomiphene citrate, metformin, tamoxifen and troglitazone. All these drugs have their own side effects. In Unani medicine, the medicinal plants as single and compound formulations have found widespread use particularly in the case of disease not amenable to treatment by modern methods. The drugs which correct *Ihtebas e tams*, *Uqr* and *Sue mizaj barid* are generally found to be useful in PCOS, but their efficacy has not been validated scientifically. The present study was designed to evaluate the effective single drugs in the management of PCOS (Beiber EJ, Sanfilippo JS, Horowitz IR, 2006)

The Unani Concept of PCOS

This disease has been described by Unani physicians under the headings of amenorrhoea, obesity, phlegmatic disease and liver disorders (Sina, 2010). Unani concept of PCOS is mainly based on the dominance of *khilt e balgham* (phlegm). It has been mentioned in classical books that *sue mizaj barid* (abnormal cold temperament) of the liver may lead to abnormal production of phlegm,(Sina, 2010) as liver is unable to convert chyme into blood, instead it converts it into phlegmatic blood or tenacious phlegm. One of the abnormal forms of phlegm is *balgham mayi*, which is thinner in consistency and can accumulate in sacs to form cysts (ABZ, 2001). Also the other predominant symptoms of PCOS like amenorrhoea,



oligomenorrhoea and obesity have been attributed to rise of phlegm (Sina, 2010) (ABZ, 2001) hence, it is claimed that PCOS arises due to predominance of phlegm in the body which leads to cyst formation in ovaries, obesity and amenorrhoea. The Unani physicians consider that the early twenty years of life are the period of childhood which is predominated by phlegm; hence the phlegmatic disorders are more likely to occur at this stage. This probably may explain the role of phlegm as a contributing factor for the onset of this disease during this age group (Begum) (ABZ, 2001) (Sina, 2010).

OBJECTIVES

To explore the traditional wisdom of Unani medicine in treating menstrual irregularities coined under the medical term of polycystic ovarian disease.

To engage in critical evaluation of efficacious single drugs of Unani medicine and their mechanism of action in treating PCOS.

METHODOLOGY

Classical texts on Unani medicine, Pharmacopoeias of Unani medicine, Modern texts of Gynaecology, books, scientific journals, review articles and web searches (Pub Med and Google scholar databases) were thoroughly studied. The search terms ('PCOS', 'effective *mufrad dawa* to treat PCOS in unani'... etc.) were used without narrowing or limiting search elements. The final summary was formulated after a thorough reading of all reading materials.

Unani related texts and other texts were thoroughly scrutinized to find out the single drugs that have actions to address the symptoms as well as minimize complications. Many single drugs were listed under the actions of emmenagogue, liver tonic, insulin sensitizers, weight reduction, ovarian tonics, hirsutism, and that containing phytohormones etc; of which ten such single drugs are broadly described under this study in terms of pharmacological actions and the experimental studies that have been conducted on few to explore pharmacological activities of these herbs are associated with diverse limitations.

RESULTS AND DISCUSSION

Women with PCOS are currently treated according to their presenting features like irregular periods, infertility and hirsutism.

Modern treatment modalities include, oral contraceptives in menstrual disturbance, Clomiphene citrate, ovarian drilling/ laser treatment and assisted reproductive techniques in anovulatory infertility, Cyproterone acetate, ethinyl estradiol and spironolactone in hirsutism and acne. Weight loss in menstrual disturbance and anovulatory infertility helps in improvement of metabolic perturbances and reduces the risk of coronary heart disease. Insulin sensitizing agents (such as metformin) in obesity, androgen excess, menstrual disturbance, anovulatory infertility and metabolic perturbances (Beiber EJ, Sanfilippo JS, Horowitz IR, 2006)

Such a complicated disease has no satisfactory treatment till now and most often patient gets only symptomatic treatment with hormones and insulin sensitizers but becomes drug dependent in the long term. Also, they are coupled with loads of side effects. Unani system employs a different mode of treatment which has no adverse effects. The main aim of Unani treatment in women with PCOS is:

Detoxification of body



Strengthening and revitalizing the female reproductive system and regularizing menstrual cycles.

Rectifying hormonal imbalances. The drugs which correct *Ihtebas e tams*, *Uqr* and *Sue mizaj barid* are generally found to be useful in PCOS (A, 2011)

Rhazes recommended regular induction of menstruation as one of the treatment modality applied for women who has developed masculine features suggestive of PCOS. He has given a line of management based on correction of temperament and menstrual irregularity by use of emmenagogue drugs (single or compound) and local application of herbs to reduce severity of hair growth, acne and hyper pigmentation. Moreover, Unani literature mentions the use of drugs for, which in turn refers for the correction of hormonal imbalance due to PCOS. These drugs are also containing phyto estrogens that mimic the estrogenic action and normalize the menstrual cycle.

The single drugs used in PCOS are categorized as follows. (Firdose KF, Begum W, Shameem I, 2013).

Emmenagogue Drugs (*Mudir e Haiz*)

Drugs to concoct and evacuate the abnormal phlegm (*Ta'deel e mizaj*)

Uterine tonics (*Muqawwi e reham*)

Drugs for weight reduction

Specific drugs – insulin sensitizers, natural drugs for hirsutism.

Though there are many single drugs that can be used for the effective management of PCOS, only ten such valuable plants have been discussed in this study for better understanding of most important ones along with experimental findings and evidence-based statistics. (Plants of the World)

TIBBI NAME (MEDICINAL NAME)	BOTANICAL NAME	VERNACULARS (ENGLISH)
<i>Abhal</i>	<i>Juniperus communis</i>	Juniper
<i>Mushktramashi</i>	<i>Mentha pulegium</i>	Pennyroyal
<i>Darcheeni</i>	<i>Cinnamomum zeylanicum</i>	Cinnamon
<i>Kalonji</i>	<i>Nigella sativum linn</i>	Black seed
<i>Satawar</i>	<i>Asparagus racemosus</i>	Asparagus
<i>Zanjabeel</i>	<i>Zingiber officinalis</i>	Ginger
<i>Aslusoos</i>	<i>Glycyrrhiza glabra</i>	Liquorice
<i>Alsi</i>	<i>Linum usitatissimum</i>	Flax seed
<i>Kharkhask</i>	<i>Tribulus terrestris</i>	Puncture vine
<i>Neem</i>	<i>Azadirachta indica</i>	Margosa

These drugs having the properties of *Muhallil e Auram* (Anti- Inflammatory), *Muffateh* (Vasodilators), *Mudire Boul-o-Haiz* (Diuretic and Emmenagogue), *Mulattif* (demulcent), *Musakkin Dard* (Analgesic), *Muqawi Meda wa Jigar* (Tonic To Stomach and Liver), *Muqawi Dimagh* (Tonic To Brain), *Muqawi Bah* (Aphrodisiac) etc. All these drugs are in the first degree of hot and dry temperament suggesting that the drugs possess moderate degree of *hararat* and *yabusat*, which suits for *Ihtebas e tams* and *uqr*, caused by *Sue mizaj barid*. Moreover, these drugs contain flavonoids which have various biological activities such as hepato-protective, anti-inflammatory, uterine stimulant, antioxidant, digestive, anti-rheumatic, immunomodulatory, antihypertensive properties. And they contain phyto estrogens as well. (Goswami PK, Khale A, Ogale S, 2012), (Sana FM, Shameem I, Roqaiya M, 2016).



Plants *Neem*, *Zanjabel*, *Kalonji* are attributed to anti- androgenic, hypo-glycemic and insulin sensitizing properties which serves as an alternate option in PCOS. The presence of phytoestrogens, steroidal saponins in *Satawar* exert hormone like actions in the body. Clinical studies on liquorice confirm that it reduces serum testosterone. Similarly, the other drugs too have promising effects in treating PCOS.

CONCLUSIONS/RECOMMENDATIONS

PCOS is a common disorder that has received much importance over the past years; we still know remarkably little about its complex etiology. The recent diagnostic criteria outlined in the ESHRE/ARM consensus statement is a move in the right, the same can be well correlated with the descriptions given by renowned Unani Physicians in their respective treatises. Potential treatment options in Unani medicines includes *Idrar haiz*, *Tadeel mizaj*, Weight reduction, Specific drugs like insulin sensitizers can be used to alleviate the ailing eves from this complicating disease. For this purpose, the above single drugs can be used alone or in combination to achieve a better result.

There is convincing evidence to suggest that the selected drugs have promising effects against PCOS and its complications. In addition, none of the studies has reported any adverse effects with the drugs. Further, there is a great need to do more research on making medicine more effective. Besides, the review article is useful for treating patients effectively by advancing the research. In order to prove significant safety and efficacy of herbs, further well-designed randomized clinical trial with double blinding, on large sample size should be conducted.

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