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Case Report

Effect of herbal medicine in male factor infertility (Oligoasthenoteratozoospermia) – A case report

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ABSTRACT

Introduction: Infertility is defined as the failure to conceive after one or more years of regular, unprotected coitus. According to the World Health Organization, male factor infertility accounts for 40 to 50 percent among the 60 to 80 million infertile couples worldwide. Semen analysis is a vital tool in the assessment of male infertility. Oligoasthenoteratozoospermia, a condition in which a semen sample comprises oligospermia/oligozoospermia, asthenozoospermia, and teratozoospermia, is common among men from infertile couples.

Case Presentation: A 32-year-old married man sought treatment for six years of infertility. His seminal fluid analysis revealed oligoasthenoteratozoospermia. Internally, *Mucuna purulence* seed powder and *Withania somnifera* root powder, 5 g each, were prescribed twice daily after meals with milk, while *Nigella sativa* seed powder was administered 2.5 g twice daily after meals. Following three months of treatment, his seminal fluid analysis revealed a consistent improvement in the sperm parameters. Sperm volume increased from 1.3 ml to 1.7 ml, sperm concentration rose from 1.3 million/ml to 3 million/ml, overall sperm motility increased from 15% to 24%, progressive motility from 00% to 04%, and non-progressive motility from 15 to 20%, while non-motile sperm decreased from 85% to 76%.

Conclusion: The seminal fluid analysis findings reveal that herbal medicine can be beneficial in managing male factor infertility by avoiding primary methods of treatment that are expensive and have a variety of undesirable side effects despite their inadequate efficacy rates, as well as secondary measures.

Keywords herbal medicine, male factor infertility, oligoasthenoteratozoospermia, seminal fluid analysis

INTRODUCTION

Failure to conceive after one or more years of regular, unprotected coitus is known as infertility.[1] Although precise figures are not yet available, the World Health Organization (WHO) estimates that between 60 and 80 million couples globally suffer from infertility. Male factor infertility accounts for 40 to 50 percent of all occurrences of infertility and is currently a growing global health concern. Over 90% of male infertility cases are caused by oligospermia and low-quality sperm.[2] An essential tool for evaluating infertile males is semen analysis.[3]

Oligoasthenoteratozoospermia is frequently found in men from infertile couples. Its etiology remains largely unknown, despite the fact that several factors contribute to its pathophysiology.[4] The WHO defines oligoasthenoteratozoospermia as a condition in which a semen sample contains oligospermia/oligozoospermia (the presence of spermatozoa in the ejaculate but the total number below the lower reference limit), asthenozoospermia (the percentage of progressively motile spermatozoa below the lower reference limit), and teratozoospermia (the percentage of morphologically normal spermatozoa below the lower reference limit). The normal reference value and lower reference (within parentheses) limit of semen analysis according to WHO have been listed in Table. 1.[1]

Factors influencing spermatogenesis can be grouped into four main categories. These include:

1) Biological, physiological, and genetic factors, including genetics, urogenital infections, varicoceles, liver diseases, and chronic kidney diseases;

2) Risk factors related to behavior and lifestyle, such as smoking, drinking, having an inappropriate body mass index, sexual behavior, diabetes mellitus, wearing tight underwear, and the use of drugs;

3) Environmental factors, such as exposure to chemicals,

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Table. 1. Semen analysis according to World Health Orgaization.[1]

Semen Analysis.	**Normal reference value and lower reference (within parentheses) limit.**
Volume	2.0 ml or more (1.5 ml)
pH	7.2–7.8
Viscosity	< 3 (scale 0–4)
Sperm concentration	20 million/ml (15 million/ml)
Total sperm count	> 40 million/ejaculate (39 million/ejaculate)
Motility	> 50% progressive forward motility(Progressive motility = 32%)
Morphology	> 14% normal form (4%)
Viability	75% or more living (58%)
Leucocytes	Less than 1 million/ml
Round cells	< 5 million/ml
Sperm agglutination	< 10% spermatozoa with adherent particles

various pesticides, mycotoxins, and testicular exposure to excessive heat (mine workers, truck drivers, tailors, and rising environmental temperatures brought on by the prevailing climate changes); and

4) Sociodemographic risk factors, such as aging.[5,6]

According to reports, only a small proportion of male factor infertility can be resolved with primary methods of treatment in the conventional system.[5] To enhance sperm count, a variety of medications are employed, such as clomiphene citrate, tamoxifen, and hCG. However, these medications are costly and have a number of side effects, which include gynecomastia, hepatic carcinoma, deep vein thrombosis, lowering HDL (high-density lipoproteins), and raising LDL (low-density lipoproteins), etc. Furthermore, the efficacy rate of these medications is likewise unsatisfactory.[6] In contrast, secondary methods such as artificial insemination, intrauterine insemination (IUI), in vitro fertilization (IVF) and embryo transfer, intracytoplasmic sperm transfer, and child fostering or adoption are typically used for dealing with male factor infertility.[5]

Manī is an Arabic term that denotes sperm or semen in the Unani system of medicine. Ibn Sina (980–1037 AD) asserts that *manī* is produced following the end result of "*haḍm chahārum*" (fourth stage of digestion), in which the extremely *laṭīf dam* (thin blood) produces *manī*.[7] Rabban Tabri (810–895) asserts that *manī* is the concocted form of blood.[8] Hippocrates and Galen (129–200 AD) claim that *manī* is the *mādda* (matter) that forms the *Janīn* (foetus).[9]

The majority of the Unani scholars, especially Ibn Sina, Zakaria Razi (865–925 AD), Ismail Jurjani (1110 AD), and Rabban Tabri, have gone into great detail about sexual illnesses. They have discussed the causes, symptoms, problems, therapy, and management of a variety of sexual illnesses under the heading of *ḍu'f al-Bãh* (anaphrodisia). *Ḍu'f al-Bãh* is actually a general phrase that includes a variety of illness entities, such as oligospermia (*Qillat i-manī*), premature ejaculation (*Sur'a al-inzãl*), erectile dysfunction (*Istirkhã' qaḍīb*), etc.[10] '*Qillat i-manī'* and '*Riqqat-i-man'ī'* captions discuss the semen abnormalities.[11] '*Qillat'* means lack, and '*Riqqa't'* indicates fluidity.[12] Sexual illnesses such as *jarayãn* (spermatorrhea), *Kathra al-iḥtilãm* (nocturnal emission), *Sur'a al-inzãl*, *'Uqr* (infertility), and *Ḍu'f al-Bãh* are mainly caused by these conditions.[11]

The *mizãj* (temperament) of certain organs must be balanced for spermatogenesis to occur. Although the precise aetiopathogenesis is not explained in classical Unani literature, it can be inferred from its cause that excessive *burûdat* (coldness), *yabûsat* (dryness), *ḥarãrat* (heat), or *ruṭûbãt* (moistness) in the *alaate manī* (testes) causes *sû al-mizãj* (morbid temperament) to alter the production of *manī*.[10] The ultimate result of the body's *sû al-mizãj* is *qillat* and *riqqat* ailments.[12] Semen production and regulation are also affected by derangement in *kayfiyãt arba'a* (physical properties), *ḍu'f al-a'ḍã 'ra'īsa* (weakness of vital organs), excessive *istifrãgh* (evacuation), malnutrition, general body weakness, excessive masturbation, excessive sexual intercourse, and drug addictions like opium and cannabis.[6]

Thus, one of the main lines of treatment in the Unani medical system is to restore or preserve the normal *mizãj* of the testes and the entire body and *kayfiyãt arba'a*. The broad term *muqawwī i-bãh* is frequently used in the Unani medical system to treat semen and issues linked to it. *Muwallid-i-manī* refers to food or medicines that increase the quantity and quality of semen. Every agent of *muwallid-i-manī* is also *muqawwī i-bãh*.[12] Therefore, drugs containing *tadil i-mizãj* (moderating the temperament) of testes, *muwallid-i-manī* (spermatogenic), *muqawwī i-aghdhiya* (nutriment), *mumsik i-manī* (semen avaricious), and *mughalliẓ i-manī* (semen viscositive) can be administered.[6,13] Several Unani medications, both single and compound, have been effectively used to treat a range of male sexual dysfunctions.[11]

MATERIALS AND METHODS

Case Profile: A 32-year-old married man sought treatment for six years of infertility. His condition was identified as oligoasthenoteratozoospermia (OAT). Unfortunately, his wife, who is 25 years old, is also receiving treatment at the same time since she has some issues on her end as well.

Medical History: He has well-developed secondary sexual characteristics. He does not have any systemic diseases, including diabetes mellitus, impotence, thyroid dysfunction, hypertension, hyperlipidemia, or a family history of subfertility.

Past Medical History: No history of diabetes, bronchiectasis, mumps orchitis after puberty, hydrocele, recurring chest infections, tuberculosis, or trauma to the gonadal part, blood transfusions, any chronic ailments, drug allergies, or bacterial or viral infections of the prostate or seminal vesicle.

Past Surgical History: None

Family History: No history of impotence or subfertility in the family

Personal History: He had a healthy appetite, slept soundly, had no history of sexual dysfunction, and his bowel movements and urine output were regular and normal. There is no history of previous marriage.

Occupation: Salesman.

Habits: He had smoked two to three cigarettes a day in the past but had never consumed alcohol.

Investigations done:
Seminal Fluid Analysis (SFA): SFA reports before and after treatment are listed in Table 2.

Therapeutic Intervention:
The patient's preferences, the individual's *mizãj* (temperament), the quality and quantity of *khilṭ* (humor) involved, and the manner in which symptoms appear all influence the therapeutic approach for a patient with Oligoasthenoteratozoospermia.

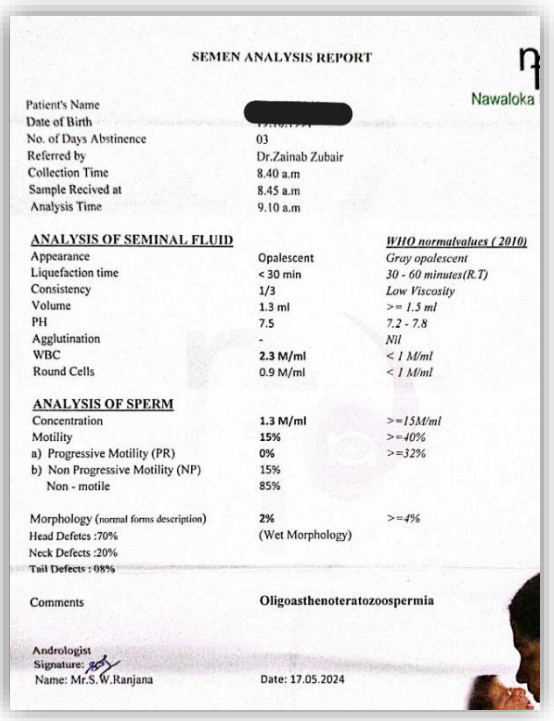
After receiving counseling regarding his condition, the patient agreed to receive treatment.

1. Advice:
    a. Adopt a healthy way of living.
    b. A healthy and balanced diet. Reduce caffeine intake.
    c. Avoid alcohol consumption and smoking.
    d. Regular exercise.
    e. Avoid wearing tight clothing and exposure to excessive heat.
    f. Adopt meditation and relaxation strategies to lower stress levels.
2. *Mucuna purulence* seed powder: 5 g twice daily orally with milk, after meals.
3. *Withania somnifera* root powder: *5 g* twice daily orally with milk, after meals.
4. *Nigella sativa* seed powder: 2.5 g twice daily orally, after meals.

Mode of Action of drugs:
It has been demonstrated that *Mucuna pruriens* seed powder, *Withania somnifera* root powder, and *Nigella sativa* seed powder possess moderating the temperament of the testes, aphrodisiac, and sperm-producing qualities. Additionally, they enhance spermatogenesis (improve sperm concentration and count), vitality, virility, vigor, blood circulation, and prevent impotence, spermatorrhea, premature ejaculation, sexual debility, etc.[14]

RESULT

The patient was assessed following three months of treatment. Analysis of the seminal fluid showed a steady improvement in the sperm parameters. The patient's general state of health also improved. The patient did not experience any adverse effects at all. In Table 2, the SFA reports are listed. The reports before and after treatment are given in Fig.1 and Fig.2.



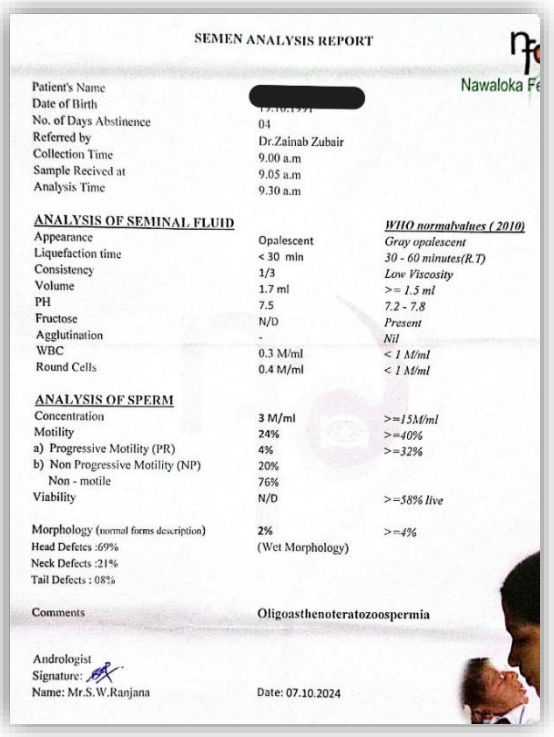
SEMEN ANALYSIS REPORT

Nawaloka

Patient's Name	[redacted]	
Date of Birth		
No. of Days Abstinence	03	
Referred by	Dr.Zainab Zubair	
Collection Time	8.40 a.m	
Sample Recived at	8.45 a.m	
Analysis Time	9.10 a.m	
ANALYSIS OF SEMINAL FLUID		***WHO normalvalues (2010)***
Appearance	Opalescent	*Gray opalescent*
Liquefaction time	< 30 min	*30 - 60 minutes(R.T)*
Consistency	1/3	*Low Viscosity*
Volume	1.3 ml	*>= 1.5 ml*
PH	7.5	*7.2 - 7.8*
Agglutination	-	*Nil*
WBC	2.3 M/ml	*< 1 M/ml*
Round Cells	0.9 M/ml	*< 1 M/ml*
ANALYSIS OF SPERM		
Concentration	1.3 M/ml	*>=15M/ml*
Motility	15%	*>=40%*
a) Progressive Motility (PR)	0%	*>=32%*
b) Non Progressive Motility (NP)	15%	
Non - motile	85%	
Morphology (normal forms description)	2%	>=4%
Head Defetes :70%	(Wet Morphology)	
Neck Defects :20%		
Tail Defects : 08%		
Comments	Oligoasthenoteratozoospermia	

Andrologist
Signature:
Name: Mr.S.W.Ranjana Date: 17.05.2024

Fig. 1. Semen analysis report before treatment



SEMEN ANALYSIS REPORT

Nawaloka Fe

Patient's Name	[redacted]	
Date of Birth		
No. of Days Abstinence	04	
Referred by	Dr.Zainab Zubair	
Collection Time	9.00 a.m	
Sample Recived at	9.05 a.m	
Analysis Time	9.30 a.m	
ANALYSIS OF SEMINAL FLUID		***WHO normalvalues (2010)***
Appearance	Opalescent	*Gray opalescent*
Liquefaction time	< 30 min	*30 - 60 minutes(R.T)*
Consistency	1/3	*Low Viscosity*
Volume	1.7 ml	*>= 1.5 ml*
PH	7.5	*7.2 - 7.8*
Fructose	N/D	*Present*
Agglutination	-	*Nil*
WBC	0.3 M/ml	*< 1 M/ml*
Round Cells	0.4 M/ml	*< 1 M/ml*
ANALYSIS OF SPERM		
Concentration	3 M/ml	*>=15M/ml*
Motility	24%	*>=40%*
a) Progressive Motility (PR)	4%	*>=32%*
b) Non Progressive Motility (NP)	20%	
Non - motile	76%	
Viability	N/D	*>=58% live*
Morphology (normal forms description)	2%	>=4%
Head Defetes :69%	(Wet Morphology)	
Neck Defects :21%		
Tail Defects : 08%		
Comments	Oligoasthenoteratozoospermia	

Andrologist
Signature:
Name: Mr.S.W.Ranjana Date: 07.10.2024

Fig. 2. Semen analysis report after treatment.

Table.2. Seminal Fluid Analysis reports before and following three months of treatment.

Parameters	Before treatment.	After three months of treatment.
Appearance	Opalescent	Opalescent
Liquefaction time	>30min	>30min
Volume	1.3 ml	1.7 ml
pH	7.5	7.5
Concentration	1.3 million/ ml	3 million/ ml
Motility	15%	24%
a. Progressive Motility	00%	04%
b. Non-Progressive Motility	15%	20%
Non-Motile	85%	76%
Morphology: (Normal Forms)	02%	02%

DISCUSSION

According to the allopathy system, male factor infertility can only be partially resolved using primary methods of treatment, which are costly and have a number of negative side effects. Secondary measures such as artificial insemination, IUI, IVF and embryo transfer, intracytoplasmic sperm transfer, and child fostering/adoption are typically used for the management.[5]

Therefore, in developing countries, medicinal plants with a variety of therapeutic and nutraceutical characteristics are largely used to treat various infertility conditions.[15]

Mucuna pruriens, Withania somnifera, and *Nigella sativa* comprise the characteristics of moderating the temperament of testes, aphrodisiac, spermatogenic, semen avaricious, and semen viscositive.

Mucuna pruriens acts as a restorative, energizing tonic and aphrodisiac in conditions marked by weakness or loss of sexual potency. It also aids in a central mechanism to boost semen secretion and decrease spermatorrhea. It controls catecholamine levels to help infertile individuals' genitourinary systems function properly.[16] A study showed that 5 g of *Mucuna* seed powder taken orally once daily enhanced sperm motility and count while also reducing psychological stress and seminal plasma liquid peroxide levels in males with reduced sperm count and motility. Additionally, it enhances semen quality, aids with stress management, and reactivates the antioxidant defense mechanism.[17]

Mucuna pruriens seeds consist of main biologically active components like L-DOPA (L-3,4 dihydroxyphenyl alanine), alkaloids (mucunine, mucunadine, prurienidine, and nicotine), b-sitosterol, glutathione, lecithin, vernolic acid, gallic acid, tryptamine, alkylamines, steroids, flavonoids, coumarins, cardenolides, and metals (magnesium, copper, zinc, manganese, and iron). According to some studies, L-DOPA has aphrodisiac characteristics. Alkaloids, coumarins, flavonoids, and alkylamines possess antioxidant qualities. Methanol extract has strong antioxidant activity, as it significantly increases the levels of seminal plasma by inhibiting 1,1-diphenyl-2-picryl-hydrazyl and hydroxyl radical and also nitric oxide and superoxide anion scavenging and hydrogen peroxide decomposing and reducing characteristics. The composition of considerable amounts of metals may provide vital supplements and nutrients. Copper and iron content in *Mucuna pruriens* seeds play a crucial role in spermatogenesis and fertility.[18]

According to several case studies, *Withania somnifera* raises the levels of testosterone, luteinizing hormone (LH), sperm motility, volume, and count.[19] Additionally, it has aphrodisiac properties.[20]

More than 80 typical phytochemicals are found in the root of the *Withania somnifera* plant, which includes steroids, alkaloids, saponins, glycosides, and volatile oil. Sitoindosides and withaferin have a significant amount of therapeutic effects. Moreover, *W. somnifera* is crucial for treating infertility issues since it contains phytochemical constituents and an appropriate amount of minerals that possess antioxidant properties. An in vitro study exhibited that hydroethanolic extract is non-toxic and non-mutagenic with membrane-stabilizing characteristics. It also potentially helps in retaining spermatozoa parameters. Additionally, it might help preserve or restore sperm functions for intrauterine insemination and in vitro fertilization.[15]

It has been demonstrated that *Nigella sativa* seed increases sperm volume, count, motility, morphology, and viability, as well as serum levels of follicular stimulating hormone, LH, and testosterone.[19]

Nigella sativa seeds contain both volatile and non-volatile oils, proteins, carbohydrates, minerals (e.g., iron, calcium, potassium, magnesium, zinc, and copper), vitamins A and C, as well as phytochemicals such as sterols (e.g., β-sitosterol, campesterol, stigmasterol, and 5-avenasterol) and saponins, phenolic compounds, alkaloids, lipid constituents, and fatty acids (e.g., linoleic, linolenic, oleic, palmitoleic, palmitic, arachidonic, and stearic acids). Essential oils consist of more than forty different compounds with varying concentrations, like trans-anethole, p-cymene, limonene, carvone, α-thujene, α-thujene, thymoquinone (TQ), thymohydroquinone (THQ), dithymoquinone (DTQ), thymol (THY), carvacrol, and β-pinene.[21] The antioxidant characteristic of thymoquinone, which is the most important compound, helps to improve spermatogenesis by preventing mitochondrial degeneration. Additionally, the antioxidants improve steroidogenesis and spermatogenesis and neutralize the free radicals in the seminal

fluid or improve the sperm factors. The linoleic acid (about 60%) and oleic acid (about 20%) present in the oil help to enhance sperm mobility and count, as well as eliminate the abnormal sperm. The phenolic and alkaloid compounds improve the levels of testosterone hormone and follicular stimulating hormone (FSH) in testicular tissues. Zinc, copper, magnesium, and vitamins enlarge the testes and epididymis. It also enhances the activity of several metabolic enzymes, secretions of steroid hormones and serum protein enzymes. *N. sativa* oil has been found to be the best form in many studies to treat infertility, while aqueous extract and TQ help to emphasize the testosterone levels and testes tissue.[22]

In numerous research studies on herbal medication for male factor infertility, no negative effects have been documented.[23]

A summarized review of some recent clinical trials and meta-analyses on *Mucuna pruriens* seeds, *Withania somnifera* roots and *Nigella sativa* seeds have been listed in Table.3.

Table.3. A summarized review of some recent clinical trials and meta-analyses on *Mucuna pruriens* seeds, *Withania somnifera* roots and *Nigella sativa* seeds.

	Drug	**Study type**	**Intervention**	**Duration**	**Main outcomes**
01	*Mucuna pruriens* - seed powder	Human study (Randomized Clinical Trial- RCT)	5 g/day orally with milk.	3 months	Sperm concentration and motility significantly improved.
02	*Mucuna pruriens* - seed powder	Human study- RCT	5 g/day orally with milk.	3 months	Sperm concentration and motility significantly improved.
03	*Mucuna pruriens* - seed powder	Human study- RCT	5 g/day orally with milk.	3 months	Sperm concentration and motility significantly improved.
04	*Mucuna pruriens* - both types of seeds (Black and white)	Human study- RCT	5 gm twice/day orally with milk.	30 days	Both types of seeds (Black and white): Erectile function, sexual desire and overall satisfaction improved significantly and orgasmic function improved marginally. Additionally, semen volume, pH, total sperm count and rapid linear progressive sperm increased, while non-progressive and immotile sperm decreased significantly. Overall, black seeds gave better results in comparison to white seeds which was not significant.
04	*Mucuna pruriens* - seed powder and *Withania. Somnifera* - root powder	Human study- RCT	Each 5 g/day orally with milk.	3 months	Sperm concentration and motility significantly improved.[24]
06	*Withania somnifera* - root extract	Human study	675 mg/day in three doses	90 days	Sperm count, semen volume and sperm motility increased.
07	*Withania somnifera* - root powder	Human study	5 g/day orally with a cup of skimmed milk	3 months	Sperm concentration and motility increased in infertile men with normozoospermia who were 'under stress'.
08	*Withania somnifera* - root extract	Human study	5 g/day orally with a cup of milk.	3 months	Semen volume increased in men with normozoospermia and oligozoospermia. Sperm concentration, motility and sperm count per ejaculate increased significantly in men with normozoospermia, oligozoospermia, and asthenozoospermia.
09	*Withania somnifera* - root extract	Charles Foster rats- Arsenic (8 mg/kg for 45 days) induced testicular impairment	100 mg/kg/day orally	30 days	Sperm count and motility improved significantly.
10	*Withania somnifera* - root Extract	Wistar rats	200 mg/kg orally	30 days	Sperm count increased in alcohol-induced testicular impairment; sperm motility improved and sperm morphological abnormality reduced in alcohol-treated rats.[25]
11	*Nigella sativa* - oil	Human	2.5 ml/ day	2 months	Count, mobility, and morphology of sperms, semen volume, pH and the stellar cells improved.
12	*Nigella sativa* - oil	Human	5 ml/ day	2 months	Semen quality including sperm count, morphology and motility and semen volume, pH and round cells in infertile men having abnormal semen parameters improved.
13	*Nigella sativa* - Thymoquinone extract	Adult male rats	25 or 50 mg/ kg daily by oral-gavage	twelve weeks	Ameliorated the testicular tissue by alleviating inflammation and apoptosis; restored the normal balance of sex hormones. (50 mg/kg showed better results).
14	*Nigella sativa* oil	Sprague-Dawley male rats	6μL/100 g body weight		Sperm motility, normal and live sperm and spermatid-sperm width improved; lumen diameter reduced.

15	*Nigella sativa* - oil	Adult male rabbits	5ml/kg body weight/day daily orally	60 days	Weight, length, circumference and volume of testis; testosterone concentration; percentage area of interstitial cells in relation to seminiferous tubules; the thickness of germinal layer, diameter, area; diameter of lumen; spermatogenic cell layer and number of spermatogonia of seminiferous tubules of testes increased. testicular function was stimulated.
16	*Nigella sativa*	Sprague-Dawley rats	200 mg/kg/ daily	1 month	Sperm concentration, motility, percentage of sperm viability, testosterone and luteinizing hormone (LH) concentration improved.[22]

CONCLUSION

According to this case study, seminal fluid analysis revealed a consistent improvement in the sperm parameters following three months of treatment. Sperm volume increased from 1.3 ml to 1.7 ml, sperm concentration rose from 1.3 million/ml to 3 million/ml, overall sperm motility increased from 15% to 24%, progressive motility from 00% to 04%, and non-progressive motility from 15 to 20%. while non-motile sperms decreased from 85% to 76%.

Consequently, herbal remedies such as the powders of *Mucuna pruriens* seed*, Withania somnifera* root*,* and *Nigella sativa* seed can be used to treat male factor infertility. Therefore, it can be stated that the Unani medical system assists in managing male factor infertility by avoiding primary methods of treatment that are expensive and have a number of negative effects despite their inadequate efficacy rates, as well as secondary measures like artificial insemination, IUI, IVF and embryo transfer, intracytoplasmic sperm transfer, and child fostering or adoption that are used in the modern medical system. However, further evaluation and treatment of the couple for infertility is required.

LIMITATION OF THE STUDY

Further research with a larger sample size is necessary to validate these findings.

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CONFLICT OF INTEREST

The authors have no conflicting financial interests.

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