International Journal of Herbal Medicine
Available online at www.florajournal.com

E-ISSN: 2321-2187
P-ISSN: 2394-0514
www.florajournal.com
IJHM 2022; 10(3): 39-49
Received: 12-02-2022
Accepted: 22-03-2022

Mohd. Khursheed Alam
Assistant Professor, Department of Tashreehul Badan, Hayat Unani Medical College & Research Centre, Hayat Complex, Hardoi Road, Sikrori, Kakori, Lucknow, Uttar Pradesh, India

Rais UR Rahman
HOD, Moalejat, A & U Tbbia College, Karol Bagh, New Delhi, India

Nasir Jamal
Assistant Professor, Department of Moalejat, Uttaranchal Unani Medical College & Hospital, Mustafabad (Padartha), Lakshar Road, Haridwar, Uttarakhand, India

Corresponding Author:
Nasir Jamal
Assistant Professor, Department of Moalejat, Uttaranchal Unani Medical College & Hospital, Mustafabad (Padartha), Lakshar Road, Dist- Haridwar, Uttarakhand, India

A clinical study on oligozoospermia and its management with Mucuna Pruriens (Tukhm-e-Kaunch), A randomized controlled trial

Mohd. Khursheed Alam, Rais UR Rahman and Nasir Jamal

Abstract
Oligozoospermia is a decrease in semen concentration below 15 million sperm per milliliter (WHO). There is a defect in sperm production which may be due to surgically treatable causes like varicocele, exposure to thermal or chemical, environmental factors suppressing spermatogenesis, hormonal factors, intrinsic testicular defect or idiopathic cause. It is responsible for 90% of male infertility. In the classical Unani literature, the semen abnormalities are mentioned under the caption of *Qillat-e-Mani* and *Riqqat-e-Mani*. The term '*Qillat*' means deficiency, '*Mani*' means semen and '*Riqqat*' means fluidity. Both these *Qillat* and *Riqqat-e-Mani* are mainly responsible for sexual disorders like *Zof-e-Bah* (Sexual dysfunction), *Surat-e-Anzal* (Premature ejaculation), *Ehtelam* (Nocturnal emission), *Uqr* (Infertility), *Jiryan* (Spermatorrhoea) etc. Decreased quantity of *Huwain-e-Manvia* (spermatozoa) in *Mani* (seminal fluid) is called oligozoospermia i.e., *Qillat-e-Mani* or *Qillat-e-Huwain-e-Manvia*. Unani physicians have been treating this not only to improve numbers of spermatozoa but also other defects of spermatozoa for so long. The causes, aetio-pathogenesis, clinical presentation, line of treatment and management for *Qillat-e-Mani* have been described in detail in almost all the classical Unani text books. This study was aimed to review the concept of *Qillat-e-Mani* (oligozoospermia) in the perspective of Unani system of medicine and to develop & evaluate the safety and efficacy of the Unani single herb, Mucuna pruriens *(Tukhm-e-kaunch)* in the management of Oligozoospermia on scientific parameters.

Keywords: Oligozoospermia, *qillat-e-mani, tukhm-e-kaunch*, mucuna pruriens, unani

1. Introduction
Oilgozoospermia or synonymously oligospermia is a condition in which sperm count gets reduced. WHO describes the condition as the one in which total sperm count is less than 15 million / ml [1]. Male infertility is a multifactorial disease process with a number of potential contributing causes. Male factors contribute to almost 50% cases of infertility; in the remainder, infertility may be due to either a female factor or a combination of male and female factors [2]. Infertility is a common social and psychological stigma for married couples and perhaps one of the tragic problems of marital life. It is estimated that about 10%-15% couples are said to be infertile [3]. The World Health Organization (WHO) defines infertility as the inability to achieve a clinical pregnancy after 12 months or more of having regular unprotected sexual intercourse [4].
For many years, sperm concentrations of less than 20 million sperm/ml were considered low or oligospermic, however, recently, the WHO reassessed sperm criteria and established a lower reference point, less than 15 million sperm/ml [5]. Sperm concentrations fluctuate and oligospermia may be temporary or permanent.
Oligospermia is classified in 3 grades:
- Mild: Sperm counts 10 million – 15 million sperm/mL
- Moderate: Sperm counts 5 million – 10 million sperm/mL
- Severe: Sperm counts less than 5 million sperm/mL [5]

The description of Oligospermia is not traceable in Unani classical literature. The term *Qillate haiwane manwiya* used in Unani Medicine is the literal translation of oligozoospermia, and is described under the caption of *Du'f al-Bah* (anaphrodisia). *Sue Mizaj* of *Alaate mani* (Testes), derangement in *kaifiyate arba* (Physical properties) [8]. excessive *Istifragh* (evacuation), *Sue Mizaj Barid Yabis* (abnormal cold and hot temperament) of testes, *Zoafe Azae Raeesa* (weakness of vital organs), malnutrition, general body weakness, excessive masturbation, excessive sexual intercourse & drug addictions such as opium and cannabis, are the various factors responsible for *Qillat e haiwan e manwia* [6,7,8]. According to Ibne Sina, *mani* (semen) is derived after the completion of '*Hazme chaharum'* (fourth stage of digestion).

He added that *mani* is produced by extremely *lateef dam* [7].
The principle of treatment of *Qillate mani* is *Tadeele mizaj* of Testes (*Alaate mani*), use of *Muqawwi aghziya*, *Muqawwie bah* and *Muwallide mani advia* [6].
In conventional system of medicine, many causes of Oligospermia ranging from varicocele to lifestyle issues e.g., cryptorchidism, varicocele, testicular torsion, Congenital anomalies i.e., Klinefelter's syndrome, Kallmann's syndrome, damaged testes due to trauma or infections like Tuberculosis, Syphilis, Mumps, UTI, filariasis, prostatitis etc. have been described. Liver diseases, Chronic kidney diseses (CKD) chronic smoking, chronic alcoholism, Metabolic & Endocrine disorders, are some of the other causes. Wearing tight under wear, workers at high temperature settings such as mine workers, truck drivers, tailors etc. are the factors responsible for diminished spermatogenesis [9,10,]. Many cases do not have clear cut origin and are referred to as idiopathic which accounts for about 30% of all cases. The process of Spermatogenesis is very sensitive to deviation of temperature, a rise or fall in testicular temperature of only 1–2-degree F may impair sperm production [11].
In conventional system, various drugs like Clomiphene citrate, Tamoxifen and HCG are being used to increase sperm count, however these drugs are expensive and produces several adverse effects like Gynaecomastia, Hepatic carcinoma, Deep vein thrombosis, lowering of HDL and rise in LDL etc [12]. Moreover, efficacy rate of such drugs is also not satisfactory.
In Unani system of medicine, a large number of single as well as compound drugs possessing the Muqawwi-e-bah (aphrodisiac) and Muwalliide mani (Spermatogogue) properties have been described for the treatment of oligospermia. These are time tested, safe, efficacious, and easily available medicines.

2. Materials and Methods

2.1 Place of study
The present study entitled as "A clinical study on Oligozoospermia and its Management with an Unani single herb, a randomized controlled trial" has been conducted in the Department of Moalejat, Ayurvedic and Unani Tibbia College Hospital, Karol Bagh, New Delhi during 2020-2021 session.

2.2 Study design
The present study was designed as a randomized standard controlled clinical trial.

2.3 Randomization
Randomization was done by lottery method. 40 patients were allocated by using lottery method into two groups, comprising 20 patients in each of the test group and control group respectively.

2.4 Sample size
40 Patients were included in the study. 20 Patients in each test and control groups.

2.5 Criteria for the selection of patients
Male patients aged between 18-65 years having history of infertility or oligospermia were enrolled from outpatient Department of Moalejat, Ayurvedic and Unani Tibbia College Hospital, Karol Bagh, New Delhi.

2.5.1 Inclusion criteria
- Patient between age of 18 to 65 years.
- Semen volume >1 ml.
- Patient having sperm count >5 million & <15 million/ml.
- Sperm motility <40%
- Informed volunteers giving written consent.
- Patients willing to participate in study
- Patients ready to discontinue ongoing treatment, if any.

2.5.2 Exclusion criteria
- Patients with any Uro-genital infection and congenital genital anomaly.
- Patients suffering from Hydrocele, Varicocele, Hypogonadism, Endocrine disorders, renal insufficiency, Liver disease & Cardiac disease(s).
- Patient having past history of mumps.
- Patient receiving anti-hyper-lipidemic drug & anti-cancerous therapy.
- Anti-depressant drugs.

2.5.3 Withdrawal criteria:
- Failure to consume the drug.
- Failure to report for follow up.
- Any marked adverse drug reaction or adverse event.

2.6 Duration of study
One and a half years.

2.6.1 Duration of protocol therapy
The treatment period in both test and control groups was fixed as 120 days (4 months).

2.7 Clinical evaluation of disease
The clinical evaluation of the patients for oligozoospermia was done on the following basis as per designed Case Record Form (CRF):
- History taking
- General physical examination
- Examination of genitalia
- Investigations

2.8 Ethical consideration
The proposed study was started after obtaining the approval from Institutional Ethics Committee and getting registered in Clinical Trial Registry of ICMR. Written informed consent to participate in the study was obtained from each patient and study was conducted as per to Good Clinical Practice (G.C.P.) Guidelines.

2.8.1 CTRI No. - CTRI/2020/11/028926
After getting approval from Institutional Ethics Committee, the trial was registered in Clinical trial registry of India.

2.9 Criteria for diagnosis of oligozoospermia
- Diagnosis was made on the basis of history of infertility and semen analysis.

2.10 Procedure
After thorough screening, diagnosed patients of oligozoospermia who fulfil inclusion/ exclusion criteria, were enrolled in the study. Patients were randomly allocated in two groups after making them understand about the study and taking their voluntary informed written consent. Test group had 20 patients and Control group too had the same number of patients. Those falling under test group were given the 50% hydro-alcoholic extract of Unani herb (*Tukhm Kaunch*), with 1 capsule (500mg) twice a day orally and the control group

was given Clomiphene citrate 50 mg once a day orally. Patients were advised to visit for follow up on weekly basis. The data for both the groups was statistically analyzed and compared with each other using appropriate statistical tests. The safety of the test drug was ensured by monitoring the kidney & liver functions and haematological parameters. Unwanted effect of the drug during study was also noticed carefully.

2.11 Justification for selecting Mucuna pruriens

There have been many scientific research papers published supporting the role of Mucunia pruriens in improving sperm count and quality. M. pruriens improves male fertility by its action on the hypothalamus–pituitary–gonadal axis. After the treatment with M. pruriens significant improvement were observed in TSH, LH, dopamine, adrenaline, and nor-adrenaline levels in infertile men and reduced levels of FSH and PRL. The sperm count and motility were significantly recovered in infertile men after treatment not only reactivates the anti-oxidant defense mechanism, but also helps in the management of stress and improves semen quality [21, 22]. M. pruriens and its Major Constituent L-DOPA Recover spermatogenic loss by combating reactive oxygen species (ROS), loss of mitochondrial membrane potential and apoptosis [23, 24]. Mucuna pruriens also enhances libido & sexual performance [25].

2.12 Study drug

2.12.1 Test drug

50% Hydro-alcoholic extract of Tukhm-e-Kauch 500 mg twice a day in capsule form.

2.12.2 Control drug

Clomiphene citrate 50 mg once a day.

2.12.3 Preparation of test drug

The test drug i.e., 50% hydro-alcoholic extract of Tukhm Kaunch (Mucuna pruriens) was procured from Vital Herbs, Uttam Nagar, Delhi-110059 along with their certificate of analysis (C.O.A).

2.12.4 Preparation of control drug

Clofert 50 (Clomiphene citrate 50 mg) of Maneesh pharmaceuticals was used.

2.13 Dosage schedule

The Test group received test drug in the dose of 1 capsule (500mg) orally twice daily with plain water for 120 days.
Control group was treated with Clofert 50 once daily orally for 120 days.

2.14 Follow up

Clinical as well as laboratory evaluation were performed and recorded at the baseline, month 2 and month 4.

2.15 Drug compliance

Compliance with test drug/ control drug was evaluated at each follow up visit by capsule count.

2.16 Assessment of Temperament (Mizaj)

Temperament of each patient was assessed on the basis of ten classical parameters (Ajnas-e-Ashra) as prescribed in Unani Classical literature.

2.17 Assessment of efficacy

To assess the adequacy of treatment of Oligozoospermia on patients in both groups, following objective parameters were used in the study.

2.17.1 Objective parameters

Semen analysis for:
1. Volume
2. Sperm count
3. Sperm motility

2.18 Assessment of safety

To establish the safety of drugs, the following investigations were carried out at baseline, on 10th day and just after termination of treatment.

- **Liver function test:** S.G.O.T, S.G.P.T and Alkaline phosphatase
- **Kidney function test:** Blood urea and Serum creatinine
- **Haemogram:** Hb%, TLC & DLC.

2.19 Adverse event documentation

No adverse reactions were observed during the trial.

2.20 Statistical analysis

After 120 days of the treatment, pre-treatment and post-treatment values of objective parameters in each group were analysed and compared to evaluate the efficacy of the treatment by applying appropriate statistical tests.

3. Observations and Results

3.1 Assessment of efficacy for test group (N=20)

Table 1: Assessment of efficacy for test group (N=20)

Parameters	0 day	30th day	120th day
Semen volume	1.36±0.38	1.665 ± 0.57	2.36 ± 0.57
Sperm count	9.6±2.76	13.12 ± 5.55	21.55 ± 11.6
Sperm motility	23.85±7.22	31.15 ± 10.8	40.1 ± 13.28

*Values with plus/minus signs are expressed as Means ± S.D.

3.2 Assessment of efficacy for control group (N=20)

Table 2: Assessment of efficacy for control group (N=20)

Parameters	0 day	30th day	120th day
Semen volume	1.32±0.35	1.705 ± 0.46	2.16 ± 0.49
Sperm count	8.55±2.53	11.4 ± 4.488	15.77 ± 5.73
Sperm motility	18.05±6.95	23.95 ± 12.26	30.5 ± 13.004

*Values with plus/minus signs are expressed as Means ± S.D.

3.3 Effect of trial drugs on semen volume

In test group, the mean values of semen volume increased insignificantly from 1.36±0.38at the baseline to 1.66 ± 0.57on 30th day, and 2.36 ± 0.57 at the termination of study (t=1.517; $p > 0.05$). While in control group, the mean values of semen volume increased significantly from 1.32±0.35on 0 day to 1.70 ± 0.46on 30th day and 2.16 ± 0.49 at the end of therapy (t=2.065; $p < 0.05$). On applying unpaired t test in both the groups, no significant difference between the mean semen volume of both groups is found (t=1.24; $p > 0.05$).

Table 3: Effect of trial drugs on semen volume

Semen volume	(Mean ± S.D.) mg/dL			t value	p value	Statistical result
	0 day	30th day	120th day			
Test drug	1.36±0.38	1.66 ± 0.57	2.36 ± 0.57	1.517	>0.15	Insignificant
Control drug	1.32±0.35	1.70 ± 0.46	2.16 ± 0.49	2.065	<0.05	Significant

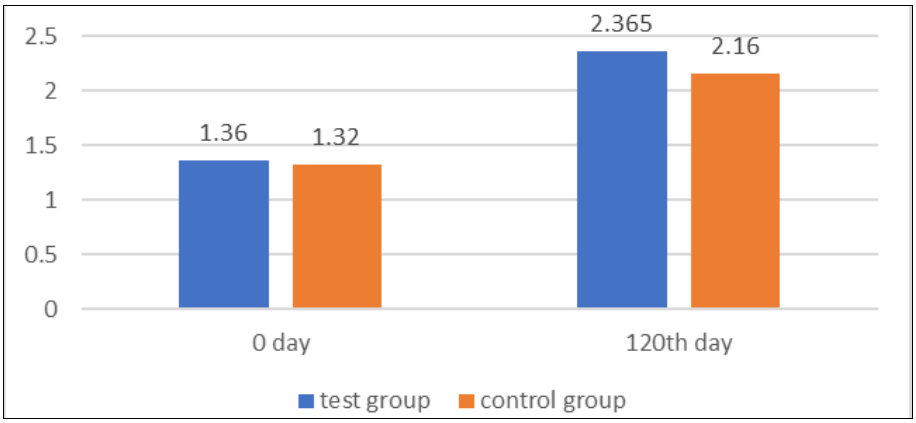

Fig 1: Effect of trial drugs on semen volume

3.4 Effects of trial drugs on sperm count

In test group, the mean values of sperm count increased extremely significantly from 9.6±2.76 at the baseline to 13.12 ± 5.55 on 30th day, and 21.55 ± 11.6 at the termination of study (t=5.718; *p*<0.001). While in control group, the mean values of sperm count increased extremely significantly from 8.55±2.53 on 0 day to 11.4 ± 4.488 on 30th day and 15.77 ± 5.73 at the end of therapy (t=6.291; *p* <0.001). On applying unpaired t test in both the groups, significant difference between the mean sperm count of both groups is found (t=2.028; *p*< 0.05).

Table 4: Effects of trial drugs on sperm count

Sperm count	(Mean ± S.D.) mg/dL			t value	p value	Statistical result
	0 day	30th day	120th day			
Test drug	9.6±2.76	13.12 ± 5.55	21.55 ± 11.6	5.718	<0.001	Extremely significant
Control drug	8.55±2.53	11.4 ± 4.488	15.77 ± 5.73	6.291	<0.001	Extremely significant

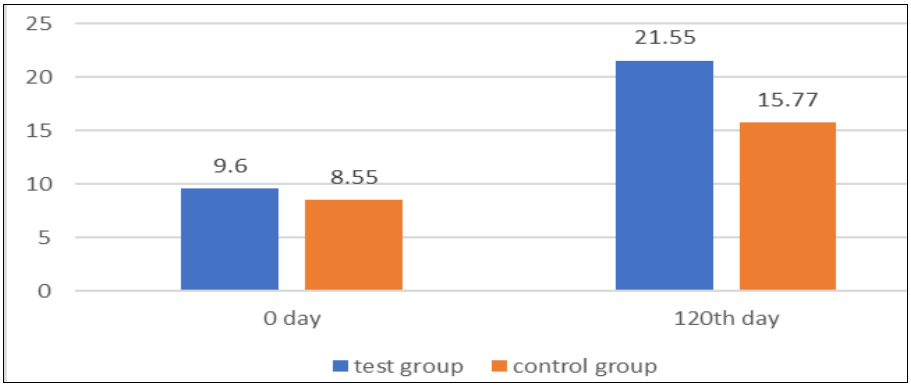

Fig 2: Effect of trial drugs on sperm count

3.5 Effect of test and control drugs on sperm motility

In test group, the mean values of sperm motility increased highly significantly from 23.85±7.22 at the baseline to 31.15 ± 10.8 on 30th day, and 40.1 ± 13.28 at the termination of study (t=2.047; *p*<0.05). While in control group, the mean values of sperm motility increased extremely significantly from 18.05±6.95 on 0 day to 23.95 ± 12.26 on 30th day and 30.5 ± 13.004 at the end of therapy (t=5.573; *p* <0.001). On applying unpaired t test in both the groups, significant difference between the mean sperm motility of both groups is found (t=2.35; *p*< 0.05).

Table 5: Effect of test and control drugs on sperm motility

Sperm motility	(Mean ± S.D.) mg/Dl			t value	p value	Statistical result
	0 day	30th day	120th day			
Test drug	23.85±7.22	31.15 ± 10.8	40.1 ± 13.28	2.047	<0.05	Highly significant
Control drug	18.05±6.95	23.95 ± 12.26	30.5 ± 13.004	5.573	<0.001	Extremely significant

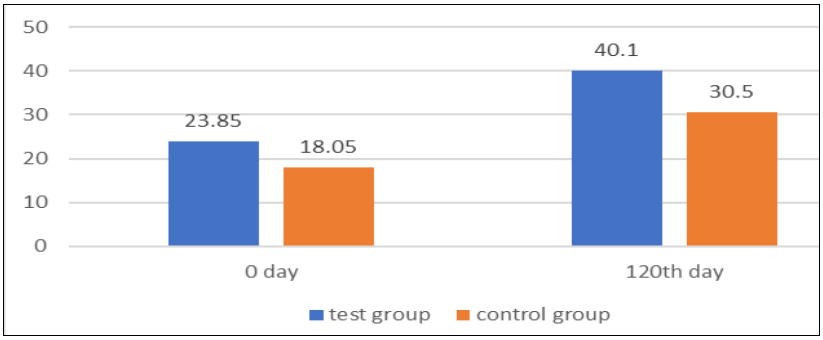

Fig 3: Effect of trial drugs on sperm motility

3.6 Intergroup comparison of test group vs control group on semen volume

Table 6: Intergroup comparison of test group vs control group on semen volume

Semen volume (Mean ± S.D.)	Test Group	Control Group
0 day	1.36±0.38	1.32±0.35
30th day	1.66±0.418	1.705±0.463
120th day	2.365±0.572	2.16±0.493
t value	1.24	
p value	>0.05	
Statistical result	Insignificant	

3.7 Intergroup comparison of test group vs control group on sperm count

Table 7: Intergroup comparison of test group vs control group on sperm count

Sperm count (Mean ± S.D.)	Test Group	Control Group
0 day	9.6 ± 2.76	8.55 ± 2.53
30th day	13.125 ± 5.553	11.4 ± 4.48
120th day	21.55± 11.67	15.77 ± 5.73
t value	2.028	
p value	<0.05	
Statistical result	Significant	

3.8 Intergroup comparison of test group vs control group on sperm motility

Table 8: Intergroup comparison of test group vs control group on sperm motility

Sperm Motility (Mean ± S.D.)	Test Group	Control Group
0 day	23.85 ± 7.22	18.05 ± 6.95
30th day	31.15 ± 10.88	23.95 ± 12.26
120th day	40.1 ± 13.28	30.5 ± 13.004
t value	2.35	
p value	<0.05	
Statistical result	Significant	

3.9 Safety assessment in test group (N=20)

Table 9: Safety assessment in test group (N=20)

Parameters		Assessments		
		0 Day	10th Day	120th Day
Heamoglobin		13.67±0.88	13.87±0.81	14.19±0.45
RBC		4.46±0.17	4.53±0.211	4.61±0.16
TLC		8630±1101.24	8580±765.43	7655±696.96
DLC	Neutrophils	74.27±2.65	73.32±2.54	71.14±3.41
	Lymphocytes	24.38±2.27	25.36±2.71	27.38± 2.39
	Eosinophils	0.83±0.65	0.61±0.44	1.07±0.46
	Monocytes	0.89±0.69	0.61±0.44	1.02±0.51
LFT	SGOT	22.89±2.07	23.29±3.28	22.92±3.22
	SGPT	28.86±1.99	27.81±2.69	26.44±3.88
	S. Alk.Phos.	100.71±10.44	102.15±7.81	99.65±4.70
KFT	B. Urea	22.51±2.50	23.95±3.51	21.51±2.90
	S. Creatinine	0.9±0.09	0.85±0.19	0.84±0.19

*Values with plus/minus signs are expressed as Means ± S.D.

3.10 Safety assessment in control group (N=20)

Table 10: Safety assessment in control group (N=20)

Parameters		Assessments		
		0 Day	10th Day	120th Day
Heamoglobin		13.43±0.98	13.54±0.64	13.87±0.68
RBC		4.49±0.10	4.47±0.18	4.65±0.17
TLC		8590±792.66	86705±839.23	7720± 713.47
DLC	Neutrophils	74±3.16	74.07±2.41	71.27±2.77
	Lymphocytes	26.92±10.30	26.7±10.08	27.16±2.48
	Eosinophils	0.66±0.54	0.84±0.64	1.16±0.64
	Monocytes	0.66±0.55	0.83±0.56	1.23±0.72
LFT	SGOT	22.78±2.34	23.03±2.70	23.18± 4.46
	SGPT	29.01±2.12	27.43±3.08	25.08±3.12
	S. Alk.Phos.	105.85±5.88	104.25±6.53	99.9±7.46
KFT	B. Urea	22.8±3.28	21.6±1.78	21.15±4.18
	S. Creatinine	0.89±0.09	0.91±0.05	0.86±0.11

*Values with plus/minus signs are expressed as Means ± S.D.

3.11 Effect on haemoglobin in both groups

In the test group the mean haemoglobin values observed were 13.67±0.88 at the baseline, 13.87±0.81 on 10th day and 14.19±0.45 on 42nd day. There was no significant change in hemoglobin in test group (t=0.0125; *p*> 0.05). The mean hemoglobin recorded in control group was 13.43±0.98 on 0 day, 13.54±0.64 on 10th day and 13.87±0.68 at the termination of therapy. There was also no significant change in hemoglobin in control group (t=0.077; *p*>0.05).

Table 11: Effect on haemoglobin in both groups

Hemoglobin gm.%	Mean ± S.D.			t value	p value	Statistical result
	O day	10th day	120th day			
Test Group	13.67±0.88	13.87±0.81	14.19±0.45	0.0125	>0.05	Insignificant
Control Group	13.43±0.98	13.54±0.64	13.87±0.68	0.077	>0.05	Insignificant

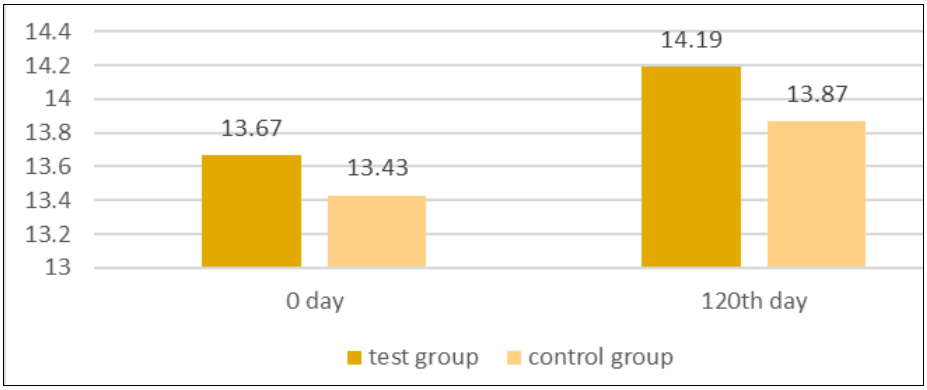

Fig 4: Effect of trial drugs on hemoglobin

3.12 Effects on T.L.C on both groups

The mean T.L.C in test group was 8630±1101.24on 0 day, 8580±765.43 on 10th day and 7655±696.96 on 120th day. On applying paired t test, this difference was found to be insignificant statistically (t=0.00012; *p*>0.05). In control group, the mean T.L.C recorded was 8590±792.66 at the baseline, 86705±839.23on 10th day and 7720±713.47 at the termination of study. The difference in mean value turned out to be statistically insignificant after application of paired t test (t=0.0009; *p* >0.05).

Table 12: Effects on T.L.C on both groups

T.L.C.	Mean ± S.D.			t value	p value	Statistical result
	O day	10th day	120th day			
Test Group	8630±1101.24	8580±765.43	7655±696.96	0.00012	>0.05	Insignificant
Control Group	8590±792.66	86705±839.23	7720±713.47	0.0009	>0.05	Insignificant

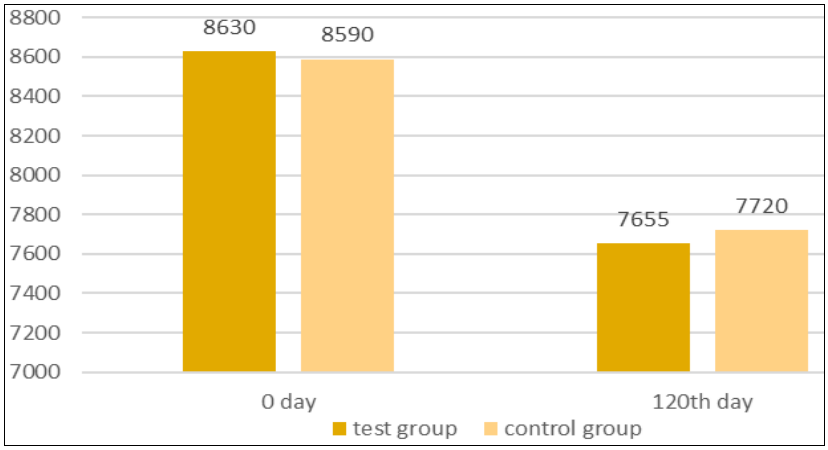

Fig 5: Effect of trial drugs on TLC

3.13 Effects on D.L.C on both groups

Table 13: Effects on D.L.C on both groups

D.L.C		Test Group	Control Group
Neutrophils (Mean ± S.D.)	0 day	74.27 ± 2.65	74 ± 3.16
	10th day	73.32 ± 2.54	74.07 ± 2.41
	120th day	71.14 ± 3.41	71.27 ± 2.77
t value		0.0014	0.0069
p value		>0.10	>0.10
Statistical result		Insignificant	Insignificant
Lymphocytes (Mean ± S.D.)	0 day	24.38 ± 2.27	26.92 ± 10.30
	10th day	25.36 ± 2.71	26.7 ± 10.08
	120th day	27.38 ± 2.39	27.16 ± 2.48
t value		0.00047	0.45
p value		>0.10	>0.10
Statistical result		Insignificant	Insignificant
Monocytes (Mean ± S.D.)	0 day	0.89 ± 0.69	0.66 ± 0.55
	10th day	0.61 ± 0.44	0.83 ± 0.56
	120th day	1.02 ± 0.51	1.23 ± 0.72
t value		0.221	0.00203
p value		>0.10	>0.10
Statistical result		Insignificant	Insignificant
Eosinophils (Mean ± S.D.)	0 day	0.83 ± 0.65	0.66 ± 0.54
	10th day	0.61 ± 0.44	0.84 ± 0.64
	120th day	1.07 ± 0.46	1.16 ± 0.64
t value		0.06	0.00052
p value		>0.10	>0.10
Statistical result		Insignificant	Insignificant

3.14 Effect on LFT in both groups

Table 14: Effect on LFT in both groups

L.F.T.		Test Group	Control Group
S.G.O.T (Mean ± S.D.)	0 day	22.89 ± 2.07	22.78 ± 2.34
	10th day	23.29 ± 3.28	23.03± 2.70
	120th day	22.92 ± 3.22	23.18 ± 4.46
t value		0.485	0.34
p value		>0.05	>0.05
Statistical result		Insignificant	Insignificant
S.G.P.T (Mean ± S.D.)	0 day	28.86 ± 1.99	29.01 ± 2.12
	10th day	27.81 ± 2.69	27.43 ± 3.08
	120th day	26.44 ± 3.88	25.08 ± 3.12
t value		0.0181	4.47
p value		>0.05	<0.001
Statistical result		Insignificant	significant
Alkaline Phosphatase (Mean ± S.D.)	0 day	100.71 ± 10.44	105.85 ± 5.88
	10th day	102.15 ± 7.81	104.25 ± 6.53
	120th day	99.65 ± 4.70	99.9 ± 7.46
t value		0.338	0.0045
p value		>0.05	>0.05
Statistical result		Insignificant	Insignificant

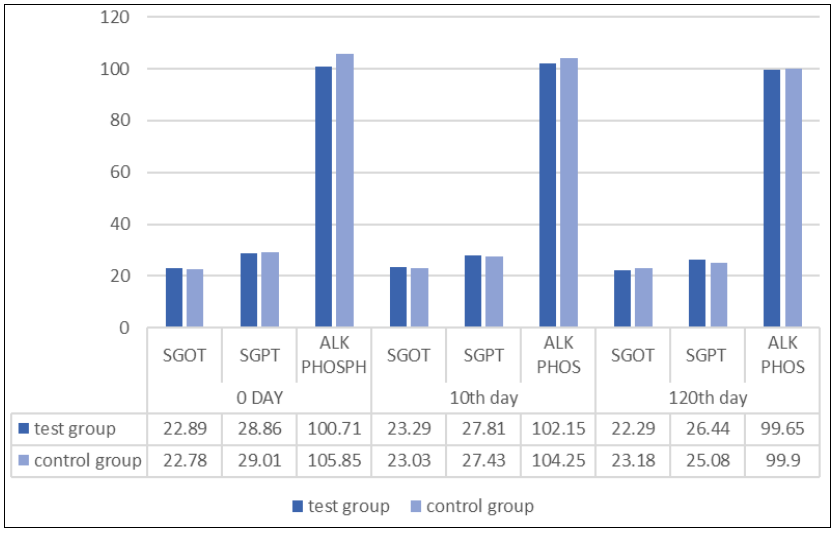

Fig 6: Effect of trial drug on LFT

3.15 Effects on K.F.T in both groups

Table 15: Effects on K.F.T in both groups

K.F.T.		Test Group	Control Group
S. Creatinine (Mean ± S.D.)	0 day	0.90 ± 0.09	0.89 ± 0.09
	10th day	0.85 ± 0.19	0.91 ± 0.05
	120th day	0.84 ± 0.19	0.86 ± 0.11
t value		0.12	0.14
p value		>0.10	>0.05
Statistical result		Insignificant	Insignificant
B. Urea (Mean ± S.D.)	0 day	22.51 ± 2.5	22.8 ± 3.28
	10th day	23.95 ± 3.51	21.6 ± 1.78
	120th day	21.51 ± 2.90	21.15 ± 4.18
t value		0.135	0.113
p value		>0.05	>0.05
Statistical result		Insignificant	Insignificant

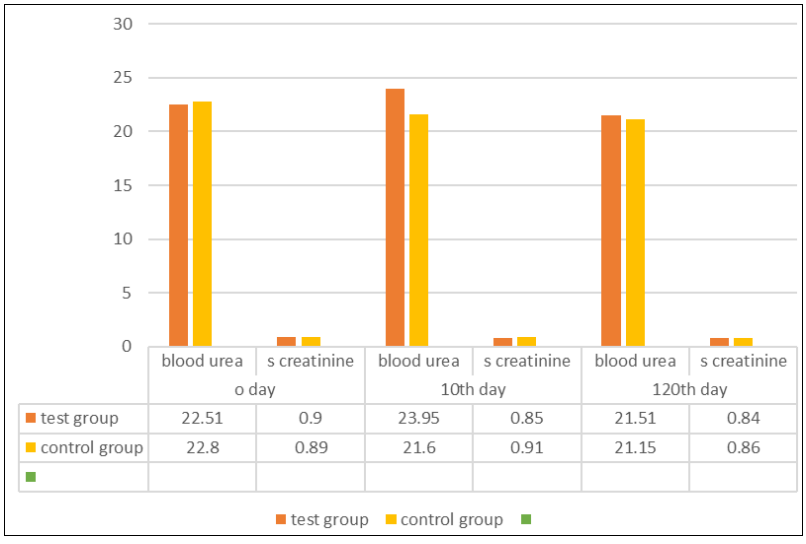

Fig 7: Effect of trial drugs on KFT

Discussion

In our Present Clinical Study following demographic observations were found:

- The higher incidence of oligozoospermia was observed in the age group of 26-35 years (65%).
- More patients were from Islam religion 25 (62.5%).
- In this study, 35 (85%) patients were from non-veg group.
- During the trial, it was observed that 7 cases were tailors, 7 cases belonged to business class, 12 cases belonged to Service class, 3 cases were driver and 11 cases belonged to other classes.
- There is higher incidence of Patients from Balghami 14 (35%) and Safravi group 13 (32.5% each).
- In the present study, 3 (7.5%) patients had history of Alcohol intake, 7 (17.5%) cases were smokers, 5 (12.5%) patients had a history of tobacco intake and 25 (62.5%) cases were non-alcoholic.

In the present study the effects of Unani test drug have been observed on all the components of semen analysis in a randomized controlled manner and safety of the drug has also been established.

The test drug (50% hydro-alcoholic extract of Mucuna pruriens) in the dose of one capsule of 500mg twice daily was found significantly efficacious in increasing sperm count and sperm motility.

4.1 Efficacy assessment

4.1.1 Semen volume

In test group, the mean values of semen volume increased insignificantly from 1.36±0.38at the baseline to 1.66 ± 0.57on 30th day, and 2.36 ± 0.57 at the termination of study (t=1.517; $p > 0.05$). While in control group, the mean values of semen volume increased significantly from 1.32±0.35on 0 day to 1.70 ± 0.46on 30th day and 2.16 ± 0.49 at the end of therapy (t=2.065; $p < 0.05$). On applying unpaired t test in both the groups, no significant difference between the mean serum semen volume of both groups is found (t=1.24; $p > 0.05$).

4.1.2 Sperm count

In test group, the mean values of sperm count increased extremely significantly from 9.6±2.76 at the baseline to 13.12 ± 5.55 on 30th day, and 21.55 ± 11.6 at the termination of study (t=5.718; $p<0.001$). While in control group, the mean values of semen volume increased extremely significantly from 8.55±2.53 on 0 day to 11.4 ± 4.488 on 30th day and 15.77 ± 5.73 at the end of therapy (t=6.291; $p < 0.001$). On applying unpaired t test in both the groups, significant difference between the mean sperm count of both groups is found (t=2.028; $p< 0.05$). Thus, test drug turned out to be more effective in increasing the sperm count.

4.1.3 Sperm motility

In test group, the mean values of sperm motility increased highly significantly from 23.85±7.22 at the baseline to 31.15 ± 10.8 on 30th day, and 40.1 ± 13.28 at the termination of study (t=2.047; $p<0.05$). While in control group, the mean values of sperm motility increased extremely significantly from 18.05±6.95 on 0 day to 23.95 ± 12.26 on 30th day and 30.5 ± 13.004 at the end of therapy (t=5.573; $p < 0.001$). On applying unpaired t test in both the groups, significant difference between the mean sperm motility of both groups is found (t=2.35; $p< 0.05$).

4.2 Safety assessment

4.2.1 Haemoglobin

In the test group the mean haemoglobin values observed were 13.67±0.88 at the baseline, 13.87±0.81 on 10th day and 14.19±0.45 on 42nd day. There was no significant change in hemoglobin in test group (t=0.0125; $p> 0.05$). The mean hemoglobin recorded in control group was 13.43±0.98 on 0 day, 13.54±0.64 on 10th day and 13.87±0.68 at the termination of therapy. There was also no significant change in hemoglobin in control group (t=0.077; $p>0.05$).

4.2.2 Total Leukocyte count (T.L.C)

The mean T.L.C in test group was 8630±1101.24on 0 day, 8580±765.43 on 10th day and 7655±696.96 on 120th day. On applying paired t test, this difference was found to be insignificant statistically (t=0.00012; $p>0.05$). In control group, the mean T.L.C recorded was 8590±792.66 at the baseline, 86705±839.23on 10th day and 7720±713.47 at the termination of study. The difference in mean value turned out to be statistically insignificant after application of paired t test (t=0.0009; $p >0.05$).

4.1.2 Differential Leukocyte count (D.L.C)

1) **Neutrophils:** The mean neutrophils in test group were 74.27 ± 2.65 on 0 day, 73.32 ± 2.54 on 10th day and 71.14 ± 3.41 on 120th day. On applying paired t test, this difference was found to be insignificant statistically (t=0.0014; $p>0.10$). In control group, the mean neutrophils recorded were 74 ± 3.16 at the baseline, 74.07 ± 2.41 on 10th day and 71.27 ± 2.77 at the termination of study. The difference in mean value turned out to be statistically insignificant after application of paired t test (t=0.0069; $p >0.10$).
2) **Lymphocytes:** The mean lymphocytes in test group were 24.38 ± 2.27 on 0 day, 25.36 ± 2.71 on 10th day and 27.38 ± 2.39 on 120th day. On applying paired t test, this difference was found to be insignificant statistically (t=0.00047 $p>0.10$). In control group, the mean lymphocytes recorded were 26.92 ± 10.30 at the baseline, 26.7 ± 10.08 on 10th day and 27.16 ± 2.48 at the termination of study. The difference in mean value turned out to be statistically insignificant after application of paired t test (t=0.45; $p >0.10$).
3) **Monocytes:** The mean Monocytes in test group were 0.89 ± 0.69 on 0 day, 0.61 ± 0.44 on 10th day and 1.02 ± 0.51on 120th day. On applying paired t test, this difference was found to be insignificant statistically (t=0.221; $p>0.10$). In control group, the mean monocytes recorded were 0.66 ± 0.55 at the baseline, 0.83 ± 0.56 on 10th day and 1.23 ± 0.72 at the termination of study. The difference in mean value turned out to be statistically insignificant after application of paired t test (t=0.00203; $p >0.10$).
4) **Eosinophils:** The mean eosinophils in test group were 0.83 ± 0.65 on 0 day, 0.61 ± 0.44 on 10th day and 1.07 ± 0.46 on 120th day. On applying paired t test, this difference was found to be insignificant statistically (t=0.06; $p>0.10$). In control group, the mean eosinophils recorded were 0.66 ± 0.54 at the baseline, 0.84 ± 0.64 on 10th day and 1.16 ± 0.64 at the termination of study. The difference in mean value turned out to be statistically insignificant after application of paired t test (t=0.00052; $p >0.10$).

4.2.4 LFT

1) **S.G.O.T:** The mean S.G.O.T in test group was 22.89 ± 2.07 on 0 day, 23.29 ± 3.28 on 10th day and 22.92 ± 3.22 on 120th day. On applying paired t test, this difference was found to be insignificant statistically (t=0.485; $p>0.05$). In control group, the mean S.G.O.T recorded was 22.78 ± 2.34 at the baseline, 23.03 ± 2.70 on 10th day and 23.18 ± 4.46 at the termination of study. The difference in mean value turned out to be statistically insignificant after application of paired t test (t=0.34; $p >0.05$).
2) **S.G.P.T:** The mean S.G.P.T in test group was 28.86± 1.99 on 0 day, 27.81 ± 2.69 on 10th day and 26.44 ± 3.88 on 120th day. On applying paired t test, this difference was found to be insignificant statistically (t=0.181; $p>0.05$). In control group, the mean S.G.P.T recorded was 29.01 ± 2.12 at the baseline, 27.43 ± 3.08 on 10th day and 25.08 ± 3.12 at the termination of study. The difference in mean value turned out to be statistically

significant after application of paired t test (t=4.47; *p* >0.001).

3) **Alkaline phosphatase:** The mean value of alkaline phosphatase in test group was 100.71 ± 10.44 on 0 day, 102.15 ± 7.81 on 10th day and 99.65 ± 4.7 on 120th day. On applying paired t test, this difference was found to be insignificant statistically (t=0.338; *p*>0.05). In control group, the mean alkaline phosphatase recorded was 105.85 ± 5.88 at the baseline, 104.25 ± 6.53 on 10th day and 99.9 ± 7.46 at the termination of study. The difference in mean value turned out to be statistically insignificant after application of paired t test (t=0.0045; *p* >0.05).

4.2.5 KFT

1) **Serum creatinine:** The mean serum creatinine in test group was 0.90 ± 0.09 on 0 day, 0.85± 0.19 on 10th day and 0.84 ± 0.19 on 120th day. On applying paired t test, this difference was found to be insignificant statistically (t=0.12; *p*>0.05). In control group, the mean serum creatinine recorded was 0.89 ± 0.09 at the baseline, 0.91 ± 0.05 on 10th day and 0.86 ± 0.11 at the termination of study. The difference in mean value turned out to be statistically insignificant after application of paired t test (t=0.14; *p* >0.05).
2) **Blood urea:** The mean blood urea in test group was 22.51 ± 2.5 on 0 day, 23.95 ± 3.51 on 10th day and 21.51 ± 2.90 on 120th day. On applying paired t test, this difference was found to be insignificant statistically (t=0.135; *p*>0.05). In control group, the mean blood urea recorded was 22.8 ± 3.28 at the baseline, 21.6 ± 1.78 on 10th day and 21.15 ± 4.18 at the termination of study. The difference in mean value turned out to be statistically insignificant after application of paired t test (t=0.113; *p* >0.05).

In assessing the safety and tolerability of drug in both the groups, L.F.T., K.F.T., haemoglobin and T.L.C. were assessed & statistically analysed and yielded insignificant results. Hence, it can be stated that the both test and control drugs are neither hepatotoxic, nephrotoxic nor has haematological / bone marrow toxicity.

4.3 Adverse effects

- No adverse effects were observed in both groups during the period of the clinical trial.

2. Summary

All the safety assessment measures were recorded at the baseline, on 10th day and after completion of study. All the efficacy assessment measures were recorded on all the follow ups. The data collected through laboratory investigations was statistically analyzed.

5.1 Demographic parameters

In our study, most of the patients were from age group of 26-35 years, Balghami & Safravi mizaj, non-addicted, non-vegetarian, belonging to service class, leading stressful life, and over indulged in masturbation. These findings are in accordance with description in Unani ancient books in which Unani scholars wrote that Riqqat E-Mani wa Qillat E mani may be due to over indulgence of masturbation, poor diet, stress and strain.

5.2 Semen volume

In test group, percentage increase in semen volume observed was 18.1% on 30th day and 42.4% on 120th day. While in control group, increment in semen volume observed was 22.4% on 30th day and 38.9% at the end of treatment.

5.3 Sperm count

In test group, percentage increase in sperm count observed was 27.3% on 30th day and 55.5% on 120th day. While in control group, increment in sperm count observed was 25% on 30th day and 45.8% at the end of treatment.

5.4 Sperm motility

In test group, percentage increase in sperm motility observed was 23.5% on 30th day and 40.6% on 120th day. While in control group, increment in sperm motility observed was 24.7% on 30th day and 40.9% at the end of treatment.

The formulation was well tolerated and not a single patient reported any adverse effect during trial.

In view of the above, it may be concluded that the test drug used in this study was found very effective in the management of oligozoospermia. During the period of study 3 patients of test group reported that their wives have conceived in the course of the treatment.

6. Conclusion

The results of this study can be concluded as under

- The Unani medicine increased sperm count and sperm motility more effectively than control drug the sperm count in this group came into the normal range i.e., >21 million (as per the guideline of WHO) while in control group it remained around 15 million.
- The Unani test drug was well tolerated and no adverse/side effects were observed during the entire period of protocol therapy.
- In view of the data in terms of safety and efficacy generated from this study, the 50% hydro-alcoholic extract of Mucuna pruriens 500 mg can safely be used in the treatment of oligozoospermia.

7. Acknowledgment

The article is recuperated from MD thesis of Dr. Mohd. Khursheed Alam under the supervision of Dr Rais ur Rahman, Head, Department of Moalejat, A & U Tibbia College, Karol Bagh, New Delhi, India.

8. Conflicts of interest

The corresponding author declares that there is no conflict of interest on behalf of other authors.

9. Funding

There was no funding from any organization for the conduct of this study or the preparation of this manuscript.

10. References

1. Hiralal Konar, Dutta DC. Textbook of Gynecology, Calcutta, New Central book agency, 2nd edition, 1994, 215pp.
2. Gopalkrishan K, Meherji PK, Juneja HS. Research in infertility, Indian Council Med. Res. Bull, 1996, 97-105pp.
3. Sengupta Sree Bijoy, Dutta DC, Chattopadhyay K Sisir. Gynecology for postgraduates and practitioners, Churchill livingstone, 1st edition, 1998, 59pp.
4. World Health Organization. Recent advances in medically assisted conception technical report series no. 820. New York: Cambridge University Press, 1995.
5. Cooper TG, Noonan E, von Eckardstein S, *et al*. World Health Organization reference values for human semen

characteristics. Hum. Reprod. Update. 2010;16(3):231-45.
6. Kabeeruddin M, Al Akseer, Ejaz Publishing House, Darya Ganj New Delhi. 2003;2:1255-1257.
7. Ibn Sina, Al Qanoon fil'tib (UrduTranslation), Idara Kitabus Shifa. 2007;(3):255-262.
8. Majusi Ibn Abbas, Kamilus Sanna, Urdu Translation by Kantoori Gulam Hussain, Idara Kitabus Shifa. 2010;479:531.
9. Bhasker Rao K, Chowdhury NN, Clinical Gynecology: Orient Longman Ltd. 4th edition, 1999, 145.
10. Cavallini G, Male Idiopathic Oligo-asthenozoospermia, Asian Journal of Andrology, 2006, 143-157.
11. Tripathi KD, Essentials of medical pharmacology, Jaypee publishers New Delhi, 6th edition. 2006;291:304-305.
12. Najmul Ghani, Khazainul-advia, Idara Kitabul Shifa, New Delhi, 1208-1209, 1248-1249.
13. Ombelet W, *et al*. Sperm morphology assessment: historical review in relation to fertility, Human Reproduction Update. 1995;1(6):543-557.
14. Cobb M. An Amazing 10 Years: The Discovery of Egg and Sperm in the 17th Century, Reprod Dom Anim. 2012;47(4):2-6.
15. Jenniffer Puerta Suárez, *et al*. Spermatozoa: A Historical Perspective, International Journal of Fertility and Sterility. 2018;12(3):182-190.
16. Michael K Skinner. Historic Considerations in Male Reproduction, Elsevier, 2018, 3-5.
17. Trevor G Cooper, *et al*. World Health Organization reference values for human semen characteristics, Human Reproduction Update. 2010;16(3):231-245.
18. Edwards Robert G, Brody Steven A. Principal and Practice of Assisted Human reproduction, Saunders 1/e, 1995.
19. Joshi Ravi Bankatlal, *et al*. Management of Oligospermia and Azoospermia through Ayurveda. IJAAR. 2017;2(11):1628.
20. Naina Kumar, *et al*. Prevalence of Male Factor Infertility in Last Ten Years at a Rural Tertiary Care Centre of Central India: A Retrospective Analysis. Indian Journal of Obstetrics and Gynaecology Research. 2015;2(3):132-136.
21. Mallika Kawatra, *et al*. Environmental and occupational factors leading to oligospermia: A pilot study. Indian Journal of Basic and Applied Medical Research. 2014;3(2):528-534.
22. Mohammad Reza Hafezi Ahmadi, *et al*. Prevalence and Risk Factors of Oligospermia in Infertile Men, Journal of Clinical and Diagnostic Research. 2014;8(9):FC11-FC13.
23. Sekar S, Elumalai P, Seppan P. Dose- and time-dependent effects of ethanolic extract of Mucunapruriens Linn. Seed on sexual behaviour of normal male rats. J Ethnopharmacol. 2009;122:497-501.
24. Natarajan K, Narayan N, Ravichandran N. Review on Mucuna- The wonder plant, Int J Pharm Sxi Rev Res. 2012;17(1):86-93.
25. Hakeem Mohd Abdul Hakeem, Bustanul Mufradat, Idara Kitab ul Shifa, New Delhi, 235.