

**THERAPEUTIC POTENTIAL OF UNANI MEDICINES IN THE PROBLEM OF
UQR(INFERTILITY): AN OVERVIEW*****Shamsa Ahmad, **Dr. Fahmeeda Zeenat, ***Prof. Suboohi Mustafa**

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ABSTRACT

Infertility, the woman has never conceived despite cohabitation, regular unprotected sexual intercourse and exposure to pregnancy for 1 year and more is an important health issue causes medical, social and financial problem worldwide. The incidence is increased continuously due to various factors like social pressure, late marriage, late childbirth which harms include heavy economic burden. According to WHO around 17.5% adult population or 1 in 6 people affected worldwide from infertility and about 50% of them are related to female infertility and other to male causes etc. Although various conventional treatment are currently available but may be contraindicated in some patient also have the limitation of unsatisfied outcomes and high cost of ART procedures find a alternative treatment always in the need. In Classical Unani literature various drugs has been mentioned for the treatment of Uqr (infertility). Unani medicine considered as suitable alternative to conventional medicines because of its phytoestrogenic, antioxidant, utero tonic, ovulation inducing, aphrodisiac and nutritional properties. An effort has been made in this paper to critically reviews the literature on the potential benefits of unani single and compound drugs as a treatment for infertility.

KEYWORDS: Uqr, Infertility, Unani medicine.**INTRODUCTION**

Infertility is a medical illness that can have psychological, physical, emotional, spiritual, and medical consequences. Infertility is defined as a couple's failure to conceive after one year of unprotected coitus. Sterility is defined as the absolute inability to conceive.^[1] Primary infertility refers to patients who have never conceived. Secondary infertility refers to past pregnancy but failure to conceive. Fecundability is the likelihood of becoming pregnant within a single menstrual cycle, whereas fecundity is the likelihood of giving birth within a single cycle.^[2] A regular couple's fecundity is believed to be between 20% and 25%. Approximately 50% of women will be pregnant at 3 months, 75% at 6 months, and more than 85% by 1 year.^[5] The frequency of infertility has risen to 10-15% as a result of several causes such as societal pressure, late marriage, and late childbirth, all of which have negative consequences such as high economic burdens and marriage failure. According to WHO, around 17.5% of the adult population, or one in every six persons, are afflicted by infertility, with approximately 40-50% being associated to female infertility, 30-40% being related to male infertility, and the remaining 10% being unexplained.^[4]

Ovulation induction, which refers to the use of pharmacological therapy to induce ovulation, and ovarian stimulation, which is conducted with the purpose of producing numerous mature ovarian follicles, are two commonly used infertility treatments. Clomiphene citrate and letrozole are the drugs used to induce ovulation. To achieve fertilisation at the moment of ovulation, timed intercourse or interuterine insemination (IUI) might be employed. Another promising option is to remove ripe oocytes directly from the ovary for fertilisation using an ultrasound-guided needle (IVF) (Soensen et al 2018). Ovulation-inducing agents have their own set of side effects, including ovarian hyperstimulation syndrome (OHSS), miscarriages, multiple pregnancies, and birth abnormalities; as a result, more couples are turning to alternative medicine, particularly herbal therapy. Advancing therapeutic options include in vitro fertilisation (IVF), intrauterine insemination (IUI), and zygote intrafallopian transfer (ZIFT), however these therapies have limitations such as unsatisfactory results and high procedure costs as well as contraindication of these therapies. Such situation invite some alternative treatment for Uqr.

PATHOPHYSIOLOGY OF INFERTILITY

In one-third of all cases, the man is directly responsible, in one-third, both partners are at fault, and in the other third, the female is fully to blame. These values may be severe, and it may be preferable to spread the fault evenly between the two spouses.

Male Character faults

1. Failure to produce sufficient numbers of spermatozoa capable of fertilisation
 - Incomplete testicular development. The prevalence of sex chromosomal abnormalities is likely to be high in males with aplastic testes and azoospermia.
 - Late descent or non-descent of the testes, which may or may not be due to the previous reason. In either situation, the testis' spermatogenetic activity is dependent on its extra-abdominal location, most likely due to the negative effects of heat on the seminiferous tubules. The scrotal testis tissue temperature is 2°C cooler than the rest of the body.
 - Orchitis caused by mumps or other severe viral fevers (including influenza) or chlamydial infection beyond the age of 14 years. Orchitis causes 25-50 complications.
 - Testicular damage caused by procedure, accident, or X-ray exposure. The harm might be to the gonad's blood supply rather than the gonad itself.
 - Heat affects spermatogenesis, at least briefly; frequent hot baths or the use of non-porous nylon pants and suspensory clothing may have this impact. Varicocele is a prevalent condition among infertile men.
 - Testicular diseases such as tumours, TB, and syphilis
 - Testicular activity is reduced by sickness of other endocrine glands (particularly the hypothalamic pituitary system, e.g. hypogonadism as in the Lawrence-Moon-Biedl or Frolich syndrome, thyrotoxicosis, diabetes mellitus), general illness, and medications and poisons. High dosages of steroids, as well as antiandrogens such as cyproterone, spironolactone, cimetidine, and cannabis, depress the hypothalamo-pituitary-testicular axis.
 - Testicular damage caused by procedure, accident, or X-ray exposure. Cimetidine and cannabis have been shown to suppress the hypothalamo-pituitary-testicular system
 - Age: Male fertility declines after the age of 40, but spermatogenesis normally continues to some extent until old age. Octogenarian dads are not uncommon.
 - Antibodies and spermagglutinins: Spermagglutinins are detectable in the blood of certain infertile men or after vasectomy reversal procedures, which may damage seminiferous tubules and cause spermatozoa to agglutinate after ejaculation. Other local and systemic antibodies to testes and spermatozoa have been reported in males¹.

2. Obstruction of the Epididymis, Vas, or Ejaculatory Ducts on both sides

These might be caused by any of the following:

- An accident or procedure, particularly herniorrhaphy
- Infections, the most common of which are gonorrhoea and TB; the lesion is frequently epididymitis
- Vascular absence or extensive hypoplasia from birth
- Congenital or developing epididymis blockage, which is commonly linked with congenital cystic illness of the lungs to constitute a defined condition.^[1]

3. Failure to Deposit Spermatozoa in the Vagina

- Impotence (including the variety in which erection and penetration occur but there is no emission)
- Premature ejaculation;
- Penis abnormalities such as hypospadias and phimosis; and
- Retrograde ejaculation into the bladder. This occurs following prostatectomy and some nerve resection procedures. It may also happen to seemingly normal males.
- Drugs that alter ejaculation include α -blockers, ganglion blockers, tricyclic antidepressants, MAO inhibitors, phenothiazines, β -blockers, and thiazides.^[1]

4. Abnormal Semen Quality

- An exceptionally high or low ejaculation volume
- Other physicochemical abnormalities that may or may not be important include low fructose or high prostaglandin content, as well as excessive viscosity
- Oligozoospermia: sperm count less than 20 million/ml
- Asthenozoospermia: less than 50% of sperm with forward development or fewer than 25% with fast advancement
- Teratozoospermia: Less than 30% of morphologically normal forms exist.
- Asthenoterato-oligozoospermia: A combination of the aforementioned.
- Azoospermia refers to the lack of sperm in the seminal fluid, whereas aspermia refers to the absence of ejaculation.^[1]

FEMALE FACTOR

1. Dyspareunia and vaginal causes: Fixed retroversion with prolapsed ovaries, inflammatory adnexal illness, and pelvic endometriosis are the most common organic causes.

Congenital genital tract defects. The obvious reasons of sterility include an absence or septate vagina, hypoplasia, and a missing uterus. Infection of the cervix and vagina. Although a moderate infection may not hinder sperms from entering the cervical canal quickly, it is important to eliminate the infection before implementing any therapeutic measures in the treatment of infertility.^[3]

2. Cervical risk factors. The cervix has an active part in conception physiology. The location of the cervix and the patency of the cervical canal allow sperms to enter the uterine cavity. The cervical canal serves as a sperm reservoir, and sperm capacitation happens here. The cervical mucus is alkaline and suitable for sperm. By phagocytosis, the ciliated endocervical cells actively pick the normal motile sperms and sift out the aberrant ones, allowing only the healthy fertilizable sperms to enter the upper genital canal. At ovulation, the cervical mucus undergoes distinct modifications that facilitate sperm penetration. These cervical variables account for around 5% of infertility.^[3]

3. Causes originating in the uterus. More than infertility, hypoplasia, deformed uterus, and incompetent os induce habitual abortion. Tube obstruction and endometrial TB producing Asherman's syndrome (adhesions) are the causes of pelvic tuberculosis. Other infections, forceful curettage, postabortal and puerperal infection can all cause Asherman's syndrome. Uterine fibroids that cause infertility include a cornual fibroid that blocks the medial end of the fallopian tube, a submucous fibroid, and a cervical fibroid that distorts sperm passage and prevents implantation. A pregnancy rate of 30-40% after myomectomy indicates that variables other than the existence of a fibroid may be involved.^[3]

4. Tubal elements. One of the most prevalent reasons of infertility is salpingitis, which occurs when adhesions form around the abdominal ostium as a consequence of inflammation, and the plicae become adherent within the lumen of the tube, obstructing the passage in the tube. Common causes of fallopian tube obstruction include gonorrhoea, chlamydial infections, or salpingitis after a septic abortion, as well as puerperal infections. Endometrial biopsy reveals that 5% of asymptomatic infertile women have genital TB, which has before been mentioned. Infertility can be caused by peritubal adhesions and fimbrial end obstruction in addition to tubal blockage.^[3]

5. Ovaries. Some of the most common reasons of infertility include endocrine problems, polycystic ovarian disease (PCOD), and corpus luteal phase deficiencies

(LPDs). Peri-ovarian adhesion in pelvic infection and luteinized unruptured follicular (LUF) syndrome are also to blame in 9% of instances. Nonovulation is caused by resistant ovarian syndrome. Corpus LPDs occur in 3-4% of infertile women because to a lack of progesterone or a shorter length of the luteal phase.^[3]

6. Peritoneal causes. By kinking the fallopian tubes, peritubal and intratubal adhesions create tube obstruction. More critically, these adhesions are an integral element of PID. These adhesions can also affect fallopian tube peristaltic motions. Macrophages in the peritoneal fluid may engulf the ovum and sperms in pelvic endometriosis, inhibiting fertilization.^[3]

7. Long-term illness. The most common causes of nonovulation are hypothalamic and pituitary illness, hypothyroidism, and adrenal cortical dysfunction. Diabetes and TB can both cause infertility. It is well established that smoking impairs ovarian function and prevents embryo implantation into the endometrium.^[3]

According to the unani concept Uqr (infertility) occurs when conception fails to occur or when conception is problematic owing to a fault in either the male or female spouse.^[6,7] According to Roofas, if the women slept after intercourse the chances to get pregnant increases. The main cause of female infertility is related to uterus, either obstruction or injury to uterus and displacement of uterus. If the cause of is excess of Hararat, then the colour of menstrual blood is orange and black. In case of excessive Baroodat menstrual bleeding will be excessive and light in colour, other cause is dryness of uterus and on examination uterus will be dry on touch. Zakriya Razi said, if Semen is thin then Garam and Khushk diet will make the semen thick and also said that, if the women desire to intercourse, then there are more chances to conceive.^[8] In Unani system of medicine the treatment is to remove the cause at first step, Ancient Unani physician testified to cure disease with several Unani drugs. Unani medicine considered as suitable alternative to conventional medicines because of its phytoestrogenic, antioxidant, utero tonic, ovulation inducing, aphrodisiac and nutritional properties, which are used from the 5th day of menstrual cycle.^[9,10]

List of single drugs used in Uqr(infertility)

Unani name	Scientific name	Mechanism of Action
Musli Safed ^[11]	<i>Chlorophytum borivilianum</i>	Aphrodisiac, antioxidant, Anti-inflammatory, anti-arthritis, antimicrobial.
Murmuki ^[11]	<i>Commiphora myrrh</i>	Aphrodisiac, antiseptic, antibacterial, diuretic, anti-inflammatory.
Shibbeyamani ^[11]	Sulphate of Al & Potash	Astringent, styptic, Antiseptic.
Mushk ^[11]	<i>Moschus moschiferus</i>	Exhilarant, tonic to vital organ, antispasmodic
Jundebedastr ^[11]	<i>Castoreum</i>	Nerve tonic, antispasmodic, anti-inflammatory, diuretic
Kakla Sigaar ^[11]	<i>Elletoria</i>	Aphrodisiac, antispasmodic, cardiac tonic, emmenagogue, diuretic, antihelmenthic.

	<i>cardomomum</i>	
Halela zard ^[11]	<i>Terminalia chebula</i>	Antibacterial, antifungal, anti ulcerogenic, antioxidant, cytoprotective, cardioprotective
Gule Nilofar ^[11]	<i>Nymphaea alba</i>	Anti-inflammatory, antiseptic, astringent, antioxidant
Mazu ^[11]	<i>Quercus infectoria</i>	Astringent, styptic, anti-inflammatory,
Gule dhawa ^[11]	<i>Woodfordia fruticosa</i>	Antimicrobial, hepatoprotective, cardioprotective, antioxidant, Immunomodulatory.
Shatavari ^[11]	<i>Asparagus racemosus</i>	Aphrodisiac, antidyspepsia, antioxidant, antiulcer, galactagogue, anticancer.
Neem ^[11]	<i>Azadirachta indica</i>	Antibacterial, antioxidant, immunomodulatory, hepatoprotective
Asgand ^[11]	<i>Withania somnifera</i>	Antioxidant, antiapoptic, cardioprotective, aphrodisiac, spermatogenic.
Joz bua (Jaifal) ^[7]	<i>Myristica fragrans</i>	Antioxidant, Immunomodulatory, radioprotective, antimicrobial, anti-inflammatory.
Dhatura ^[7]	<i>Datura stramonium</i>	Antiasthmatic, anticholinergic, antimicrobial, anticancer, anti-inflammatory.
Zafraan ^[7]	<i>Crocus sativus</i>	Aphrodisiac, stimulant, uterine tonic, cardiotonic, Emmenagogue, antispasmodic, resolvent, Exhilarant, Diuretic, Astringent.
Ood ^[11]	<i>Aquilaria agallocha</i>	Cardiotonic, Aphrodisiac, antiseptic, Deobstruent, Exhilarant,
Filfil Siyaah ^[11]	<i>Piper nigrum</i>	Nerve tonic, Aphrodisiac, diuretic, antimicrobial, antihypertensive, antioxidant, anti-inflammatory.
Qinnab ^[11]	<i>Cannabis sativa</i>	Antiparasitic, antiemetic, antipyretic, antiepileptic, carminative, antiinflammatory, antitumor.
Utangan ^[11]	<i>Blepharis edulis</i>	Anti-inflammatory, antioxidant, hepatoprotective, antimicrobial.
Lisanul-Asafeer ^[7]	<i>Wrightia tinctoria</i>	Aphrodisiac, Emmenagogue, antihelminthic, carminative, antiinflammatory,
Khyaar shanbar ^[7]	<i>Cassia fistula</i>	Antimicrobial, antiulcer, Antioxidant, antiinflammatory, CNS activity, Hypolipidemic.
Anbul Salab ^[7]	<i>Piper longum</i>	Stomachic, aphrodisiac, laxative, antiasthmatic, antidiarrhoeic, antidysentery.
Piyabansa ^[11]	<i>Barlerias prionitis</i>	Diuretic, gastroprotective, cytotoxic, antiviral, CNS depression, antiinflammatory, antifungal.

List of Compound drugs used in infertility

● Itriful Sageer ^[11]	Cardiotonic,
● Jawarish Kamooni ^[11]	Stomachic, aphrodisiac
● Usara bartang ^[11]	Aphrodisiac stimulant, uterine tonic, Anti-inflammatory, antioxidant
● Majoon Hamal Anbari Alwi khan	Uterotonic, aphrodisiac, anti-inflammatory.
● Majoon Nishara Ajwali	
● Majoon Supari park ^[7]	
● Habbe Hamal ^[11]	Uterotonic, aphrodisiac

Pre-clinical and clinical studies

Punica granatum (Pomegranate): Pomegranate seeds include phytoestrogens such as genistein, daidzein, coumestrol, glutamic amino acids, and aspartic acids.^[13] According to animal studies on PCOS rats, pomegranate extract, which includes phytoestrogens, can manage and treat PCOS symptoms. This plant extract promotes mucus production by increasing uterine blood flow (vasodilation) and uterine wall thickness. This increase in mucosal secretions facilitates implantation through anti-inflammatory mechanisms.^[14,15]

In a randomised controlled triple-blind parallel experiment including 23 women with PCOS, pomegranate fruit extract reduced blood levels of sex

hormones (testosterone reduction) and their lipid profile.^[16]

Withania somnifera (Ashwagandha): Premature ejaculation, polyarthritis, painful swellings, lumbago, oligospermia, vitiligo, general debility, ulcers, impotency, uterine infections, leucorrhoea, and orchitis have all been historically treated with the herb.^[17]

Saiyed et al. (2016) reported that blood LH levels reduced, FSH levels increased, and preantral and antral follicles and corpus luteum decreased in a 22-day study on letrozole-induced polycystic ovarian syndrome in rats.^[18]

According to Bhattarai et al. (2010), Ashwagandha extract boosted gonadotropin hormone production and, eventually, improved oogenesis via GABA mimetic characteristics, which was believed to be owing to enhancing the HPG axis and increasing serum oestrogen balance.^[19]

Cinnomomum: Cinnamomum extracts and active components have also been used to treat asthma, bronchitis, diarrhoea, headache, inflammation, cardiovascular disease, and PCOS, as well as to increase female/male sexual potency and female sexual desire.^[20] Kort and Lobo (2014) found in a randomised controlled trial that six months of Cinnamomum treatment improved the menstrual cycle, insulin resistance, and testosterone production in women with PCOS.^[21] Cinnamomum also controlled the HPG axis and increased GnRH secretion, perhaps by boosting norepinephrine and NO production via compounds like delta-Cadinene.^[22]

Cinnamon promotes glucose absorption by activating the glycogen synthase enzyme and decreasing glycogen synthase kinase 3 (GSK3) activity. Cinnamon also activates the insulin receptor kinase enzyme and inhibits insulin receptor dephosphorylation. All of these activities have been shown to diminish insulin resistance.^[23]

Vitex Agnus-castus (Verbenaceae): This plant extract also stimulates the release of the corpus luteum following ovulation, which results in the production of progesterone, which regulates the female reproductive cycle (Askari, 2017). Blood levels of oestrogen and progesterone increased in the Verbenaceae extract group compared to the control group in an animal study done by Yakubu and Akanji (2011), however LH and prolactin, as sexual function interfering hormones, decreased.^[24] Furthermore, as compared to the control group, an extract of this plant reduced the number of preantral and antral follicles as well as the corpus luteum in rats with induced PCOS after 28 days. Furthermore, the diameter of antral follicles increased, as did the thicknesses of follicular theca and ovarian tunica albuginea when compared to the control.^[25]

Butea frondosa: Gholami et al. (2016) observed that giving male rats, both young and old, a bark methanol extract of *B. frondosa* resulted in an increase in sperm production and a decrease in abnormal spermatozoa.^[26]

Matricaria chamomilla (Chamomile): In a study on the growth and maturation of isolated mouse ovarian follicles in a three-dimensional culture system, chamomile extract increased progesterone, 17-estradiol, and dehydroepiandrosterone levels in the culture medium, decreased ROS, follicular diameter, and antrum formation, and prolonged oocyte survival²⁷. Furthermore, Gholami et al. (2016) discovered that after one week of taking chamomile extract-containing capsules on 80 post-term pregnant women with a

gestational age of 40 weeks or more, labour symptoms appeared, and labour pain and contraction duration decreased when compared to the control group.^[26]

DISCUSSION

Infertility may have a significant impact on a couple's life, thus it is critical to optimise their reproductive health. The frequency of infertility has risen to 10-15% as a result of several causes such as societal pressure, late marriage, and late childbirth, all of which have negative consequences such as high economic burdens and marriage failure. Infertility has become a big problem in many couples' lives, causing many to divorce and live apart. As a result, it is critical to educate couples and society about infertility and its treatment. Various medical therapies are accessible in traditional medicine, however there are negative effects and contraindications to these treatments. As a result of the necessity for alternative treatment, the Unani system has a variety of single and compound medications that are employed in infertility. Unani literature review provides a list of herbal drugs used in Uqr (infertility). Unani medicine considered as suitable alternative to conventional medicines because of its phytoestrogenic, antioxidant, utero tonic, ovulation inducing, aphrodisiac and nutritional properties.

CONCLUSION

There are few drug which has been proved scientifically their efficacy which justify upto some extent yet now. Further more studies required to validate the role of other unani medicines in Uqr (Infertility) on scientific parameters.

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