Research Article

A Non Randomized, Open-Label, Non Comparative, Prospective Study To Investigate The Efficacy Of A Herbal Preparation (Super Active) In The Treatment of Oligospermia, Erectile Dysfunction, Premature Ejaculation and Loss of Libido

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and
Microdose Lifescience (SMO), 6D Krishnaram Bose Street,
Kolkata – 700 004, India.

1. Study Synopsis

<table>
<tr><td>Name of Sponsor/Company:
Pitrashish Marketing Enterprises Pvt. Ltd.,
GA- 126 Rajdanga Main Road,
Kolkata – 700 107</td><td>Name of Investigational Product:

Super Active Capsule (500mg)</td><td>Name of Active Ingredients: (in 500 mg)
1. Gingseng 65 mg
2. Ashwagandha 85 mg
3. Shilajit 75 mg
4. Safed Musali 35 mg
5. Akarkara 40 mg
6. Vidarikhand 50 mg
7. Shatavari 50 mg
8. Kounch 50 mg
9. Salam Panja 50 mg</td></tr>
<tr><td colspan="3">Title of Study: A non randomized, open-label, non comparative, prospective clinical study to investigate the efficacy of Super Active Capsule in the treatment of Oligospermia & Erectile dysfunction as adjuvant therapy.</td></tr>
<tr><td colspan="3">SMO: MICRODOSE LIFESCIENCE, KOLKATA.</td></tr>
<tr><td colspan="3">Study Period: From 1st May 2017 to 15th July 2017</td></tr>
<tr><td colspan="3">Objectives: To evaluate safety and efficacy of Super Active Capsule in the treatment of Oligospermia, Erectile Dysfunction, Premature Ejaculation And Loss Of Libido as adjuvant therapy.</td></tr>
<tr><td colspan="3">Methodology: This is a non randomized, open-label, non comparative, prospective study to investigate the efficacy of Super Active Capsule in the treatment of Oligospermia, Erectile Dysfunction, Premature Ejaculation and Loss Of Libido. Subjects were evaluated at screening/enrolment, and at the end of treatment. Patients were treated with 1 capsule of Super Active 2 times per day for a period of 60 days.</td></tr>
<tr><td colspan="3">Number of Patients: 20</td></tr>
<tr><td colspan="3">Diagnosis and Main Criteria for Inclusion:
1. Male outpatients aged 25 to 50 years
2. Patients with Oligospermia, Erectile Dysfunction, Premature Ejaculation and Loss Of Libido.
3. The patient will take his regular medicines, if any, along with this adjuvant therapy.
4. Patients ready to give written informed consent and willing to comply with the study protocol.</td></tr>
<tr><td colspan="3">Test Product: Super Active Capsule (500 mg)
Dose & Mode of Administration: 1 Capsule of Super Active (500 mg) 2 times per day for a period of 60 days.</td></tr>
<tr><td colspan="3">Duration of Treatment: 60 days</td></tr>
<tr><td colspan="3">Criteria for Evaluation: Efficacy:
Primary Efficacy End Point. To evaluate Sperm Count in patients with Oligospermia.
Secondary Efficacy End Point. To determine the development in Erectile Dysfunction, Premature Ejaculation, General Health & debility assessment by subjective scoring (VAS) and clinical assessment.</td></tr>
<tr><td colspan="3">Criteria for Evaluation: Safety: 1. Adverse Events
2. Overall safety will be assessed by local symptoms of itching, rash or any other allergic reactions.</td></tr>
<tr><td colspan="3">Statistical Methods: Data of efficacy and safety were presented descriptively. Descriptive statistics was used for efficacy end points. Sperm count was examined using baseline demographics and at the end of study. General Health & debility was assessed by subjective scoring (VAS) and clinical assessment.</td></tr>
<tr><td colspan="3">Conclusion: Super Active Capsule has been found to be a safe and effective herbal product as the adjuvant therapy of Oligospermia, Erectile Dysfunction, Premature Ejaculation And Loss Of Libido.</td></tr>
<tr><td colspan="3">Date of Report: 25th July 2017</td></tr>
</table>

1 List of Abbreviations

AE	=	adverse event
CI	=	confidence interval
d	=	days
CRF	=	electronic case report form
GCP	=	Good Clinical Practice
ICF	=	informed consent form
ICH	=	International Conference on Harmonization
IEC	=	Independent Ethics Committee
SAE	=	serious adverse event
SAP	=	statistical analysis plan
SD	=	standard deviation
SOP	=	standard operating procedure
WHO	=	World Health Organization
WMA	=	World Medical Association

2 Ethics

2.1 Independent Ethics Committee

The study was carried out according to the protocol approved by the Sponsor. The study would be conducted in accordance with the "Good Clinical Practices for Clinical Research in India" guidelines and pertinent regulatory requirement.

The investigators would report promptly to the Sponsor new information that may adversely affect the safety of the patients or the conduct of the trial. The investigator would submit written summaries of the trial status to the Sponsor if requested. Upon completion of the trial, the investigator would provide the Sponsor with a brief report of its outcome, if required. The original documents would be sent to the sponsor and the investigator would keep a copy.

2.2 Ethical Conduct of the Study

The study was performed in accordance with the requirements of the International Conference on Harmonization (ICH) guidelines for current Good Clinical Practice (GCP)as well as the demands of national drug and data protection laws and other applicable regulatory requirements.

2.3 Patient Information and Consent

The investigator was responsible for ensuring that no patient enters in the trial before obtaining his written informed consent. Informed Consent means that the person involved is capable to give consent and he is able to exercise free power of choice. It is the explicit acceptance that the individual's data would be known to the investigator(s), sponsor and possibly the regulatory authorities. The consent shall be given in writing after detailed information about the trial and trial medication is provided. Informed written consent will be obtained from each patient in the form provided by the investigator. The patient who refuses to give written informed consent shall not be included in the trial. The investigators will give the patient complete information about the nature, meaning and importance of the study and description of the procedures to be followed by the investigator. They were further given a description of any foreseeable risks and discomforts. Patient will also be told that they have the right to opt out of the trial at any time without having to give reasons if they so wish and without prejudice to further treatment. The patient/guardian will be given sufficient time to consider the implications of the study before deciding whether or not to participate in the trial. The patient and the principal investigator must sign the informed consent form. A copy of the ICF signed by the investigator and subject and/ or LAR and/ or independent witness will be given to the subject. The patient should have legal capacity and be able to comprehend the nature, meaning, importance and risks of the study and to make up his mind accordingly. If the patient is unable to comprehend and understand the necessary information pertaining to his participation in the study, then, an impartial witness (a person, who is independent of the trial and who cannot be influenced by people involved in the trial) would attend the informed consent process and would explain the contents of the informed consent form, in a language understood by the patient.

2.4 Investigators and Study Administrative Structure

2.5 Study Centres

2.6 Administrative Structure

This was a non randomized, Prospective, Open Label, Non-Comparative study in subjects having Oligospermia, Erectile Dysfunction, Premature Ejaculation and Loss Of Libido.

Each patient received treatment for the duration of 60 days. Outpatients (male aged between 10-80 years) who had Oligospermia & Erectile dysfunction were enrolled.

A total of 20 patients were enrolled and analyzed in order to receive the proper data.

3 INTRODUCTION

Use of Herbal preparations are widely used for prevention and treatment of Oligospermia & Erectile dysfunction. There are several preparations available for Oligospermia & Erectile dysfunction. The selection of any herbal preparation depends on its antimicrobial spectrum, minimal risk of irritation and allergenicity. Te following herbs are used to prepare the investigational product

Ginseng

Ginseng herb has a long history of use as an alternative medicine going back over 5,000 years, and appears on several continents. Ginseng root is adaptogen, cardio-tonic, demulcent, sedative, sialagogue, stimulant, tonic and stomachic. Ginseng has been studied over the past 30 years in many countries. Its remarkable ability to help the body to adapt mental and emotional stress, fatigue, heat, cold, and even hunger is confirmed and documented.

The major constituents in Ginseng are Triterpenoid saponins, Ginsenosides (at least 29 have been identified), Acetylenic compounds, Panaxans, and Sesquiterpenes. Taken over an extended period it is used to increase mental and physical performance. A very powerful medicinal herb, it both stimulates and relaxes the nervous system, encourages the secretion of hormones, improves stamina, lowers blood sugar and cholesterol levels and increases resistance to disease. The ginsenosides that produce these effects are very similar to the body's own natural stress hormones. It is used in the treatment of debility associated with old age or illness, lack of appetite, insomnia, stress, shock and chronic illness and also increases immune function, resistance to infection, and supports liver function. It stimulates and increases endocrine activity in the body, promotes a mild increase in metabolic activity and relaxes heart and artery movements. Stimulates the medulla centers and relaxes the central nervous system.

Ginseng's main use in Traditional Chinese Medicine was to enhance sexual function. Modern medical science confirms the effectiveness of this use. In fact, ginseng has several different benefits for sexuality. Though women can also enjoy many benefits of ginseng, the sexual health benefits may be more noticeable in men.

According to recent statistics, there are approximately 48.5 million couples worldwide who want to conceive a child but are suffering from infertility. Almost half the time, infertility between couples is at least partially due to physical problems on the male's side. There are several distinct causes of male infertility, but low sperm quality is a very prominent one. There is solid research, stretching back to the 1970s, showing that Panax ginseng promotes optimal sperm quality. Taking ginseng can also support healthy sperm count, i.e. the concentration of sperm cells in your semen; it can also increase sperm motility, or the sperm cells' ability to travel through your female partner's reproductive tract.

Erectile dysfunction greatly diminishes sexual satisfaction. Ginseng has also shown benefits in this area. In one study, 45 men who suffered from moderate to severe erectile dysfunction showed improvement after taking Panax ginseng for eight weeks. Another similar study involving 60 participants found that men had better erections after taking the herb for 12 weeks. Ginseng may provide these benefits because its active ingredients increase your body's levels of nitric oxide, a chemical that helps blood vessels to expand. Ginseng relaxes the muscles and opens the blood vessels inside the penis, making it easier for blood to fill the Corpus Cavernosum.

Libido is another important component of male sexual function. Studies done on rodents have found that ginseng increases sex drive. This is due to its testosterone-boosting effects; researchers speculate that ginsenosides act like testosterone in the body because their molecules are structurally similar to steroid hormones. The effects of ginseng on libido are also partially due to the herb's influence on neurotransmitters. There is also a small amount of research done on humans.

Taking a supplement containing ginseng to improve sex life or fertility will also come with a range of other benefits. Ginseng promotes a healthy immune response in body as well as a healthy response to stress. It also boosts energy levels. Herbs with these properties are collectively known as adaptogens. Regularly taking an adaptogen supplement like ginseng can help to avoid the common cold and other illnesses. Long-term use may help to avoid inflammatory health conditions like diabetes, asthma and rheumatoid arthritis. Research even suggests that taking ginseng can help to prevent anxiety and depression, two stress-related mental health problems.

Ginseng's benefits for circulation are by no means limited to the genital region. The whole cardiovascular system can benefit from ginseng. The antioxidant effects of ginsenosides can also reduce stress on the cells of blood vessels and heart. Though more research is needed, this implies that taking ginseng could possibly decrease the risk of cardiovascular health problems.

Due to its effects on hormones, ginseng could help prevent osteoporosis, a disease that lowers the bone density, making bones very fragile.

Research shows that ginseng also promotes cognitive health. In one study, researchers gave 97 volunteers either Panax ginseng powder or a placebo for a period of 12 weeks. The scientists tested the participants' cognitive function during and after the 12-week course. The group that received real

ginseng powder showed improvements in cognition after taking the herb for 12 weeks. These cognitive improvements are probably due to the way ginsenosides promote neurogenesis.
However, the cognitive benefits of Panax ginseng only showed up after the study volunteers took the herb for 12 weeks. The benefits also slowly went away after they discontinued the supplement. Most other studies on Panax ginseng also involve taking it for at least 8-12 weeks. This means that ginseng is best used as a long-term supplement; with a short-term course of ginseng, you may not be able to enjoy the benefits.

Ashwagandha

Ashwagandha belongs to the Solanaceae family and its scientific name is Withania somnifera. It is also known as Indian ginseng or winter cherry. In Sanskrit, it is known as Ashwagandha, which means the odor of a horse. It is named so because of the odor of horse sweat that the roots seem to emanate. The plant originated in India and it grows best in dry regions. It is a robust plant that can survive in very high and low temperatures too, ranging from 40°C to as low as 10°C. Ashwagandha grows from sea level to an altitude of 1500 meters above sea level.
The use of Ashwagandha for so many centuries has aroused the curiosity of modern medical science, leading to an interest in investigating the medicinal properties of the plant. Preliminary studies on Ashwagandha indicated the presence of potential therapeutic abilities and it also showed no associated toxicity to the chemical constituents of the plant.
Also known as Indian ginseng, has a wide range of health benefits, which include its ability to fight cancer and diabetes, reduce inflammation, and prevent arthritis, asthma, hypertension, stress, and rheumatism. Furthermore, it boosts the supply of antioxidants and regulates the immune system. It also has antibacterial and anticonvulsant properties. It is also useful for men as a remedy for infertility and erectile dysfunction.
Ashwagandha has had a great significance in Oriental medical schools of thought, especially in the ancient Indian system of medicine, Ayurveda, for many centuries. Regular consumption of Ashwagandha can result in various health benefits; some of which are listed below:
Controls Cholesterol Levels Ashwagandha, with its anti-inflammatory and anti-oxidant properties, is good for cardiovascular problems. It strengthens the heart muscles and can also control cholesterol. A study at the University of Arizona indicated that it possesses hypolipidemic properties that help in bringing down blood cholesterol levels. Ashwagandha is good for enhancing the libido in men and is used to treats Erectile Dysfunction. Increases Fertility in Men In addition to increasing libido, and also helps in improving the semen quality. It plays an important role as an aphrodisiac as well as a way to improve semen quality by increasing the sperm count and sperm mobility. Ashwagandha helps in reducing anxiety. In India, Ashwagandha has been traditionally used in Ayurveda to improve both physical and mental health. The effects of this medicine, particularly on depression, were studied at the Institute of Medical Sciences at Banaras Hindu University, India. The study supported the benefits of Ashwagandha in relation to anxiety and depression. It is believed to possess anti-stress properties. Traditionally, it had been administered to induce a soothing and calming effect on a person., Consumption of Ashwagandha led to significant modulation of immune system reactivity and prevented myelosuppression in mice induced by immunosuppressive drugs. It was also observed that Ashwagandha increased the red blood cell, white blood cell, and platelets count.

Shilajit, pronounced shil-ah-jeet, is an organic tar-like substance that naturally occurs in mountains around the globe, from the Himalayas to the Andes. Ayurvedic doctors began using it hundreds of years ago for its potent health-supportive properties.
Shilajit contains several potent substances including antioxidants and Humic and Fulvic acid. The plant contains over 80 minerals that support the body, and many have an incredible effect on a man's health. There are many health benefits of Shilajit for men. It supports Fertility. A study gave shilajit to 60 men suffering from infertility twice daily for 90 days. At the end of the trial period, sperm counts in the men increased by more than 60%, and sperm activity improved by 12% or more. It promotes Testosterone Levels Naturally. It enhances Performance and acts at the cellular level to improve energy production at its source, the mitochondria.
Encourages Healthy Aging. Studies report shilajit's antioxidant activity protects against cellular damage, and it's this cellular damage that speeds the aging process in the heart, lungs, liver, and skin. The fulvic acid in shilajit delivers antioxidants and minerals directly to cells where they're needed. This keeps them safe from free radical damage and accelerated aging.

Safed Musli is a healing plant which is generally used for Sexual Weakness and Impotence. It is most important herb described in Ayurveda for vigorous. Safed Musli plants are small in size, it generally have white flowers and are grown in scattered panicles up to 120 cm long. It is a rich source of

vitamins and of about more than 25 alkaloids, beside this it have proteins, steroids, polysaccharides and carbohydrates. Due to its vigorous properties it is also known as such as “Indian Viagra”, “Golden Roots”, “Herbal Viagra”, “The Wonder Harvest” etc. It is a herb that can boost the immune system. Chlorophytum borivilianum has immunization stimulating properties which can be helpful for overall health. The research done on rat also stated that they found an increases in sperm count within 60 days of regular doses given regular given to the rats.
So we believe that roots of Chlorophytum borivilianum can be useful to cure of certain forms of sexual deficiencies such as premature ejaculation or oligospermia. In other reports, rats have benefited from this plant and shown increased sexual activity and increased libido as well as having a significantly higher sperm increase.
It has been used as a tonic for sexual condition by Indians for centuries. It has a powerful activator agent used for restoring male reproductive system disorders like impotency, low sperm count and premature ejaculation, etc.
Apart from revitalizing the reproductive system, the herb avoids premature ejaculation as well as is also used in chronic leucorrhoea.

Vidarikhand Vidarikand (Pueraria tuberosa) is a creeper which has circular leafless stems. Underground fruits are found attached to its roots. Fruits vary in shape and size and its taste is very similar to that of Yashtimadhu. This is why it is known as swadu kand (tasty fruit). Vedari is nourishing tonic, diuretic, anabolic, alterative and Vajikarak. It reduces Pitta-Vata and increases Kapha. It mainly works on plasma, blood, muscles and reproductive system. It increases Shukra dhatu. It stimulates milk production in nursing mothers.. It has Estrogen like properties. Estrogen is the female hormone responsible for development and regulation of the female reproductive system and secondary sex characteristics. In males estrogen helps in maturation of the sperm and maintenance of a healthy libido. Vidarikhand Vidari / Vidari Kanda and is a rejuvenating drug of Ayurveda. It is mainly used as reproductive tonic that promotes sexual desire, treats nocturnal emission in males and for females treats menstrual disorders, menopause syndrome and uterus weakness. It is cooling, nourishing, and tonic. Vidari cures weakness. It is aphrodisiac and improves sperms in males.

Shatavari, or Asparagus racemosus, has been used for centuries in Ayurveda to support the reproductive system, particularly for females, and as a support for the digestive system, especially in cases of excess pitta. Shatavari’s name gives reference to its traditional use as a rejuvenative tonic for the female reproductive system. This support is not only for the young woman, but also for women in their middle and elder years, to help them gracefully transition through the natural phases of life, including menopause. The nourishing properties of Shatavari are used traditionally to support a number of systems and functions in the body like:

- ✓ A healthy female reproductive system
- ✓ Healthy levels of breast milk production
- ✓ Supports to balance female hormones
- ✓ Supportive of male reproductive system as well
- ✓ Soothing effect on the digestive tract
- ✓ Healthy peristalsis of bowels
- ✓ Moisturizing support of the respiratory tract
- ✓ Promotes healthy energy levels and strength
- ✓ Supports the immune system
- ✓ Natural antioxidant properties
- ✓ Supporting women through every stage of their lives, Shatavari's main constituents are steroidal saponins that suggest its use as an oestrogen regulator. This modulation helps to regulate menstrual cycles, manage PMS symptoms, alleviate menstrual cramps and control the amount of blood lost. Shatavari greatly helps with fluid retention and may also be helpful with the uncomfortable bloating often suffered before a period.
- ✓ This versatile herb can be very helpful to women who have fertility issues due to stress or immune-mediated problems, with Shatavari supporting proper immunological function. It supports the mucous membranes as it contains mucilage, this lines and protects the membranes of the cervix which is helpful for women with low cervical mucous. Adequate cervical mucous allows sperm to swim freely through the cervix.
- ✓ The saponins contained in Shatavari have been shown to have an "anti-oxytocin" effect which in turn may help uterine contractions subside- protecting against threatened miscarriage. Consultation with an Ayurvedic or Naturopathic Practitioner is advised before using Shatavari for this condition.
- ✓ Due to its oily, heavy nature, Shatavari nourishes the female reproductive system from within to relieve menopause symptoms such as vaginal dryness, hot flashes and

insomnia. This phytoestrogen-rich herb naturally helps to balance the hormones responsible for many of the more unpleasant symptoms associated with this change in life. Shatavari also stimulates and balances the production of happy hormones; Endorphins, Serotonin and Dopamine- meaning it can greatly reduce mood swings, irritability and menopause induced depression.

- ✓ Shatavari works as an aphrodisiac for women by bringing all the symptoms of women's sexual health, through all the changes of a woman's life, into balance. Research shows that Shatavari increases blood flow to the female genital area, enhancing sexual sensation, sensitivity and increasing vaginal lubrication. It is known to have a hormone balancing effect, making it useful for women who experience loss of libido as a side effect of the menopause.
- ✓ In men, studies show it to be an excellent aphrodisiac when combined with Ashwagandha. It promotes the size, strength and stiffness of the penis and can treat impotence and sexual debilitation. It has also been shown to increase spermatogenesis in men, providing higher sperm counts and a larger percentage of healthy sperm.
- ✓ **Kounch Beej (Mucuna prurita)** has been used as an aphrodisiac, it is used to increase libido in both men and women, and helps in treating erectile dysfunction & impotency. It is used as a nervine tonic for nervous system disorders. Kounch Beej is beneficial for reducing cholesterol, lowering blood sugar levels and enhancing mental alertness all without stimulating the central nervous system. It has the following benefits
- ✓ Central nervous system: It is used in paralysis, hemiplegia and other nervine disorders and spasms associated with Parkinson's or Bell's Palsy
- ✓ Digestive system: It is used in intestinal worms and colic
- ✓ Reproductive system: It is used as an aphrodisiac and is used in seminal weakness, spermatorrhea.
- ✓ Genito- urinary system: It is used in leucorrhea and profuse menstruation.

Salam Panja is an herb, used in the Unani and Ayurvedic systems of medicines as a powerful stimulant and virility enhancer. The botanical name of this plant is Dactylorhiza Hatagirea. It is a tonic, which boosts the libido with its strong aphrodisiac properties. This herb is known by different names in different parts of the world such as Marsh Orchis in the Europe, Salem Panja in Kashmir, and Ambolakpa in Ladakh. The different health benefits of Salam Panja are as follows:

Low libido: Salam Panja has been used traditionally in the management of low libido in men. It has been shown to increase the libido. It acts as a powerful aphrodisiac and also produces a testosterone boosting effect. It increases the virility and vigor in men and increases their physical performance. It has the ability to enhance the stamina and strength in men, which has a favorable effect on their physical powers. It also increases the production of a male hormone called testosterone, which plays a major role in the fertility in men.

Erectile dysfunctions and premature ejaculation: Salam Panja can be used to treat male health problems like erectile dysfunctions. It can increase the strength of the muscles in the penile tissue and also increase the blood supply into the organ thus allowing a man to get an erection. This herb is known to possess a strong penile erection index, which is a measure of how long a man can maintain an erection. Hence, it is considered useful for treating premature ejaculation also.

Male infertility: Salam Panja is a potent herbal medication used for treating male impotency arising out of low sperm count or lack of sperm motility. Salam Panja increases the sperm count by boosting the testosterone levels in the blood and improves the quality and motility of the sperms. Hence, it is considered an effective treatment for oligospermia and oligozoospermia. Nocturnal emission: Nocturnal emission, also called night fall or night pollution, is a complaint more common among the men above the age of 50 years. Though it is a natural process and can occur infrequently in most men, it can result in a more serious problem like erectile dysfunctions, obliquity of penile tissue, and premature ejaculation, if not treated properly. Salam Panja offers an effective and safe treatment option for nocturnal emission. It works by promoting the production of nitric oxide in the muscles of the penile tissue that results in the relaxation of the smooth muscles, which, in turn, helps to prevent nightfalls.

4 Study Objectives

4.1 Primary & Secondary Objectives

To evaluate increase in Sperm Count in patients with Oligospermia.

To evaluate gradual development in Erectile Dysfunction, Premature Ejaculation and Loss Of Libido.

Selection of Study Population

4.1.1 Inclusion Criteria

To be eligible for study entry patients had to satisfy all of the following criteria:

1. Male outpatients aged 25 to 50 years.
2. Patients with Oligospermia, Erectile Dysfunction, Premature Ejaculation & Loss of Libido.
3. The patient will take his regular medicines along with this adjuvant therapy, if any.
4. Patients ready to give written informed consent and willing to comply with the study protocol.

4.1.2 Exclusion Criteria

Patients were excluded from the study if one or more of the following criteria were applicable:

1. Patients with deep cuts and wounds, raw wound and weeping wounds.
2. Patient with known allergy to any ingredients used Super Active.
3. Patients with signs of cellulitis, osteomyelitis, necrotic or avascular bed.
4. Patients with documented sexually transmitted diseases/ VD.
5. Patients with Cancer.
6. Patient receiving corticosteroids or any other immunosuppressive treatment
7. Patient with clinical evidence of anemia or malnutrition
8. Patients who have received any investigational drug within 6 months prior to study entry or such treatment is planned for during the study period.

4.1.3 Removal of Patients from Therapy or Assessments

Patients would be free to withdraw from the study anytime without stating the reason, however, every attempt would be made by the investigator to find out and record the reason for the same. Conversely, if the principal investigator feels appropriate he may withdraw the patient from the study. A record of reasons for the same would be made in the patient CRF. In the event of a patient requiring any other medication/intervention during the course of the trial, which can interfere with the study, that patient will be withdrawn from the trial. The withdrawn patients would be subjected to physical and systemic examination and efficacy endpoint assessment.

It would be documented whether or not each patient completed the study phase. If for any patient either study treatment or observations were discontinued, the reason for the same would be recorded. Reasons that a patient may discontinue study treatment may be one of the following:

- ✓ Adverse event(s)
- ✓ Abnormal laboratory value(s)
- ✓ Unsatisfactory therapeutic effect
- ✓ Patients conditions no longer requires study treatment
- ✓ Protocol violation
- ✓ Patient withdrew consent
- ✓ Administrative problems
- ✓ Lost to Follow up

4.2 Investigational Products

4.2.1 Investigational Products Administered

The investigational product is Super Active Capsule. 1 Capsule of 500 mg was taken two times daily after meals with little amount of water for a period of 60 days.

4.2.2 Identity of Investigational Products

The details of the investigational products are described below.

The investigational products should be stored at a temperature from 15^{o}C to 30^{o}C.

4.2.3 Method of Assigning Patients to Treatment Groups

As it is a single arm study, all the patients were assigned the same treatment without any randomization.

4.2.4 Selection of Doses in the Study

Dose selection was not the case in this study.

4.2.5 Selection and Timing of Dose for Each Patient

1 Capsule of 500 mg was taken two times daily after meals with little amount of water for a period of 60 days. No specific timings were followed and required.

4.2.6 Blinding

The treatment was administered without any randomization. So, blinding was not performed and maintaining was not required.

4.2.7 Prior and Concomitant Therapy

Medications other than the study drugs which would be considered necessary for the patient' welfare and which would not interfere with the study medication or efficacy evaluation may be allowed at the discretion of the investigator, and an appropriate record would be maintained in the CRF.

4.3 Efficacy, and Safety Variables

4.3.1 Efficacy, and Safety Measurements Assessed

4.3.1.1 Efficacy Assessments

Parameters

Sperm Count was evaluated at the beginning and at the end of therapy. Also the signs and symptoms of General Health and Debility was assessed before and after of treatment by VAS score.

Primary Efficacy End Points

Proportion of patients achieving Improving in Sperm Count Level.

Secondary Efficacy End Point

To Determine the development in Erectile Dysfunction, Premature Ejaculation, General Health & debility assessment by subjective scoring (VAS) and clinical assessment.

4.3.1.2 Safety Assessments

Assessments of safety were based on the following:

- ✓ Adverse Events
- ✓ Overall safety was assessed by local symptoms of itching, rash or any other allergic reactions.

4.3.1.2.1 Adverse Events

Expected Adverse Events

There is no significant adverse event expected with Super Active. However, few patients may develop constipation or irritation.

Serious Adverse Event

Any "serious adverse effects" resulting in withdrawal from the study must be notified by the Investigator within 24 hours to the study sponsor. In case of "Death", it should be reported to Sponsor within one working day. Any unexpected serious adverse event (SAE) occurring during a clinical trial should be communicated promptly (within 14 calendar days) by the Sponsor to the Licensing Authority and to the other Investigator(s) participating in the study.

All the serious adverse effects (SAE) occurring during study at each centre will be recorded into SAE reporting form.

A serious adverse event or reaction is any untoward medical occurrence that at any dose:

1. Is life threatening [Note: The term "life threatening" in the definition of "serious" refers to an event in which the patient was at risk of death at the time of the event; if appropriate help was not available (it does not refer to an event, which hypothetically might have caused death, if it were more severe)].
2. Results in death.
3. Requires in patient hospitalization or prolongation of existing hospitalization
4. Results in persistent or significant disability / incapacity.
5. Results in congenital anomaly

Causality Assessment

Causality of adverse Event were based on investigator's assessment of the event as certain, probable, possible, unlikely, unclassified and un-assessable as per WHO scale (as given in the table below).

Relationship	Description
CERTAIN	A clinical event, including laboratory test abnormality, occurring in a plausible time relationship to drug administration, and which cannot be explained by concurrent disease or other drugs or chemicals. The response to withdrawal of the drug (dechallenge) should be clinically plausible. The event must be definitive pharmacologically or phenomenologically, using a satisfactory rechallenge procedure if necessary.
PROBABLE	A clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, unlikely to be attributed to concurrent disease or other drugs or chemicals, and which follows a clinically reasonable response on withdrawal (dechallenge). Rechallenge information is not required to fulfil this definition.
POSSIBLE	A clinical event, including laboratory test abnormality, with a reasonable time sequence to administration of the drug, but which could also be explained by concurrent disease or other drugs or chemicals. Information on drug withdrawal may be lacking or unclear
UNLIKELY	A clinical event, including laboratory test abnormality, with a temporal relationship to drug administration which makes a causal relationship improbable, and in which other drugs, chemicals or underlying disease provide plausible explanations.
UNCLASSIFIED	A clinical event, including laboratory test abnormality, reported as an adverse reaction, about which more data is essential for a proper assessment or the additional data are under examination
UNASSESSIBLE	A report suggesting an adverse reaction which cannot be judged because information is insufficient or contradictory, and which cannot be supplemented or verified

Intensity of adverse events

Intensity of adverse events was assessed as per the following classification:

Mild

An event that is usually transient, and requires no special treatment or intervention. The event does not generally interfere with usual daily activities. Includes transient laboratory test alteration.

Moderate

An event that is alleviated with simple therapeutic treatments. The event impacts usual daily activities, which includes alteration in the laboratory tests indicating injury, but without long-term risk

Severe

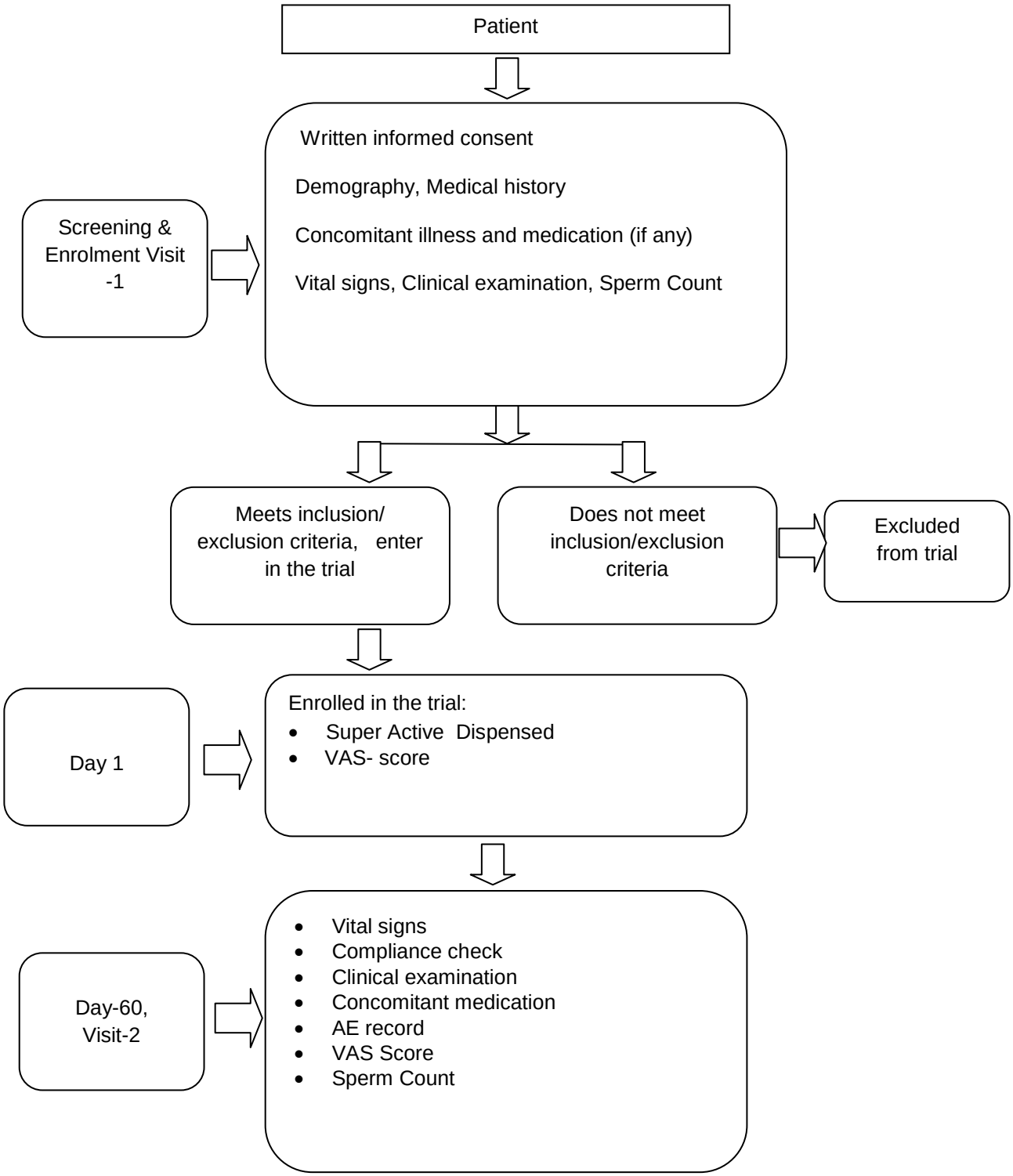
An event that requires therapeutic intervention. The event interrupts usual daily activities, which also include laboratory test indicating a serious health threat or permanent injury. If hospitalization is required for treatment it becomes a serious adverse event.

Abnormal laboratory values will be reported as adverse events under the following circumstances:

- ✓ When the abnormal lab report is accompanied with associated symptoms.
- ✓ When medical/surgical intervention is required.
- ✓ When an additional diagnostic test is required.
- ✓ Leads to a serious adverse event.
- ✓ When it is considered by clinical investigator as an adverse event.

Flow Chart

The schedule of planned study assessments is shown in the following flow chart.



4.3.2 Drug Concentration Measurements

Not applicable.

4.4 Data Quality Assurance

The Sponsor implemented and maintained quality assurance and quality control systems with written Standard Operating Procedures (SOPs) in accordance with the Guidelines of Good Clinical Practice of CDSCO.

The study was monitored as per the requirement of CDSCO GCP guidelines. A monitor or auditor appointed by the sponsor could meet the investigator and visit the study facilities at any time in order to maintain current knowledge of the study through review of the records, comparison with source documents, observation and discussion of the conduct and the progress of the study. Prior to the start of the study, the principal investigator will be contacted and informed of any impending visits and the frequency of such visits. The investigator will allow and assist the Sponsor's study monitor to review study progress, allow source data verification (checking of CRFs against original source documents) for accuracy of data recording, review of study drug logs and facilities, collect completed documents. Any deficiency found will be reported, and signed by the principal investigator and Sponsor Monitor. Also action taken for the last visits decision will be signed. Site monitoring visit log will be updated after every monitoring visit.

In addition, a study site might be audited by the Sponsor's Quality Assurance unit (QA) or by an external Auditor on behalf of Sponsor and/or inspected by the representative of Regulatory Authority. This audit might include review of all source documents, drug records, original clinical case notes, facilities used in the trial.

4.5 Changes in the Conduct of the Study or Planned Analyses

4.5.1 Changes in the Conduct of the Study

No amendments were generated for the study.

4.5.2 Changes in the Planned Analyses

No changes in the conduct of the study or planned analyses were instituted after the start of the study.

5 Study Patients and Results

5.1 Disposition of Patients

A total of 20 male patients were screened at 1 centre in Kolkata, India. A total of 20 patients were assigned and all of them received study medication and completed the study. The patients were recruited from Namita Medical Hall, Amarapuri, Sodepur, Kolkata - 700 111, West Bengal, India for this study.

5.2 Demographic and Other Baseline Characteristics

Demographic data are summarized for all the patients in the following table.

(Demographic Characteristics)

Serial Number	Subject Initials	ICF Signed by subject	Age years	Weight Kg	Height cm
1	L-B	02-05-2017	25	35.00	175
2	M-J	02-05-2017	27	55.00	150
3	H-N	02-05-2017	36	60.00	160
4	U-B	03-05-2017	41	72.00	164
5	T-K-C	03-05-2017	45	74.00	168
6	B-H	03-05-2017	29	64.00	170
7	T-S	03-05-2017	41	75.00	174
8	R-D	05-05-2017	33	40.00	150
9	B-T-M	05-05-2017	47	35.00	138
10	L-D	05-05-2017	29	55.00	160
11	C-R	05-05-2017	38	60.00	175
12	N-J	06-05-2017	44	72.00	150
13	T-L	06-05-2017	37	55.00	160
14	N-B	06-05-2017	42	78.00	164
15	J-M	06-05-2017	37	40.00	170
16	P-N	09-05-2017	50	35.00	172
17	T-S	09-05-2017	30	70.00	174
18	K-C	09-05-2017	25	44.00	150
19	J-L	10-05-2014	31	39.00	138
20	T-B	10-05-2014	45	81.00	160
Mean				**56.95**	**161.1**

5.3 Vital Signs

Sl No.	Visit 1 Date	Visit -1 Vital Signs				Visit 2 Date	Visit-2 Vital Signs			
		PR	BP	RR	Temp		PR	BP	RR	Temp
1	02-05-2017	80	124/80	14	98	02-07-2017	80	120/84	16	98
2	02-05-2017	76	122/82	14	99	02-07-2017	74	124/80	14	98
3	02-05-2017	76	130/86	14	99	02-07-2017	72	130/84	14	99
4	03-05-2017	84	150/100	16	99	03-07-2017	76	146/100	14	98
5	03-05-2017	80	154/100	14	99	03-07-2017	78	154/100	16	98
6	03-05-2017	74	120/80	16	99	03-07-2017	74	120/80	14	99
7	03-05-2017	80	140/90	16	99	03-07-2017	80	140/90	16	99
8	05-05-2017	74	120/80	14	99	05-07-2017	79	120/80	14	98
9	05-05-2017	74	120/80	14	99	05-07-2017	80	120/80	16	99
10	05-05-2017	74	120/80	14	99	05-07-2017	80	120/80	14	99
11	05-05-2017	90	124/80	18	99	05-07-2017	90	120/80	20	99
12	06-05-2017	74	120/80	14	99	06-07-2017	80	120/80	14	98
13	06-05-2017	76	120/80	16	99	06-07-2017	82	120/80	16	99
14	06-05-2017	74	120/80	14	99	06-07-2017	80	120/80	14	98
15	06-05-2017	76	120/80	14	98	06-07-2017	84	120/80	14	99
16	09-05-2017	74	120/80	14	99	09-07-2017	80	120/80	14	99
17	09-05-2017	80	120/90	14	99	09-07-2017	78	120/90	14	98
18	09-05-2017	81	110/85	15	98.6	09-07-2017	78	110/80	14	98.6
19	10-05-2014	79	100/80	17	98.3	10-07-2014	72	100/80	17	98.7
20	10-05-2014	76	120/80	15	98.9	10-07-2014	78	120/80	17	98.1
	Mean	**77.60**		**14.85**	**98.84**		**78.75**		**15.10**	**98.52**

No significant or medically important change has been observed in vital signs of the subjects between baseline data and the data recorded after treatment with Super Active for 60 days.

5.4 Medical History and Examinations

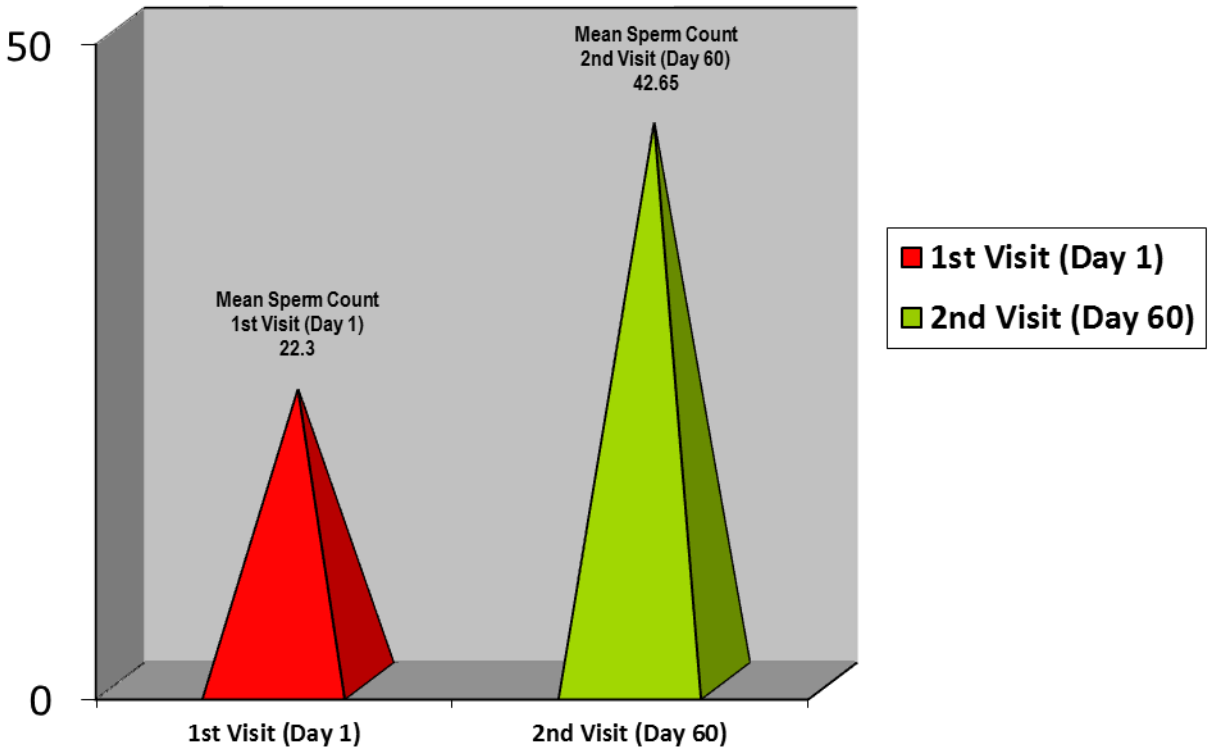
Sl No	Subject Initial	Physical Examination	Medical History	Allergies	Recent Hospita-lization	Surgical History
1	L-B	None	None	None	None	None
2	M-J	None	None	None	None	None
3	H-N	None	None	None	None	None
4	U-B	None	Diabetic	None	None	None
5	T-K-C	None	None	None	None	None
6	B-H	None	None	None	None	None
7	T-S	None	Hypo-Thyroidsm	None	None	None
8	R-D	None	None	None	None	None
9	B-T-M	None	None	None	None	None
10	L-D	None	None	None	Dehydration	None
11	C-R	None	None	None	None	None
12	N-J	None	None	None	None	None
13	T-L	None	None	None	None	None
14	N-B	None	None	None	None	None
15	J-M	None	None	None	Accident	Wrist Fracture
16	P-N	None	None	None	None	None
17	T-S	None	None	None	None	None
18	K-C	None	None	None	None	None
19	J-L	None	None	None	None	None
20	T-B	None	None	None	None	None

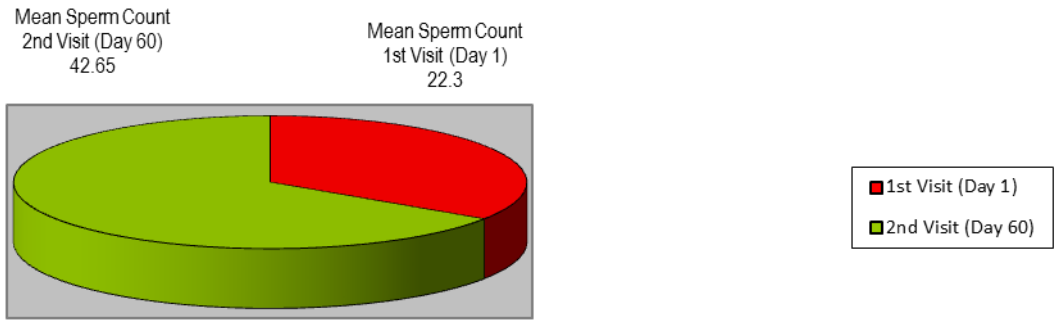
8.5 Baseline Characteristics (Visit 1)

Sl. No.	Subject Initial	Sperm Count in million/ml.
1	L-B	22
2	M-J	17
3	H-N	26
4	U-B	30
5	T-K-C	12
6	B-H	19
7	T-S	32
8	R-D	34
9	B-T-M	05
10	L-D	22
11	C-R	11
12	N-J	26
13	T-L	19
14	N-B	31
15	J-M	27
16	P-N	30
17	T-S	19
18	K-C	14
19	J-L	18
20	T-B	32
Mean Sperm Count in million/ml = 446/20= 22.3		

8.5 End Characteristics (Visit 2)

Sl. No.	Subject Initial	Sperm Count in million/ml.
1	L-B	42
2	M-J	47
3	H-N	56
4	U-B	42
5	T-K-C	32
6	B-H	32
7	T-S	52
8	R-D	64
9	B-T-M	31
10	L-D	47
11	C-R	34
12	N-J	46
13	T-L	51
14	N-B	42
15	J-M	38
16	P-N	41
17	T-S	43
18	K-C	34
19	J-L	32
20	T-B	47
Mean Sperm Count in million/ml = 853/20= 42.65		

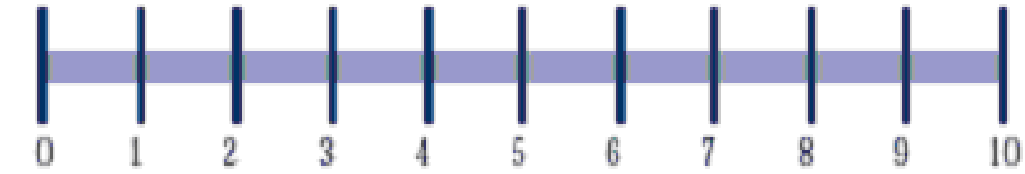




Graphical Representation of study start and close mean data of Sperm Count

5.5 Quality of life Analysis by Visual assessment & voluntary subjective declaration. Patients were asked about the difficulties they are facing in sex life due to erectile dysfunction, premature ejaculation and loss of libido at the beginning and end of treatment.

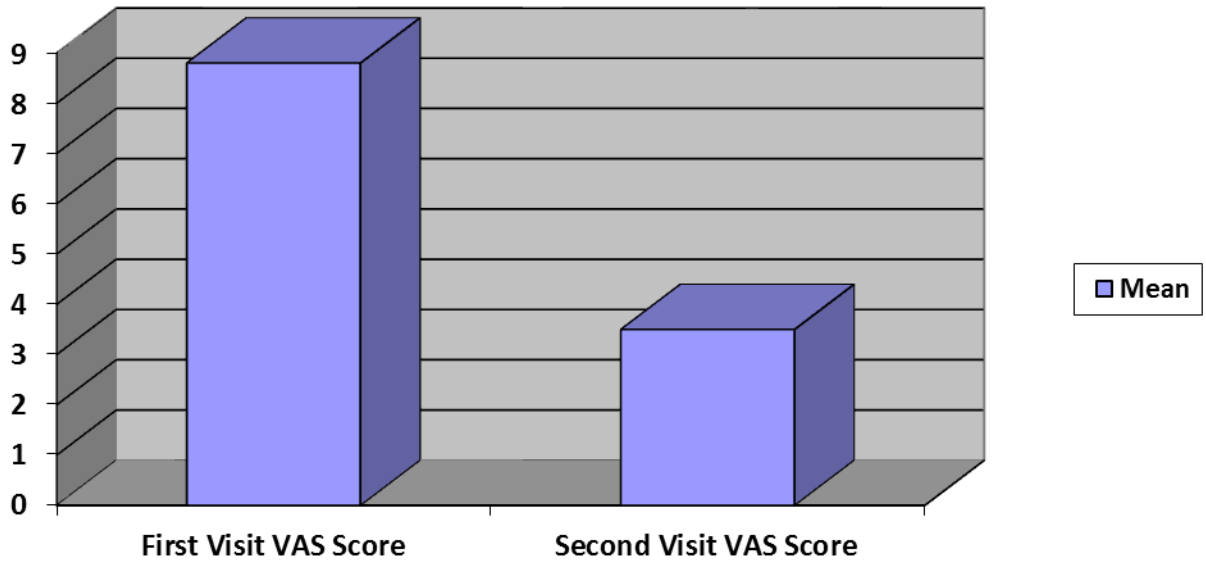
The Visual Analog Scale (VAS) is a psychometric response scale which can be used in questionnaires. It is a measurement instrument for subjective characteristics or attitudes that cannot be directly measured. When responding to a VAS item, respondents specify their level of agreement to a statement by indicating a position along a continuous line between two end-points. This continuous (or "analogue") aspect of the scale differentiates it from discrete scales such as the Likert scale. There is evidence showing that visual analogue scales have superior metrical characteristics than discrete scales, thus a wider range of statistical methods can be applied to the measurements.

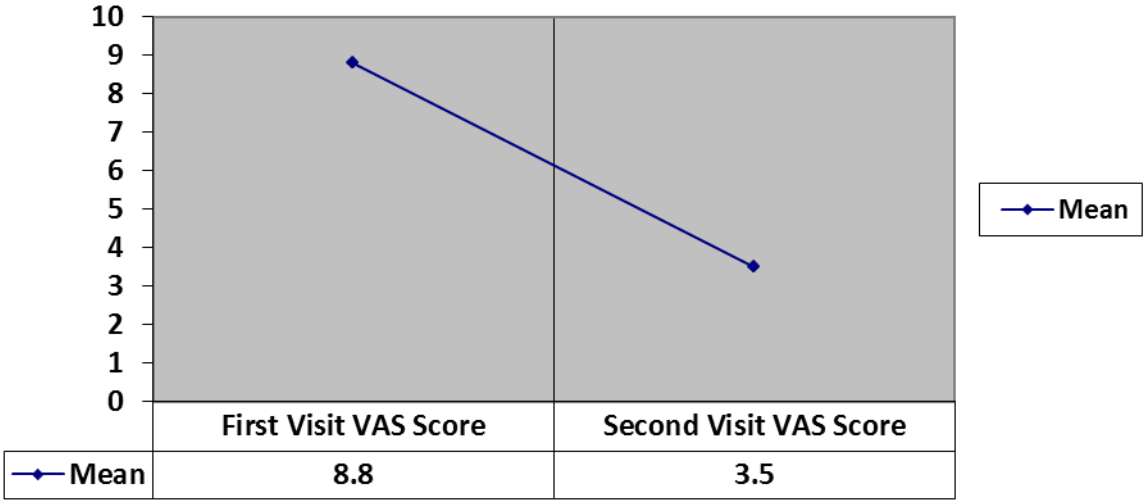


Enjoying Normal Life (No UI) **Worst Possible (Severe UI)**

Subject No	Quality of Life (In terms of difficulties they are facing in sex life due to erectile dysfunction, premature ejaculation and loss of libido (Visit 1)	Quality of Life (In terms of difficulties they are facing in sex life due to erectile dysfunction, premature ejaculation and loss of libido (Visit 2)
1	10	3
2	10	4
3	08	3
4	10	4
5	09	4
6	10	3
7	08	3
8	08	2
9	08	4
10	09	5
11	08	4
12	10	4
13	08	2
14	07	3
15	08	2
16	10	5
17	07	3
18	08	3
19	10	5
20	10	4
Mean	**8.8**	**3.5**

The mean VAS score has been decreased from 8.8 (Visit 1) to 3.5 (Visit 2). This decrement in VAS score is statistically significant for reduction of erectile dysfunction, premature ejaculation and loss of libido from Visit 1 to Visit 2. The analyzed data is graphically presented below.





Summary

VAS score	Visit 1	Visit 3
Score	8.8	3.5
Inference	**Highly significant development**	

5.5.1 Efficacy Conclusions

After application of **Super Active** for 60 days on 20 patients.

- ✓ This increase in number of sperm count mean at the end of treatment is statistically significant in support of efficacy of Super Active in treatment of Oligospermia.
- ✓ The decrement of VAS score from Visit 1 to Visit 2 is statistically significant in support of development of QUALITY OF LIFE of the patients suffering from erectile dysfunction, premature ejaculation and loss of libido.

5.5.2 SAFETY CONCLUSIONS

After application of **Super Active** for 60 days on 20 patients.

- ✓ No medically important adverse change in vital signs has been observed
- ✓ No adverse event either treatment related or unrelated has been reported during the course of the study.

6 CONCLUSION

Super Active has been found to be a safe and effective herbal product and excellent for the treatment of Oligospermia, erectile dysfunction, premature ejaculation and loss of libido.