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Hirsutism due to polycystic ovarian syndrome: An integrative review of pathophysiology and management

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Abstract

Hirsutism -excessive male pattern terminal hair growth in women, is a distressing clinical manifestation commonly associated with Polycystic Ovarian Syndrome (PCOS), arising from complex endocrine and metabolic dysfunctions. This integrative review explores the pathophysiology and management of hirsutism from both modern biomedical and Unani perspectives. In modern medicine, hyperandrogenism, insulin resistance, and altered ovarian steroidogenesis lead to elevated androgen levels and decreased sex hormone-binding capacity, stimulating hair follicles in androgen-sensitive areas. Unani medicine explains these symptoms through concepts of deranged *Mizaj* (temperament), accumulation of morbid humors (*Su-i-Mizaj*), phlegmatic dominance, and menstrual disturbances, causing internal waste (*fuzlat*) to be expelled via abnormal routes such as excessive hair growth. Conventional treatments include lifestyle modification, weight management, oral contraceptives, anti-androgens, insulin sensitizers, and cosmetic procedures, while Unani approaches emphasize *Ilaj bil Tadbeer* (regimenal therapies), herbal and compound formulations, dieto-therapy, and temperament correction. The review advocates an integrative approach combining modern and Unani therapies to provide holistic, individualized care. Future research should focus on clinical trials comparing treatment outcomes, integration of *Mizaj* assessment with biochemical markers, and standardization of Unani protocols to enhance efficacy, safety, and patient adherence.

Keywords: Hirsutism, polycystic ovarian syndrome, unani medicine, mizaj, hyperandrogenism, su-i-mizaj, integrative therapy

Introduction

Hirsutism, defined as excessive terminal hair growth in women in a male-pattern distribution, is a common endocrine disorder that significantly affects physical appearance and psychological well-being ^[1]. Among the various underlying causes, Polycystic Ovarian Syndrome (PCOS) is the most prevalent, accounting for approximately 70–80% of cases of hirsutism ^[2]. PCOS is a complex condition characterized by hormonal imbalance, chronic anovulation, and polycystic ovaries, often accompanied by metabolic disturbances such as insulin resistance and obesity ^[3]. From the modern biomedical perspective, hirsutism in PCOS is primarily attributed to hyperandrogenism and altered hypothalamic-pituitary-ovarian axis function. Insulin resistance further exacerbates androgen production, leading to the stimulation of hair follicles in androgen-sensitive areas ^[4].

In the Unani system of medicine, conditions resembling hirsutism and PCOS are interpreted through the lens of humoral theory and temperament (*mizaj*). An abnormality in the *Mizaj* of organs, particularly the uterus and ovaries, along with accumulation of morbid humors (*Akhlat-e-Fasida*), is believed to disturb normal reproductive and metabolic functions. *Su-i-Mizaj* (derangement of temperament) plays a central role in the development of such disorders, including the growth of unwanted hair ^[20].

Despite the increasing prevalence of PCOS and associated hirsutism, conventional treatment options often present limitations, including side effects and recurrence. Unani medicine offers an individualized, holistic approach based on natural therapies and lifestyle modifications, which may complement modern strategies. This review aims to explore the pathophysiology and management of hirsutism due to PCOS from both modern and Unani medical perspectives, highlighting areas of convergence and opportunities for integrative treatment protocols.

Etiology

Hirsutism, defined as excessive growth of androgen- dependent sexual hair may be due to

excessive production of androgens, increased sensitivity of hair follicle to androgens, or increased conversion of weak androgens to potent androgens. Potential sources of increased androgens include the ovaries, the adrenal glands, exogenous hormones and other medications ^[12].

Ethnicity:

Ethnic differences do exist. Individuals of Mediterranean descent have a higher concentration of hair follicles than northern Europeans, and a much higher concentration than Asians (Speroff, 1999). For this reason Asians with PCOS are much less likely to present with overt hirsutism than other ethnic groups. Additionally, there is also a strong familial tendency for the development of hirsutism, due to genetic differences in target tissue sensitivity to androgens and in the activity of 5 α -reductase ^[5].

Pathophysiology of Hirsutism due to PCOS:

PCOS is the most common disorder diagnosed in women presenting with symptoms and signs of androgen excess. A survey taken in 2012 suggested that it accounts for 71% of women presenting with hirsutism (Escobar-Morreale, 2012) ^[6]. The development of hirsutism in PCOS patients is a direct result of androgen excess and metabolic disturbances originating from the pathophysiological mechanisms of the syndrome itself ^[7].

• Hyperandrogenism: The Central Mechanism-

PCOS is characterized by excessive androgen production by the ovaries mainly. The major androgens are dehydroepiandrosterone sulfate (DHEA-S), dehydroepiandrosterone (DHEA), androstenedione, testosterone (T).

Androgens ^[12]	Potency	Circulating Levels	Source
Testosterone (T)	2 nd most potent (Major androgen)	20-80ng/dL	25% ovary, 25% adrenals, 50% conversion of androstenedione
Dihydrotestosterone (DHT)	Most potent (1/10th of T)	2-8ng/dL	Ovary, adrenals, peripheral conversion of testosterone by 5 α reductase
Androstenedione	Not very potent (20% of effective T)	0.5-2ng/ml	Ovary, adrenals, 10% peripherally
Dhea & Dheas	Weak androgens (3% of effective T)		60-70% adrenals, ovary, hydrolysis of DHEAS

These androgens stimulate the transformation of fine vellus hair into coarse terminal hair in androgen-sensitive areas (upper lip, chin, arm, chest, abdomen, back, thigh and leg), resulting in hirsutism.

Ovary produces excess androgens due to: a) stimulation of theca cells by high LH; b) P450 C17 enzyme hyperfunction; c) Defective aromatization of androgens to estrogen; d) Stimulation of theca cells by IGF-1 (insulin growth factor-1). Decreased level of SHBG (Sex Hormone-Binding Globulin) resulting in increased free testosterone ^[8]. Hyperandrogenism manifests in females as hirsutism, acne, frontal and temporal balding, deepening voice, increased muscle mass, and in severe cases, virilization involving clitoromegaly ^[10].

Women with PCOS with hyperandrogenism are reported to

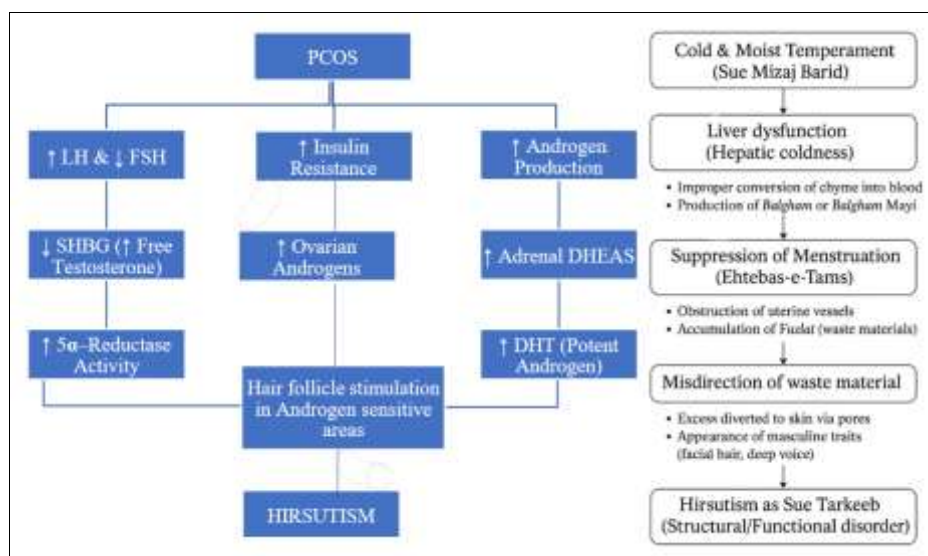
have much worse cardiometabolic risk as compared to women without hyperandrogenism ^[9].

• Insulin Resistance and Its Amplifying Role-

Insulin resistance is present in 65-95% of women with PCOS and plays a key role in the pathogenesis of hirsutism ^[11]. Women with PCOS tend to be insulin resistant with accompanying hyperinsulinemia. To overcome insulin resistance, the body secretes more insulin, thus causing a hyperinsulinemic state. These are all predictive of type 2 diabetes. Increased circulating levels of testosterone are noted in women with PCOS because high levels of insulin decrease circulating levels of SHBG. This, in turn, leads to increasing levels of free testosterone and worsening of the signs of hyperandrogenism ^[10].

• Adrenal Involvement in Selected Cases-

There is non-specific hyperandrogenemia due to exaggerated androgen response to ACTH. It occurs primarily from ovarian thecal cells and the adrenal glands ^[10].



Peripheral Factors: Hair Follicle Sensitivity-

The skin and hair follicles are androgen-responsive and thus have the capacity to metabolize androgens. DHEA, androstenedione, and testosterone enter the target cell and reduced to dihydrotestosterone by 5 α -reductase. Dihydrotestosterone is then bound to a cytoplasmic receptor protein that transports the androgen into the cell nucleus, where it is bound to chromatin and initiates transcription of stored genetic information. In the hair follicle, this promotes hair growth, leading to increased hair growth and initiating the conversion of vellus (fine unpigmented hair) to terminal hair (thick, coarse, pigmented hair)^[8, 12].

Hirsutism due to PCOS arises from a cascade of hormonal disruptions. These mechanisms together create a pathophysiological state where hair follicles in certain areas become overstimulated, leading to the development of coarse, male-pattern hair growth — the hallmark of hirsutism.

Unani concept

Introduction

According to Buqrat (Hippocrates), disease arises from an imbalance in the bodily humours (*Akhlat*), a concept known as the Hippocratic humoral theory (*Nazariya-e-Akhlat*). Each individual has a unique composition of these humours, referred to as *Mizaj* (temperament), which reflects their natural state of health. When this balance is disturbed and not restored, it can lead to the onset of disease^[16]. An individual's *mizaj* is classified into four types: Sanguine (*Damwi*) – hot and moist; Phlegmatic (*Balghami*) – cold and moist; Choleric (*Safrawi*) – hot and dry; Melancholic (*Saudawi*) – cold and dry. Any disturbance in the balance of humours affects the *mizaj*, and the Unani system of medicine offers therapeutic measures to restore this balance^[17]. This foundational theory guides the understanding of various diseases, including Polycystic Ovarian Disease (PCOD) and its complications like hirsutism.

Unani Understanding of PCOD-

The Unani term for PCOD, *Marz Akyas Khusyatur Reham*, is essentially an Arabic translation of the modern term. In Unani medicine, the pathophysiology of PCOD is predominantly attributed to the dominance of *khilt-e-balgham* (phlegmatic humour). Classical texts mention that a *su-i-mizaj barid* (abnormally cold temperament) of the liver may impair its function. Instead of converting chyme into healthy blood, the liver produces *balghami* blood or tenacious phlegm. A thinner, more fluid variant of phlegm called *balgham mayi* may accumulate within bodily sacs, eventually forming ovarian cysts^[18].

Hirsutism as a Complication of Amenorrhoea-

According to Unani concept, hirsutism is classified under *su-i-tarkeeb – amraz adad*^[19], and is considered a complication of prolonged amenorrhoea^[20]. The temperament of women is generally colder and wetter compared to men. Due to this, *fuzlat* (excess substances) that in men are expelled through thick hair and beard are, in women, expelled via menstruation. When menstruation is disrupted or insufficient, these substances may manifest as masculine features, such as facial hair growth and deepening of the voice^[21, 24]. Women engage in less physical activity, have narrower vessels, and slower humoral breakdown. As a

result, waste material accumulates and is expelled via menstruation. If this natural outlet is blocked, it leads to pathological manifestations, including hirsutism^[22, 23].

Pathological Changes Behind Hirsutism-

Amenorrhoea is commonly seen in women with a fair complexion and phlegmatic temperament. It can arise due to the dominance of *barid* (cold) or *galeez* (dense) humours, especially *balgham* and *saudawi*. Liver dysfunction also plays a role, as it impairs the production of healthy blood, leading to accumulation of abnormal phlegmatic matter^[24]. This dense matter may travel in the bloodstream, obstruct uterine vessels, and suppress menstruation (*ehtebas-e-tams*). The unexpelled waste is then diverted through alternate channels, like skin pores, manifesting as excess hair growth and hirsutism^[25].

Classical Insights on Hair and Humours-

According to Galen, hair is formed from vapours rising from waste material. As long as these vapours are warm, thick, and strong, hair continues to grow. Similarly, Muhammad bin Zakariya noted that a woman with facial hair should have her menstruation regulated and undergo *fasd* (bloodletting) to remove impurities^[26]. Classical Unani texts state that when menstruation is obstructed, harmful blood accumulates in the body leading to weakness, heaviness, and redirection of waste through the skin, resulting in conditions like hirsutism^[27].

Waste Redirection and Hair Growth-

The body's waste, when not expelled through menstruation, finds alternate exits including skin impurities or perspiration. This is why hirsutism is often a sign of internal waste retention. Regular physical exertion and therapeutic exercise can help break down and remove this waste material, restoring balance^[25].

From a Unani perspective, hirsutism in PCOS is a result of cold, moist temperament (especially of the liver) and dominance of phlegmatic humour, leading to amenorrhoea and waste accumulation. This waste is then expelled through alternate channels like the skin, leading to excessive hair growth. The classical views of Galen and Zakariya support this by linking hair growth to internal waste processes. Hence, hirsutism in Unani medicine is not merely a cosmetic issue but a reflection of deep systemic imbalance, particularly related to menstrual health and humoral dominance.

Clinical presentation and Diagnosis

Ferriman-Gallwey (1981) scoring system was developed to quantify the degree of hirsutism. Abnormal hair distribution is assessed in 11 body areas and is scored from 1 to 4. Score of 8 or more has been accepted as hirsutism^[8].

Evolution of PCOS Diagnostic Criteria^[13].

- **1990 – NIH Criteria**
PCOS as: Hyperandrogenism + Oligo/Anovulation;
Ultrasound not diagnostic.
- **2003– Rotterdam Criteria (ESHRE + ASRM)** Requires any 2 of 3: Oligo/Anovulation
Hyperandrogenism
Polycystic Ovarian Morphology (PCOM) on ultrasound
- **2006 – Androgen Excess Society (AES) Criteria**

Hyperandrogenism mandatory, with either Oligo/Anovulation or PCOM

- 2012 – NIH Workshop- Identified 4 phenotypes within it: Androgen excess + Ovulatory dysfunction
Androgen excess + PCOM Ovulatory dysfunction + PCOM All three features
- 2018 – International Guideline
Rotterdam Criteria reaffirmed as the most accepted. Despite multiple definitions over time, the Rotterdam Criteria (2003) remains the global standard for PCOS diagnosis, allowing for broader inclusion and sub-phenotyping for better management.

Exclusion of other causes^[12]

Before attributing hirsutism to PCOS, it's important to exclude other etiologies, including: Ovarian non neoplastic causes (Tumors), Adrenal causes (congenital hyperplasia, tumors, Cushing's syndrome, hyperprolactinemia), Iatrogenic causes (methyltestosterone, danazol, anabolic steroids, nortestosterones), Idiopathic hirsutism.

Investigations:^[8, 12]

The following guidelines are prescribed in an attempt to pinpoint the diagnosis. History of intake of an offending drug producing androgenicity is to be excluded first. Family history of excess hair growth is too often correlated.

Physical examination

- a) Modified FG score
- b) Measurement of BMI by waist-to-hip ratio (central/android obesity)
- c) Signs of insulin resistance (acanthosis nigricans)
- d) Others- acne, deepening of voice, clitoromegaly.

Laboratory findings

Screening tests

- 1) Testosterone - >200ng/dL- suspect ovarian tumor
- 2) DHEAS- >700-800 µg/dL- suggest adrenal tumors
- 3) 17α hydroxyprogesterone- diagnostic test for CAH (>400 ng/dL diagnostic)

Directed tests:

- 1) Serum values of LH:FSH is >3:1
- 2) Estrone and Prolactin levels are markedly elevated
- 3) SHBG level is reduced
- 4) Raised Sr testosterone (> 1.5ng/mL) & DHEAS, DHT levels
- 5) Androstenedione is raised (3-5ng/mL)
- 6) Raised fasting insulin levels >25 mIU/L

Laparoscopy: Bilateral polycystic ovaries are characteristics of PCOS. Ovaries are enlarged in volume (>10cm³)

Increased number (>20) of peripherally arranged follicles per ovary (2-9 mm)

Management of Hirsutism due to PCOS: Integrative approach

To remove the sources of excess androgen.

To suppress or neutralize the action of androgen. To remove the excess hair.

Lifestyle Modifications-

- **Weight reduction:** It is an important step of management (PCOS). Weight loss is associated with

reduction of hyperinsulinemia and androgen excess. Ideal body mass index (BMI) should not be more than 25^[8]. Weight reduction will elevate SHBG and find free testosterone thus reducing its peripheral action on hair follicles^[14].

- **Diet:** Foods recommended are of low glycemic index, limiting simple & complex carbohydrates and foods high in PUFA are advised.
- **Exercise:** Moderate physical activity, 30-60 mins/day. Aerobic exercise should be encouraged^[10]. Stress reduction and cognitive behavioral therapy help regulate the hypothalamic-pituitary-ovarian axis^[15].

Pharmacological Therapy-

The drugs most commonly used to treat Hirsutism include oral contraceptives, GnRH analogs, androgen receptor antagonist and corticosteroids.

Combination oral contraceptives (COCs) treat hirsutism by suppressing LH and ovulation, reducing ovarian androgen (testosterone) production. Estrogen increases SHBG, lowering free testosterone. Effects begin within a week, normalize in ~3 months, reducing hair growth by 50–60%. GnRH agonists suppress pituitary gonadotropins, reducing ovarian androgen and estrogen production. This lowers estradiol, testosterone, and androstenedione but not adrenal androgens. Studies show GnRH agonists, alone or with oral contraceptives, improve hirsutism more than contraceptives alone, though some show similar efficacy.

- 1) **Androgen receptor antagonist:** Cyproterone acetate 50-100mg on days 1-10 of menstrual cycle combined with oral estrogen on days 1-21. Spironolactone 50 and 200 mg/d for 2-5 months. Flutamide 250mg 1-3 times daily. Finasteride 5mg over 3 months-1year^[12].
- 2) **Insulin sensitizing drugs:** Women with insulin resistance PCOS are treated with metformin and thiazolidinediones. These drugs decrease circulating insulin and androgen levels.

Cosmetic and Physical Therapies:

Eflornithine hydrochloride (13.9% cream) when used topically prevents hair growth. Bleaching, twitching, depilation, epilation, waxing, lasers, shaving or electrolysis^[8].

Unani System of Medicine- Management:

Unani treatment targets the root causes by restoring the balance of *Mizaj* (temperament), *Akhlat* (humours), and *Tadbir* (lifestyle)^[28].

Usul-i-Ilaj (Principles of Treatment)

The management of hirsutism due to PCOS is based on the following principles:

- *Tadil-i-Mizaj* – Correction of abnormal temperament.
- *Tanqiya-i-Akhlat* – Elimination of morbid humors.
- *Izala-i-Sudad* – Removal of obstruction in uterine and metabolic pathways.
- *Taqwiyat-i-A'da Ra'isa* – Strengthening of vital organs such as *Reham* (uterus), *Jigar* (liver), and *Dimagh* (brain)
- *Taqil-i-Siman* – Reduction of obesity to restore

hormonal balance.

- *Mudirr-i-Hayd* – Stimulation of regular menstruation (Mudir-e-Hayd therapy).
- *Izala-i-Sha'r-e-Ghayr Zaruri* – Removal of excessive or unwanted hair growth.

Ilaj bi'l Taghdhiya (Dieto-therapy):

Use *qalil al-taghziya wa kasir al-kamiyat ghiza* [29].

Use *mulattif aghzia* like luke warm water or *sirka/kanji* in empty stomach [20]. Add spices such as *filfil*, *raai*, *zeera*, *lehsan* to the vegetables [25].

Chane ka pani (chickpea water) – to support uterine health *Asfedaj* – for moderate nutrition without phlegmatic build-up [24]. Avoid: Restrict junk, fatty and fried diet.

Cold and moist foods [30]

Ilaj bi'l Dawa (Pharmacotherapy):

Tadil-i-Mizaj-

Mundij: Gaozabaan, Parsiaavashan., Asl-us-soos, Biranjaasif, Maveez Munaqqa Mushil: Sana maki, Turbud, Gariqoon, Aftimoon vilayati, Hab ayarij
Tabrid: Khameera Gaozabaan Sada wrapped in Warqe Nuqra [31].

Taqwiyat-i-A'da Ra'isa- *Majun e muqawwi rehm*
Sufoof dabit ul ward Majun falasafa

Taqil-i-Siman- *Sufoof muhazzil with arq zeera*

Dawa e luk with arq ajwain Jawarish bisbasa with arq Kasni [32]

Mudirr-i-Hayd (Emmenagogues) [20, 24, 26, 30, 33, 34].

Amenorrhea can occur due to the dominance of dense (galeez) or cold (barid) humors, as described in traditional Unani medicine. Treatment involves herbal decoctions, use of hematologic thinning agents, administration of vaginal suppositories and the use of emmenagogues to stimulate menstrual flow.

1. Oral use:

1) *Jushandas (Decoctions)*

Post Khayashamber, Mushk Taramashi, Parsiaavashan, Qand Siyah → boiled & strained
Nankhwah, Badiyan, Wajturki → boiled & strained

2) *Mufarrad advia (Single drugs)*

Asaroon, Izqar, Abhal, Nankhwah, Beeq sosan, Sudab, Maryam jad, Satar, Qust, Chiraita, Roghan qaisoom, Parsiaavashan, Darchini, Hurfa, Tuqm karafs, Shaljam, Shooneez, Mushkatramashee, Majeeth, Pudina nehri, Pudina kahi, Afsanteen, Kibr, Anisoon.

3) *Murakkab dawa (Compound formulations)*

Qurs mur with Jushanda abhal, Hab mudirr, Majun mudirr tams, Majun abhal, Sharbat kasoos, Sharbat mudirr tams.

2. Local use:

1) *Farzaja (Suppositories)*

Kutki siyah + Indrayeen shaped as suppositories → *expels moisture then blood Farfiyoon* suppository → *instant menses induction*

Sufoof Murmaki, Pudina, Abhal, Sudab khushk, Maveez Munaqqa in *Gaaye ka Pitta* (used after 7 years of amenorrhea – classical formulation)

2) *Humool (Vaginal pessaries)*

Branjasif + Mur paste – inserted for Mudir effect

Barg Pudina khushk, Barg Marzanjosh, Zaravand taveel va mudhiraj

3) *Abzan (Sitz bath)*

In a decoction of resolvent herbs like *Shibt, Marzanjosh, Pudina, Sudab, Babuna, Satar, Abhal, Karafs, Biranjasif, Mushktaramashee*

4) *Dhooni (Fumigation)*

Maryam, Hanzal, Nankhwah, Hilteet, Sakbeenaj, Tukhm Karafs, Heeng.

5) *Zimad (Paste)*

Apply paste of *Biranjasif* over suprapubic region

Tukhm Bedanjeer over umbilical region

Specific drugs

1. Insulin sensitizers: [36]

Satawar, Gilo, Saunf, Elva, Triphala, Darchini, Kalonji

2. Herbs for Hirsutism: [35]

Spearmint, Fennel, Saw palmetto, Soy, Nutgrass

Ilaj bil Tadbeer (Regimenal Therapy): [21, 25, 26]

Modality Use

- *Fasd* (Venesection) Saphenous vein for excessive menstruation
- *Hijamah* (Dry cupping) Lower abdomen to promote uterine detox
- *Alaq* (Leeches) Applied to calves in case of abnormal blood congestion
- *Riyazat* (Exercise) Essential for obesity and metabolic health

Modality Use

Abzan (Sitz bath) In herbs like *Marzanjosh, Pudina, Sudab, Babuna Hammam* (Bath) Herbal steam baths for *Rutubat* reduction

Ilaj bil Yad / Jirahat (Physical / Hair Removal Methods):[22,26]

1) *Topical Hair Suppressants*

Jundbedastar with *Honey* – applied regularly

Tukhme Utangan with *roghan*– slows hair regrowth

Gil-e-Qaimooliya, Safeda, Phitkari, Bhang leaves boiled in *vinegar* – applied locally

2) *Depilatory Formulas:*

Hadtal + Chuna – strong depilatory, may be corrosive
Samundar Jhaag, Elva, Hadtal, Chuna – removes hair
Bhang, Afiyoon, Post Khashkhash + Sirka – prevent regrowth

Conclusion and future directions

Hirsutism in PCOS stems from hormonal imbalances and metabolic dysfunction, posing a persistent clinical challenge. While modern medicine targets symptom control through pharmacological means, Unani medicine offers a holistic, temperament-based approach aimed at restoring systemic balance. This review highlights the potential of integrating both paradigms to enhance therapeutic outcomes and patient compliance.

Future research should focus on well-designed clinical trials evaluating Unani interventions through standardized biomedical metrics, investigating combined treatment protocols, and formulating individualized models based on hormonal and Mizaj profiles. Such integrative strategies may lead to more effective, patient-centered management of

PCOS-related hirsutism.

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