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# The Gut–Fertility Axis: A Potentially Overlooked Determinant in Unexplained Infertility

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## ABSTRACT

**Background:** Unexplained Infertility (UI) accounts for approximately 10–30% of infertility cases despite normal clinical evaluation, suggests an important determinants of reproductive dysfunction remain unidentified. Emerging evidence identifies the gut microbiota as a key regulator of endocrine, metabolic, immune, and inflammatory pathways that influence reproductive physiology. This has led to the concept of the Gut-Fertility Axis, a bidirectional communication network linking intestinal microbial homeostasis with reproductive health. Although extensively investigated in modern biomedical research, its conceptual relevance to classical Unani medicine has not been comprehensively explored.

**Objective:** To critically review current evidence on the Gut–Fertility Axis in unexplained infertility and explore its conceptual convergence with classical Unani principles, providing an integrative framework for understanding reproductive health.

**Methods:** A narrative review of peer-reviewed biomedical literature and classical Unani texts was conducted. Evidence relating to gut microbiota, endocrine regulation, immune modulation, oxidative stress, intestinal barrier function, and reproductive physiology was synthesized and conceptually correlated with Unani principles, including Quwwat-e-Hazima, Mizaj, Akhlat, Sue Mizaj-e-Meda, Fasad-e-Akhlat, and Tabiat.

**Findings:** Gut dysbiosis may impair reproductive function through interconnected mechanisms including estrobolome-mediated hormonal regulation, metabolic dysfunction, immune dysregulation, oxidative stress, and intestinal barrier disruption. These alterations may adversely affect ovulation, implantation, endometrial receptivity, and spermatogenesis. In Unani medicine, impaired Quwwat-e-Hazima, Sue Mizaj-e-Meda, and Fasad-e-Akhlat conceptually resemble systemic disturbances arising from impaired gastrointestinal homeostasis. Traditional interventions such as Ilaj bil Ghiza and Ilaj bil Tadbeer may complement contemporary microbiota-targeted strategies.

**Conclusion:** The Gut-Fertility Axis represents a promising yet under-recognized determinant of unexplained infertility. Integrating microbiome science with the holistic principles of Unani medicine provides a systems-based perspective that may support future preventive and personalized therapeutic approaches. However, further experimental and clinical studies are required to validate these conceptual associations.

**Keywords:** Gut microbiota; Estrobolome; Gut dysbiosis; Unani medicine; Quwwat-e-Hazima; Reproductive health.

## 1. INTRODUCTION

According to World Health Organization (WHO), positive reproductive health of a woman is a state of complete physical, mental and social well-being and not merely the absence of disease related to reproductive system and functions [1]. Infertility is a major global public health concern affecting millions of individuals during their reproductive years. According to WHO (Apr 2023), around 17.5% of the adult population [i.e 1 in 6 people] experience infertility during their lifetime [2]. It imposes significant psychological, social, and economic burdens on affected couples [3] [4]. Despite advances in reproductive endocrinology and assisted reproductive technologies (ART), approximately 10–30% of infertility cases remain unexplained after normal assessment of ovulation, tubal patency, uterine anatomy and semen parameter [5][6]. This diagnostic uncertainty suggests that systemic factors influencing reproductive function may escape conventional fertility evaluation [7].

Recent advances in microbiome research have demonstrated that the gut microbiota functions as a dynamic regulator of metabolism, endocrine signaling, immune homeostasis, and inflammation. Through microbial metabolites and neuroendocrine–immune interactions, intestinal microorganisms influence multiple organ systems, including the reproductive axis [8]. Consequently, the concept of the Gut–Fertility Axis (GFA) has emerged, describing the bidirectional relationship between gut microbial homeostasis and reproductive health.

Classical Unani medicine has long emphasized digestion as the foundation of systemic and reproductive health [9]. Concepts including Quwwat-e-Hazima, Mizaj, Akhlat and Tabiat describe gastrointestinal function as central to maintaining physiological equilibrium [9][10]. Although these principles are not equivalent to modern microbiome science, they demonstrate notable conceptual similarities in recognizing digestive health as a determinant of reproductive well-being. Therefore, this review critically evaluates the emerging evidence supporting the gut–fertility axis in unexplained infertility while exploring its conceptual convergence with classical Unani medicine.

## 2. THE GUT–FERTILITY AXIS (GFA): AN EMERGING BIOLOGICAL PARADIGM

The human gastrointestinal tract harbors a diverse community of microorganisms including bacteria, archaea, viruses, fungi, and protozoa, collectively known as the Gut Microbiota (GM) [11][12]. Among the bacterial community, Firmicutes and Bacteroidetes constitute nearly 90% of the intestinal microbiota, followed by Actinobacteria, Proteobacteria, Fusobacteria, and Verrucomicrobia [8] [12]. This microbial ecosystem possesses a vast genetic repertoire that expands the host's metabolic capacity. Owing to its essential role in metabolism, immunity, and physiological regulation, the gut microbiota is increasingly regarded as a virtual metabolic organ [13].

Under physiological conditions, the gut microbiota exists in eubiosis, a balanced state that supports nutrient metabolism, vitamin synthesis, short-chain fatty acid (SCFA) production, intestinal barrier integrity, immune maturation, and endocrine regulation [11]. Disruption of this balance, known as Gut Dysbiosis, is characterized by reduced microbial diversity and altered microbial composition [12]. Increasing evidence indicates that these disturbances may also impair reproductive physiology through systemic rather than localized gastrointestinal effects [14].

These observations have led to the concept of the Gut–Fertility Axis. Instead of a single signaling pathway, this axis involves coordinated interactions among the gut microbiota, hypothalamic pituitary gonadal (HPG) axis, immune system, metabolic pathways, and reproductive organs through microbial metabolites, endocrine mediators, inflammatory signals, and neuroimmune mechanisms [15]. Current evidence suggests that gut microbial homeostasis influences fertility through multiple interconnected pathways, including regulation of estrogen metabolism, maintenance of metabolic homeostasis, immune modulation, preservation of intestinal barrier integrity and control of oxidative balance. Together, these mechanisms contribute to ovarian function, endometrial receptivity, implantation, spermatogenesis, and overall reproductive competence [16].

## 3. BIOLOGICAL MECHANISMS UNDERLYING THE GUT–FERTILITY AXIS (GFA)

The biological basis of the gut–fertility axis lies in the ability of the gut microbiota to regulate endocrine, metabolic, immune and oxidative pathways beyond the gastrointestinal tract. Rather than acting through a single pathway, these interconnected mechanisms collectively influence fertility in both females and males.

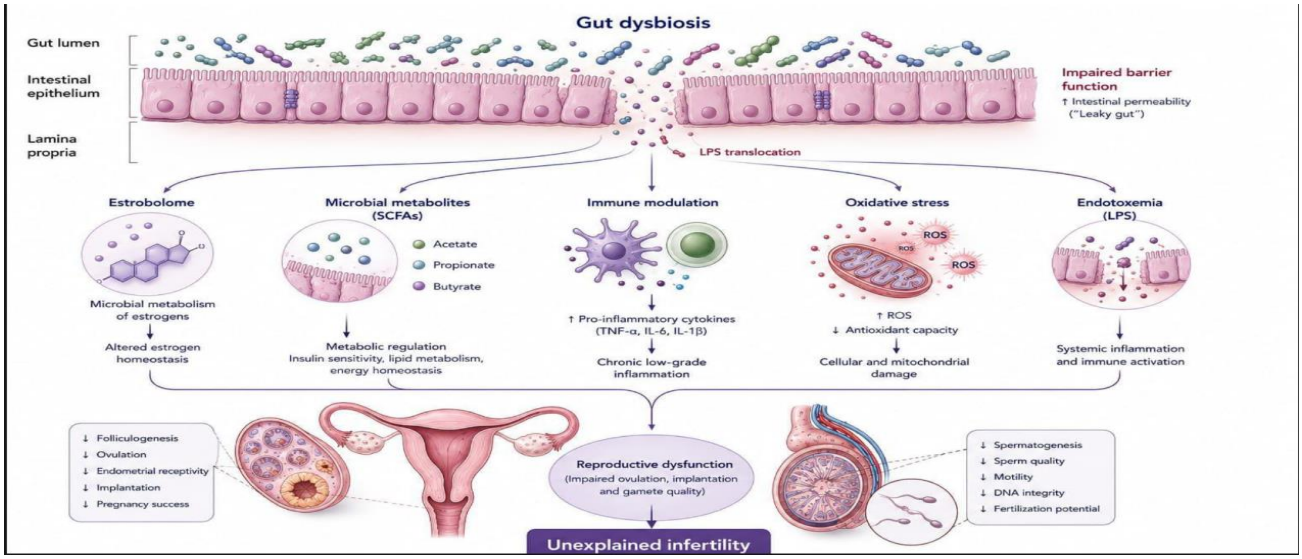


**Fig:1 Gut Dysbiosis and Its Impact On Male And Female Reproductive Health**

### 3.1 Hormonal Regulation: The Estrobolome and Reproductive Endocrine Homeostasis

One of the most extensively studied mechanisms linking the gut microbiota with female reproductive health is the estrobolome, a collection of intestinal bacteria capable of metabolizing estrogens through the enzyme β-glucuronidase (GUSB) [17]. After hepatic conjugation and biliary excretion, estrogens entering the intestine may be deconjugated by microbial β-glucuronidase, allowing their reabsorption through enterohepatic circulation. Consequently, the gut microbiota plays an important role in maintaining physiological estrogen levels and endocrine homeostasis [18].

Alterations in the composition or activity of the estrobolome may disrupt estrogen metabolism, contributing to hormonal imbalance that adversely affects follicular development, ovulation, endometrial proliferation, and implantation. Such disturbances have been implicated in disorders including polycystic ovary syndrome (PCOS), endometriosis, and other estrogen-dependent gynecological conditions [17][18]. Although direct evidence in unexplained infertility remains limited, these findings support a biologically plausible role for gut microbial regulation of reproductive endocrinology.

### 3.2 Metabolic Endocrine Dysregulation

The gut microbiota contributes significantly to metabolic homeostasis through fermentation of dietary fiber into short-chain fatty acids (SCFAs), including acetate, propionate, and butyrate. These metabolites regulate glucose metabolism, insulin sensitivity, lipid metabolism, and energy balance [17].

Gut dysbiosis may impair these metabolic processes, leading to insulin resistance and chronic low-grade inflammation. Since insulin signaling closely interacts with the hypothalamic pituitary gonadal (HPG) axis and ovarian steroidogenesis, metabolic dysfunction may compromise follicular maturation, ovulation, and endocrine balance [19]. Similar alterations may also impair testicular endocrine function and spermatogenesis, indicating that microbiota mediated metabolic regulation is important for fertility in both sexes [12].

### 3.3 Immune Endometrial Crosstalk

Successful reproduction depends on a finely regulated immune environment that supports fertilization, embryo implantation, and maternal immune tolerance. The gut microbiota plays a pivotal role in shaping innate and adaptive immune responses through continuous interaction with intestinal immune cells and microbial metabolites, thereby maintaining immune homeostasis [20].

Gut dysbiosis may disturb this balance, resulting in chronic inflammation and altered cytokines (TNF-alpha, IL-1, IL-6) production that impair endometrial receptivity and implantation. Emerging evidence also suggests communication between the intestinal and female reproductive tract microbiota, whereby alterations in gut microbial composition may influence vaginal and uterine microbial ecosystems. This gut–reproductive tract crosstalk may further contribute to reproductive dysfunction by modifying the local immune microenvironment [12][21].

### 3.4 Oxidative Stress and Intestinal Barrier Dysfunction

Intestinal barrier integrity prevents the systemic dissemination of microbial products. Gut dysbiosis may disrupt epithelial tight junctions, increasing intestinal permeability ("Leaky Gut") and allowing microbial associated molecular patterns (MAMPs), particularly lipopolysaccharide (LPS), to enter the circulation. This activates inflammatory pathways and excessive production of reactive oxygen species (ROS), resulting in oxidative stress that damages cellular proteins, lipids, DNA and mitochondria [12].

Persistent oxidative stress adversely affects oocyte quality, folliculogenesis, endometrial receptivity, embryo viability, and sperm function. Similarly, circulating inflammatory mediators may compromise the blood–testis barrier and testicular microenvironment, contributing to impaired spermatogenesis. Although the precise molecular mechanisms continue to be investigated, these findings support the role of intestinal barrier dysfunction as an important contributor to reproductive impairment [12].

Collectively, hormonal, metabolic, immune, and oxidative pathways provide a mechanistically supported framework linking gut microbial homeostasis with reproductive competence. While current evidence primarily supports biological plausibility rather than direct causality, these mechanisms establish the scientific basis for evaluating the clinical evidence relating the gut fertility axis to unexplained infertility.

## 4. CURRENT EVIDENCE SUPPORTING THE GFA IN UNEXPLAINED INFERTILITY

Despite considerable advances in reproductive medicine, infertility cases remain unexplained after comprehensive evaluation [21]. This persistent diagnostic gap suggests that conventional investigations may overlook systemic factors influencing reproductive function. Consequently, the gut fertility axis has emerged as a promising area of research.

Most available evidence is derived from reproductive disorders rather than unexplained infertility itself. Altered gut microbial composition has been consistently reported in conditions characterized by endocrine, metabolic, and immune dysregulation, including polycystic ovary syndrome (PCOS), endometriosis, obesity-associated infertility, thyroid dysfunction, and male reproductive disorders [22]. Although clinically distinct, these conditions share common biological pathways, suggesting that gut dysbiosis may represent a common systemic contributor to impaired fertility [15][17].

Evidence also supports a role for gut microbiota in male reproductive health. Western dietary patterns, characterized by high intake of processed foods, refined carbohydrates, sugary beverages, and saturated fats, have been associated with deterioration in semen concentration, motility, and morphology [23]. Since diet is a major factor of gut microbial composition, these findings indirectly support the contribution of gut microbial homeostasis to male fertility. Similarly, studies in patients with inflammatory bowel disease (IBD) have demonstrated impaired sperm chromatin integrity and increased antisperm antibodies (ASA), indicating that chronic intestinal inflammation may adversely affect testicular function through systemic immune activation [12].

Despite these encouraging findings, direct studies evaluating gut microbiota in unexplained infertility remain limited. Most published investigations are observational, involve relatively small cohorts, and differ substantially in participant characteristics, dietary habits, sequencing techniques, and analytical methods. Furthermore, the gut microbiota is highly dynamic and influenced by age, medications, antibiotic exposure, lifestyle, and environmental factors, making it difficult to identify a consistent microbial signature associated with unexplained infertility.

Overall, the Gut Fertility Axis represents a biologically plausible yet underexplored determinant of unexplained infertility. Rather than replacing established etiological factors, it expands the understanding of reproductive dysfunction by highlighting the contribution of systemic physiological networks that are not routinely assessed during conventional fertility evaluation. This evolving evidence also provides a scientific rationale for revisiting traditional medical systems such as Unani medicine, which has long recognized digestive health as a cornerstone of systemic and reproductive well-being.

## 5. DIGESTIVE HEALTH IN CLASSICAL UNANI MEDICINE: IMPLICATIONS FOR REPRODUCTIVE FUNCTION

Classical Unani medicine regards digestion as the cornerstone of systemic health [9]. Unlike the organ specific approach of modern medicine, Unani philosophy considers the human body an integrated biological system in which the gastrointestinal tract, metabolism, circulation, and reproductive organs function interdependently [9]. Consequently, reproductive health is viewed as the outcome of balanced digestive, metabolic, and humoral processes rather than the integrity of the reproductive organs alone. Although classical scholars did not describe the intestinal microbiota in modern scientific terms, they emphasized that disturbances originating in the digestive system could influence distant organs, including the reproductive system. This holistic perspective provides a valuable conceptual framework for interpreting the emerging evidence on GFA.

### 5.1 Foundations of Health: Mizaj, Akhlat, and Tabiat

The theoretical basis of Unani medicine centers on the balance of *Mizaj* (temperament), *Akhlat* (humours), and *Tabiat* (the body's innate governing power). It adopts a profoundly holistic approach, viewing the human body as an integrated system where physical, mental and spiritual aspects are interconnected and interdependent. *Sehat* (health) is maintained when these remain in equilibrium, whereas disturbances in temperament or humoral composition result in disease, collectively described as *Sue Mizaj* [24].

According to classical scholars such as Hippocrates, Galen, Al-Razi, Ibn Sina, and Ali Ibn Abbas Al-Majusi, the four humours- *Dam*, *Balgham*, *Safra*, and *Sauda* are generated through digestion and nourish all body tissues [9][10]. *Tabiat* preserves this internal balance by regulating physiological functions and supporting self-healing. Thus, efficient digestion and balanced humours are considered essential for maintaining systemic and reproductive health.

### 5.2 Quwwat-e-Hazima: The Central Role of Digestion

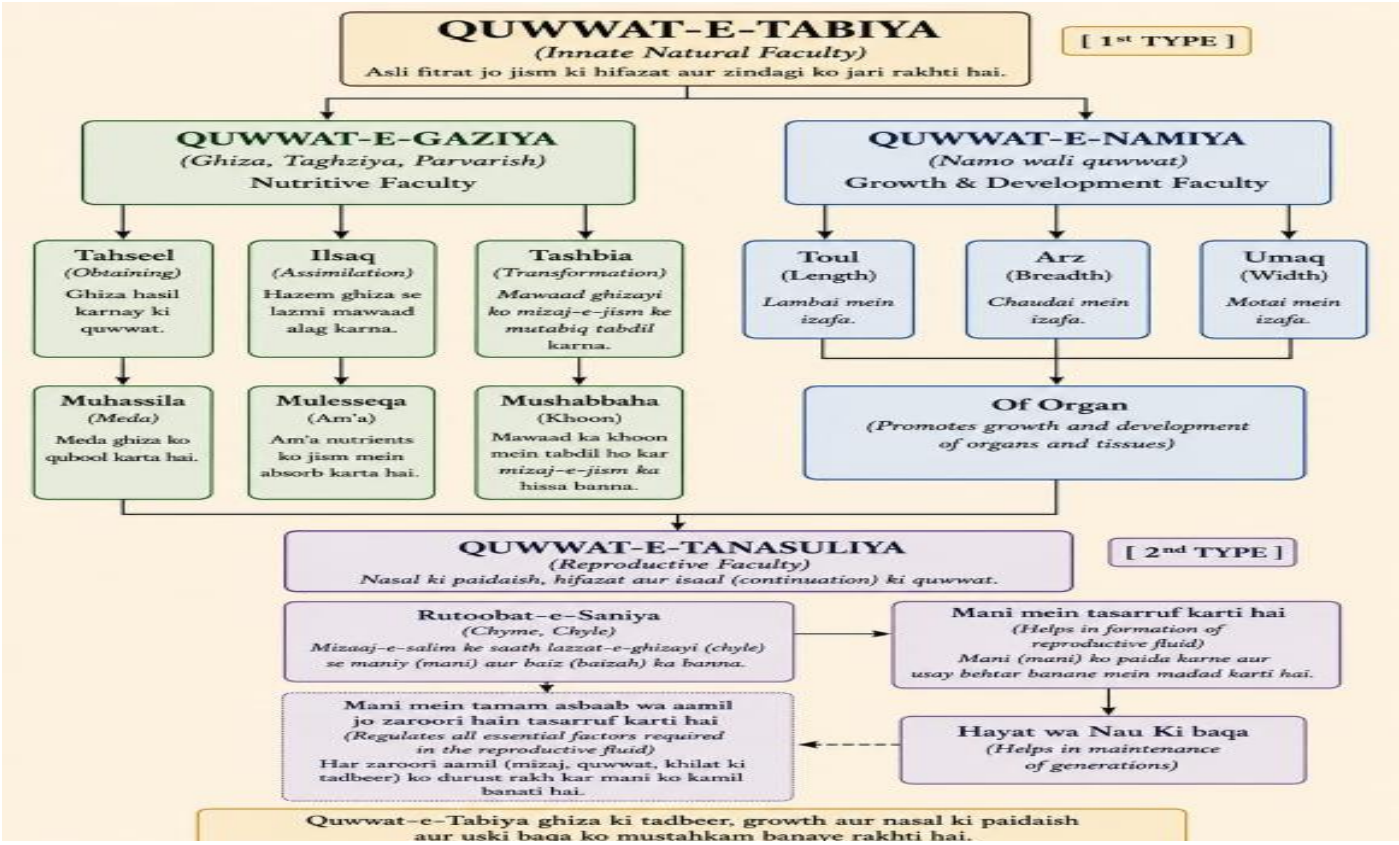


**Fig:2 Unani Concept Of Quwwat e Tabaiya :The Triad Of Nutrition ,Growth and Reproduction.**

**Hippocrates (460-370 BC) states "All diseases begins in the gut."[8]**

Quwwat-e-Hazima (digestive power) occupies a central role in Unani physiology as it governs the transformation of food into healthy humours [10]. Classical texts describe digestion as a sequential process involving Hazm-e-Medi (gastric), Hazm-e-Kabidi (hepatic), Hazm-e-Urooqi (vascular), and Hazm-e-Uzwi (tissue) digestion, each contributing to the formation, distribution, and utilization of nutrients throughout the body [10][25].

Impaired digestion results in Fasad-e-Akhlat (abnormal humours) and Sue Mizaj-e-Meda (gastric temperament imbalance), leading to inadequate nourishment of tissues and systemic dysfunction [26]. Therefore, digestive health is regarded as the foundation of disease prevention and therapeutic intervention.

### 5.3 Digestive Dysfunction and Reproductive Disorders

In Unani medicine, healthy *Nutfa* (reproductive fluid) is believed to originate from properly digested nutrients and balanced humours [25][27]. Consequently, infertility is considered a manifestation of systemic imbalance rather than an isolated reproductive disorder.

Disturbances in digestion, humour formation, or temperament may impair the quality & quantity of reproductive fluids, thereby reducing fertility potential[27].

Particular emphasis has been placed on *Sue Mizaj*, especially excessive *Burudat* (cold temperament), which is believed to diminish reproductive vitality by weakening semen quality in males and impairing uterine function in females. Similarly, excessive adiposity and nutritional imbalance were regarded as systemic conditions capable of disturbing reproductive physiology through alterations in humoral equilibrium and tissue nourishment [27][28]. Although expressed in traditional terminology, these concepts reflect the view that reproductive dysfunction often arises from generalized physiological disturbances.

### 5.4 A Classical Basis for the Gut Fertility Axis

Collectively, these classical principles demonstrate that Unani medicine has long recognized digestion as the foundation of systemic and reproductive health. The concepts of *Quwwat-e-Tabiya*, *Quwwat-e-Gaziya*, *Quwwat-e-Tanasuliya* collectively propose that disturbances arising within the gastrointestinal system may propagate throughout the body, ultimately influencing reproductive function [10][25]. While these concepts predate the discovery of the gut microbiota, they similarly propose that disturbances within the gastrointestinal system can influence distant organs through systemic physiological imbalance.

## 6. MODERN MICROBIOME SCIENCE AND CLASSICAL UNANI MEDICINE: A CONCEPTUAL CONVERGENCE

The emerging concept of the GFA offers an opportunity to interpret classical Unani principles in light of contemporary microbiome science. Although the two systems differ fundamentally in origin, methodology, and scientific foundation, both recognize the central role of digestive health in maintaining systemic physiological balance and reproductive function.

Current evidence demonstrates that gut microbial homeostasis regulates endocrine function, metabolism, immune responses, intestinal barrier integrity, and oxidative balance, all of which contribute to reproductive competence [15][17]. Similarly, Unani medicine attributes reproductive well being to efficient *Quwwat-e-Hazima*, balanced *Mizaj* and *Akhlat*, and the regulatory role of *Tabiat* [25][27]. Despite differences in terminology and theoretical framework, both paradigms emphasize digestive integrity as the basis of overall health.

The similarities identified in this review represent conceptual convergence rather than scientific equivalence. Recognizing these parallels may generate novel hypotheses for translational research and support the development of evidence informed integrative approaches for unexplained infertility.

**Table 1. Conceptual Convergence Between Modern Microbiome Science and Classical Unani Medicine**

| Modern Microbiome Science | Classical Unani Concept | Area of Conceptual Convergence |
|---|---|---|
| Gut Microbial Homeostasis | Quwwat-e-Hazima | Digestive integrity as the foundation of systemic health |
| Gut Dysbiosis | Sue Mizaj-e-Meda | Digestive dysfunction leading to systemic disturbances |
| Metabolic Dysregulation | Fasad-e-Akhlat | Formation of abnormal physiological constituents affecting distant organs |
| Physiological Homeostasis | Mizaj | Maintenance of internal equilibrium |
| Host Regulatory Mechanisms | Tabiat | Preservation of normal physiological function |
| Gut–Fertility Axis | Digestive–reproductive relationship | Digestive health influences reproductive competence |

## 7. THERAPEUTIC MODULATION OF THE GFA: AN INTEGRATIVE PERSPECTIVE

Although direct evidence supporting microbiota targeted therapy for unexplained infertility remains limited, growing evidence suggests that restoration of gut microbial homeostasis may improve endocrine, metabolic, immune, and inflammatory pathways essential for reproductive health. Current strategies focus on restoring eubiosis through dietary modification, probiotics, prebiotics, lifestyle optimization, and complementary therapies. These approaches closely align with the Unani principle that restoration of digestive health precedes systemic recovery.

### 7.1 Dietary Modulation of the Gut Microbiota [23][29]

Diet is one of the strongest modifiable determinants of gut microbial composition. Diets rich in dietary fiber, fruits, vegetables, legumes, whole grains, nuts, fermented foods, and polyphenols promote beneficial bacteria, enhance SCFA production, maintain intestinal barrier integrity, reduce inflammation, improve insulin sensitivity, and support reproductive health.

Among healthy dietary patterns,
**Mediterranean diet** emphasis whole plant- based foods, healthy fats, lean proteins; has the strongest evidence for improving microbial diversity, reducing inflammation, and enhancing metabolic and fertility outcomes.
**Atlantic diet** rich in seafood, vegetables, legumes, whole grains, and dairy; provides omega-3 fatty acids, iodine, and B vitamins that further support metabolic and reproductive function.

In contrast, **Western dietary patterns** rich in processed foods, refined carbohydrates, saturated fats, and sugary beverages promote gut dysbiosis, intestinal permeability, chronic inflammation and adverse reproductive outcomes [23][29].

**Micronutrients** including vitamin D, vitamin A, zinc, selenium, folate, iron, and omega-3 fatty acids

**Functional foods** such as yogurt, kefir, garlic, onions, oats, barley, flaxseed, chia seeds, berries, green leafy vegetables, walnuts, almonds, and resistant starch-rich foods

**Probiotics**, particularly Lactobacillus and Bifidobacterium species, improve gut microbial balance, strengthen intestinal barrier function, reduce inflammatory cytokines, and enhance metabolic regulation. Gagliardi A et al. have demonstrated beneficial effects in women with PCOS, obesity, metabolic syndrome and bacterial vaginosis.

**Prebiotics** such as inulin, fructooligosaccharides (FOS), galactooligosaccharides (GOS), and resistant starch selectively stimulate beneficial gut bacteria and increase SCFA production. Combined administration as **Synbiotics** may provide synergistic effects on microbial restoration and immune modulation.

### 7.2 Lifestyle Modification [30]

Lifestyle factors substantially influence gut microbial diversity and reproductive health. Regular physical activity, adequate sleep, stress reduction, smoking cessation, avoidance of unnecessary antibiotics, and maintenance of healthy body weight promote eubiosis and metabolic homeostasis. Conversely, chronic psychological stress activates the hypothalamic pituitary adrenal axis, alters intestinal permeability, promotes dysbiosis, and may impair reproductive function.

### 7.3 *Ilaj bil Ghiza* [31][32]

Since dietary requirements differ according to *Mizaj*, Unani physicians recommend individualized nutritional interventions, a concept that parallels the modern approach of personalized nutrition based on individual microbiome composition.

**Examples of fertility-supportive foods according to temperament include:**

***Cold & Dry Mizaj*:** Milk with dates, honey, ginger or cinnamon, young chicken, lamb, shrimp, fish eggs, walnuts, almonds, pistachios, hazelnuts; garlic, onion, sesame, fenugreek, saffron, ginger, grapes, bananas, figs, carrots, melons and wheat sprouts.

***Cold & Wet Mizaj*:** Wheat, chickpeas, red beans, bananas, apples, sweet pomegranates, pears, mangoes, walnuts, pistachios, hazelnuts, fenugreek, garden cress, cinnamon, saffron, ajwain, ginger, garlic, celery, olive oil, chicken, pigeon, rooster, pheasant and mint.

***Hot & Dry Mizaj*:** Cow's milk, goat meat, lamb, chicken, fish, watermelon and pumpkin seeds, peaches, apricots, sweet pomegranate, watermelon, cucumber, spinach, lettuce, purslane, almond oil and sesame oil while avoiding excessively hot spices.

***Hot & Wet Mizaj*:** Whole-wheat bread, olive oil, sweet pomegranate, apples, lettuce, dried figs, walnuts, pistachios, hazelnuts, poppy seeds, chicken and lamb.

### 7.4 *Ilaj bil Dawa*

| S. No | Unani Medicine /Herb | Major Phytochemicals | Unani Actions [35][36][37][38] | Potential Benefits |
|---|---|---|---|---|
| 1 | *Badiyaan* [Foeniculum vulgare ][33] | Anethole, Fenchone, Estragole | Hazim, Muwallid e mani, Muqawwi e Rahem | Digestive tonic, antimicrobial, phytoestrogenic, supports healthy gut microbiota |
| 2 | *Asgandh* [Withania somnifera ][34] | Withanolides, Withaferin A, Sitoindosides | Muqawwi e bah, muqawwi e aam, muffareh | Adaptogenic, reduces stress ,antioxidant ,immune modulator |
| 3 | *Seer* [Allium sativum][39] | Allicin, Allin, Diallyl, Sulfides, Ajoene. | Hazim, Dafe taffun | Antimicrobial, prebiotic, antioxidant, supports metabolism |
| 4 | *Amla* [Phyllantus embilica ][40] | Embilicanin A&B, Gallic acid ,Quercetin | Muqawwi-e meda wa jigar ,muharrik e bah, musaffi e dam | Enhances microbial diversity, potent antioxidant |
| 5 | *Isaphghol* [ Plantago ovata ][41] | Arabinoxylans, Soluble fiber, Mucilaginous | Mussakin-e hiddat, Musleh e-meda, mulayyin | Prebiotic, improves metabolic homeostasis, increases SCFA, strengthens intestinal barrier |
| 6 | *Haldi* [Curcuma longa][42] | Curcumin, Demethoxycurcumin | Muhallil-e Waram, Musaffi e damm | Modulates gut barrier, anti inflammatory, improves insulin sensitivity. |

| | | | | |
|---|---|---|---|---|
| 7 | *Mulethi* [Glycyrrhiza glabra][43] | Glycyrrhizin, Glabridin, Glycyrrhetinic Acid | Mullatif, Muhallil e waram | Anti inflammatory,gut mucosal protection, immunoregulator, endocrine modulator. |
| 8 | *Kalonji* [Nigella sativa][44] | Thymoquinone, Nigellone, Carvacrol | Muqawwi-e meda, Muqawwi-e bah, Muhallil e-waram | Anti inflammatory, antioxidant, immunomodulator, supports ovarian function |
| 9 | *Zanjabeel* [Zingiber officinale][45] | 6- gingerol, Zingerone | Muqawwi-e meda, Muqawwi-e bah, Hazim | Reduces gut inflammation, antioxidant, improves endocrine function |
| 10 | *Hulba* [Trigonella foecum graceum][46] | Trigonelline, Diosgenin, 4-hydroxyisoleucine | Musleh-e meda, Muhallil e waram, Muwallid e mani | Prebiotic, improves insulin resistance, improves metabolic function |

Tukhm e Jarjeer, Tukhm e Karafs, Barg e neem ,Zeera also have similar properties [47].

Compound Formulations[48][49] :

| Sno. | Formulation | Properties | Usage |
|---|---|---|---|
| 1 | *Majun Arad khurma* | Muqawwi wa muharrik- e-meda, mughalliz, mumsik-e-madda-e-manwiya, muqawwi e bah | 1 tola majoon + kushta e qalai ,2 chawal mix & use in morning regularly. |
| 2 | *Jawarish Jalinoos* | Muqawwi,muharrik, mufarreh azaa e raaesa . | 5-7g twice daily after meals |
| 3 | *Jawarish fawakeha* | Muqawwi e meda | 5-7g twice daily after meals |
| 4 | *Jawarish Zafran* | Muffareh meda | 5-7g twice daily after meals |
| 5 | *Jawarish Darchini* | Muqawwi e jigar | 5-7g twice daily after meals |
| 6 | *Laboob Asraar* | Muqawwi-e-azaa-e-raesa, muharrik-wa-mufarreh asaab . | 7 masha + Arq maul laham ambari 4 tola to be taken every morning. |

7.5 Ilaj bil Tadbeer[32][49]

*Riyazat* (Exercise),*Dalk* (Massage)*Hammam* (Bath),Adequate sleep, Stress reduction -Enhances circulation and supports digestive function promotes detoxification and relaxation, maintains gut microbial balance and hormonal homeostasis, Lowers systemic inflammation and preserve *tabiat* indirectly support reproductive function.

**Future Perspectives:** The gut–fertility axis is a promising target for future infertility research. Well-designed longitudinal and randomized clinical studies integrating microbiome profiling, microbiome metabolite analysis, microbiome sequencing and metabolomics are needed to establish causality and validate microbial biomarkers. These advances may enable personalized diagnostic and therapeutic strategies for unexplained infertility.

## CONCLUSION

Current evidence supports a strong biological association between gut microbiota and reproductive health, although causal relationships remain to be established. Integrating microbiome science with classical Unani principles provides a novel, holistic framework for understanding unexplained infertility. This conceptual convergence may enhance future diagnostic approaches and promote personalized, evidence-based management strategies for improving reproductive outcomes.

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