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# AN OPEN LABEL, INTERVENTIONAL, MULTI-CENTER, PROSPECTIVE CLINICAL STUDY TO EVALUATE EFFICACY AND SAFETY OF 'AYUVIGO FORTE CAPSULE' IN PATIENTS SUFFERING FROM MILD TO MODERATE ERECTILE DYSFUNCTION

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## ABSTRACT

**Objectives**: The main objective of the study was to evaluate the efficacy and safety of 'Ayuvigo Forte' capsule in subjects suffering from mild to moderate erectile dysfunction (ED). **Methods**: It was an open label, interventional, multi-center, prospective, phase II clinical trial. Study was completed in 31 subjects. All the subjects were advised to take two Ayuvigo Forte capsules thrice daily orally after meals with water for 30 days. After screening visit (day -3), all the subjects were called for baseline visit (day 0) and follow-up on day 15 and day 30. Data describing quantitative measures were expressed as mean ± SD. **Results:** At the end of the treatment, IIEF questionnaire showed significant improvement in erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction domains. Evaluation of male sexual health on EDITS questionnaire (patient & partner version) and quality of sexual life on SQoL questionnaire showed a significant improvement at the end of the study period. Global evaluation by the physician and patient showed excellent response to the study treatment. Almost all patients showed excellent tolerability to the study drug. No significant change in vital parameters and safety laboratory parameters were observed at the end of the study. **Conclusion:** The study provides good evidence in support of the efficacy and safety of Ayuvigo Forte capsule in loss of libido and mild to moderate cases of erectile dysfunction.

**KEYWORDS:** Ayuvigo Forte capsule, IIEF questionnaire, EDITS questionnaire, SQoL questionnaire.

## INTRODUCTION

Erectile dysfunction (ED) is a persistent inability to achieve or maintain penile erection sufficient for satisfactory sexual performance. ED is a complex condition involving the physical and psychological factors. It adversely impacts on a man's self-esteem and quality of life.[1] After premature ejaculation, ED is the most common disorder of sexual dysfunction. Worldwide estimates of ED prevalence range from 2% in men younger than 40 years to 86% in men 80 years or older.[2] According to the Massachusetts Male Aging Study, the overall probability of complete impotence tripled from 5% in men 40 years of age to 15% in those 70 years of age. It has been estimated that in 1000 consecutive patients with sexual disorders attending a psychosexual clinic in India, ED was the presenting complaint of 23.6%.[1]

Penile erection is a neurovascular phenomenon, which occurs by different mechanisms involving tactile stimulation, erotic stimulation (of para-ventricular nucleus and medial pre-optic area of the hypothalamus) and nocturnal erection. Though, the exact central pathway involved in penile erection is unclear, various neurotransmitters within penile tissues are involved in erection process of which the most important is nitric oxide (NO). NO has been released from penile nerve endings. Nitric oxide causes relaxation of smooth muscles of penile arteries and spongy tissues of corpora cavernosa which leads to the arterial dilatation and cavernosal relaxation, respectively. These activities cause increase pooling of blood within the trabecular spaces of corpora and obstruction of venous outflow (veno-occlusion) of penis. These combine mechanisms of pooling of blood in corpora and veno-occlusion lead to rigid penile erection.[3]

Several causes viz. psychogenic, neurogenic, vascular, drug related and endocrine are responsible for ED. The commonest causes of ED are hypertension, smoking,

hyperlipidaemia and diabetes. These causes are also called as organic causes of ED. Functional ED is commonly found in young and healthy men in which psychogenic causes are considered to be involved.[4-5] Testosterone deficiency is rare but potentially reversible cause for ED.[1] There are four types of ED viz. mild, mild to moderate, moderate and severe. Generally, Erectile Function (IIEF) score is well accepted criteria to stratify ED as No ED (IIEF score from 25–30), mild ED (IIEF score from 19–24), mild to moderate ED (IIEF score from 13–18), moderate ED (IIEF score from 7–12) or severe ED (IIEF score from 0-6).[6]

Management of ED usually involves psychotherapeutic and pharmacological approaches. Psychotherapy includes patient counseling, addressing primary issues, resolving conflict and settlement of psychogenic problems. Pharmacological therapy includes first line management i.e. use of oral medicines such as phosphodiesterase (PDE) type-5 inhibitors. PDE inhibitors are potent selective inhibitors of cyclic GMP, specifically phosphodiesterase type 5 (PDE-5), the predominant isoform of the enzyme found in the human penis, which results in smooth muscle relaxation. The currently available PDE 5 inhibitors are Sildenafil, Tadalafil and Vardenafil. Other therapies such as testosterone replacement, vacuum erection devices, prosthesis, intra-urethral prostaglandin E and vascular surgery have also been used to treat ED.[1]

Though, above treatment approaches are effective, these treatment options have many side effects and disadvantages. Patient counseling has very high recurrence rate of ED. PDE-5 inhibitors are associated with cardiac contraindications and may cause systemic side-effects. Testosterone replacement is an effective option but other causes of testicular failure such as carcinoma of the prostate and outflow obstruction of the bladder should be ruled out before prescribing testosterone. Use of vacuum erection devices can cause unnatural erections, petechial rash, pain, cold penis and partner dissatisfaction. The prosthesis use may cause infection and fibrosis. Intra-urethral prostaglandin E may lead to pain and hypotension. The vascular surgery is an expensive method and requires expertise.[1] These facts about conventional methods motivate medical practitioners and patients to use alternative medicines.[1-4]

In Ayurveda, *Klaibya* refers to impotence i.e. a man who is unable to perform sexual intercourse, being powerless, helpless or the inability to carry out sexual activities. According to Ayurveda, penile erection is a complex phenomenon of physical and psychological mechanisms. Physiological erection occurs through *Sankalpa* (determination and feeling), *Pidana* (specific stimulations) and *Cheshta* (acts), in which *Sankalpa* and *Pidana* are related to mind whereas *Cheshta* is related to the physic. Thus, any abnormality in physiological process of erection can cause *Klaibya*. In Ayurveda, *Vajikarana* (aphrodisiac) treatment has been used to manage almost all types of sexual disorders. In the management of *Klaibya* three types of treatment methods have been used viz. *Shodhana Chikitsa* (purification therapy), *Shamana Chikitsa* (conservative therapy) and *Manas Chikitsa* (psychological treatment). *Manas Chikitsa* includes patient counseling. *Shodhana Chikitsa* mainly emphasized on the use of *Uttar-Basti* (enema through the genital openings). In *Shamana Chikitsa* use of herbs such as *Ashvagandha*, *Shveta Musali*, *Gokshura*, and various classical formulations such as *Shatavaryadi Churna*, *Ashvagandhadi Churna*, *Vanari Gutika*, *Shilajeet Rasayan*, *Gokshuradi Vati* have been advised.[4,7-8]

Keeping in mind the basic concept of Ayurveda, Welex Laboratories Pvt. Ltd., has developed Ayuvigo Forte capsule for effective management of erectile dysfunction. Ayuvigo Forte capsule is a unique combination of 5 herbs and Shilajit. Most of the ingredients of Ayuvigo Forte capsule possess aphrodisiac, rejuvenator and libido enhancer activities. Few ingredients help to facilitate penile erection through nitric oxide (NO) pathway. Few ingredients of Ayuvigo Forte capsule help to increase androgen levels, sexual desire and performance in males. Few ingredients are also useful to promote stamina, a sense of well-being vigor, semen and sperm count. Most of the ingredients of Ayuvigo Forte capsule improve cognition and memory, ensure normal sleep, improve physical work capacity, endurance, tolerance and compatibility during stressful states and relieve different age-related symptoms.[9-31]

Looking at the various activities of the ingredients present in Ayuvigo Forte capsule, a hypothesis is postulated that Ayuvigo Forte capsule was helpful in the management of erectile dysfunction. Hence, to test this hypothesis, a clinical study titled as "An open label, interventional, multi-center, prospective clinical study to evaluate efficacy and safety of 'Ayuvigo Forte capsule' in patients suffering from mild to moderate erectile dysfunction" was planned.

## MATERIALS AND METHODS

### 1. Study Design

The study was an open label, interventional, multi-center, prospective, phase II clinical study.

### 2. IEC Approval

Before the initiation of the study, the study protocol and related documents were reviewed and approved by Institutional Ethics Committee (IEC) of KVTR Ayurvedic College, Boradi, Taluka - Shirpur, Dist - Dhule, 425428 and IEC of Govt. Ayurvedic College, Nanded, Maharashtra. The study was conducted in accordance with the approved protocol and GCP guidelines (issued by AYUSH in 2013). No changes in study plan or protocol were implemented during the trial.

**3. CTRI Registration**

The clinical study data was uploaded on Clinical Trial Registry of India (CTRI) website on 22.12.2015. The reference no for the trial is REF/2015/12/010336.

**4. Study Objectives**

The primary objectives were to evaluate efficacy of Ayuvigo Forte capsule in patients suffering from mild to moderate erectile dysfunction by assessing erectile function of penis on Erectile function subscale of IIEF Questionnaire and hardness of penis on Erection Hardness Score (EHS).

The secondary objectives were to evaluate the efficacy of Ayuvigo Forte capsule by assessing male sexual health on EDITS questionnaire (patient & partner version), quality of sexual life on Sexual Quality of Life Questionnaire (SQoL-M), changes in serum testosterone level, sexual encounter profile, drug compliance, global assessment for overall improvement by patient and by physician at the end of the treatment. Also, secondary objectives were to evaluate the safety of Ayuvigo Forte capsule by assessing tolerability of the study drug, AEs/ADRs and pre & post treatment changes in laboratory investigations i.e. liver function tests (LFT), renal function tests (RFT), lipid profile, complete blood count (CBC), ESR, Hb%, Urine Examination and ECG.

**5. Sample Size**

Anticipating 20% dropouts, we enrolled 36 subjects to get 30 evaluable cases at the end of the study.

**6. Subject Selection**

Subjects were recruited after signing the Informed Consent Document. Consent was taken after providing complete information to the subject in written document (Subject Information Sheet). Information was given to the subjects in the language that the subjects could read and write. Subjects were given opportunity to ask questions and their queries were resolved. All the process of screening/consent and recruitment were documented by the Clinical Research Coordinator (CRC) in the informed consent process document. The subject selection was done as per following details.

Married male subjects between 21 to 50 years of age suffering from mild to moderate erectile dysfunction and who were attending the outpatient clinic at trial sites were selected for the study. Subjects who scored 13 to 24 on the Erectile Function (EF) domain of the International Index of Erectile Function (IIEF) at screening were included in study. Subjects without any organic cause of erectile dysfunction, with active stable sexual relationship for the duration of study were included in the study. Subjects with known hypersensitivity to trial medicine or its components were not included in the study. Subjects with total erectile failure or any other sexual disorder, hypogonadism or anatomical deformity of the penis such as severe penile fibrosis or Peyronie's disease or penile trauma were excluded from the study. Subjects having history of major psychiatric disorder, central nervous system disorders such as stroke, transient ischemic attacks or spinal cord injury or pelvic surgery, disorders that may cause priapism were excluded from the study. Subjects with preexisting systemic diseases necessitating long-term medications, genetic and endocrinal disorders, major illnesses and sexual dysfunction due to anatomical, surgical or pharmacological causes; hypotension or uncontrolled hypertension uncontrolled diabetes, hepatic impairment, renal impairment or hematological disorders and continuing history of alcohol and / or drug abuse were excluded from the study. Subjects, who failed to keep abstinence for antioxidant agents, vitamins, anti-inflammatory drugs, hormones, Ayurvedic /herbal /homeopathic /naturopathy medications for erectile dysfunction were excluded from the study. Subjects whose ECG demonstrating any signs of uncontrolled arrhythmia / acute ischemia and X- ray chest showing any active lesion of tuberculosis, subjects with significant abnormal laboratory parameters were not included in the study.

**7. Investigational Drug**

The investigational product i.e. Ayuvigo Forte capsules was manufactured by the Sponsor i.e. Welex Laboratories Pvt. Ltd., following GMP and all applicable regulatory guidelines. The composition of the drug is given in Table 1.

**8. Study Procedure**

On screening visit (day -3), written informed consent was obtained from each subject for participation in the study. Subject's demographic data was noted. Subject was asked for his sexual relationship and advised to keep an active stable sexual relationship for the entire duration of the study. Subject was asked for any concomitant medical illness/medications. All subjects were asked for the use of antioxidant agents, vitamins, anti-inflammatory drugs, hormones, antibiotics and herbal /Ayurvedic /homeopathic /naturopathy medications. Subject's general and systemic examinations were done. Subject's *Dosha Prakriti Parikshan* was done. Subject's examination for erectile dysfunction was done and subject was assessed for any organic cause of erectile dysfunction. All the subjects were assessed for penile erection as per Erectile Function (EF) domain of the International Index of Erectile Function (IIEF). If subject EF- IIEF score was 13 to 24 then subject was considered for further evaluation as per the inclusion and exclusion criteria.

On screening visit, subject's assessment for hardness of penis was done on Erection Hardness Score (EHS). Subject's assessment for sexual health was done on EDITS questionnaire (Patient & Partner version). Subject's assessment for quality of sexual life was done on Sexual quality of life Questionnaire (SQoL-M). All the subjects were given a daily diary card to record their sexual encounter profile on daily basis

from the screening visit to the end of the study. Subject's chest X-ray PA view and ECG were done. If chest X-ray and ECG were within normal limits, then subjects were called on next day morning with empty stomach for laboratory tests. On next day morning, subject's blood sample was collected at the respective study center for lab tests i.e. serum total testosterone level, CBC, ESR, Hb%, liver function tests, lipid profile, renal function tests and fasting blood sugar. Subject's urine routine and microscopic examination was also done.

A wash out period of 3 days was advised to all the subjects. During wash out period and till the completion of the study, all the subjects had to refrain from antioxidant agents, vitamins, anti-inflammatory drugs, hormones, antibiotics and herbal / Ayurvedic / homeopathic / naturopathy medications. The use of concomitant medicines was assessed and advised by investigator as per the requirement. All the subjects were advised to continue the diet and exercise regimen (which they were already following during wash-out period and till the completion of study.

On baseline visit (day 0), subjects were asked for any AE/SAE occurred. Subject's general and systemic examinations were done. Subject's examination for erectile dysfunction was done and clinical symptoms were recorded. The daily diary card given to subject on last visit was collected and assessed by investigator/co-investigator for sexual encounter profile. The daily diary card was returned to subject to keep daily record of his sexual encounter profile up to next follow-up visit.

After baseline visit, all the subjects were called for follow-up visits viz. visit I (day 15) and visit II (day 30). On baseline visit an every follow-up visit (except last follow-up visit), all subjects were provided 2 HDPE containers each containing 60 Ayuvigo Forte capsules (90 capsules for 15 days + additional 30 capsules for use if the follow up is delayed maximum by 5 days). All the study subjects were advised to consume given medication in a dose of 2 capsules thrice daily orally after meals with water for 30 days. Subjects were advised to return empty containers after 15 days when they came for next follow up visit. On baseline visit (day 0) and on every follow up visit (except last follow-up visit) a dose chart (in the languages best understood by subjects) was given to subjects to keep daily record of use of study drug. Drug compliance was assessed by the investigator as per the dose chart.

On every follow up visit, subjects underwent general and systemic examinations. Subjects were asked for details of the AE/SAE (if any). Subject's examination for erectile dysfunction was done. On every follow-up visit except day 30, the daily diary card was returned to subject to keep daily record of his sexual encounter profile up to next follow-up visit. Drug compliance was assessed by the investigator as per the dose chart. On each follow up visit, subject's assessment for hardness of penis was done on Erection Hardness Score (EHS). Subject's assessment for quality of sexual life was done on Sexual quality of life Questionnaire (SQoL-M).

On last follow up visit (day 30), all the subjects were assessed for penile erection as per Erectile Function (EF) domain of the International Index of Erectile Function (IIEF). Subject's assessment for sexual health was done on EDITS questionnaire (Patient & Partner version). On last follow up visit (day 30), subject's serum testosterone level, CBC, ESR, Hb%, liver function tests, lipid profile, renal function tests and urine routine and microscopic were also done. Subject's ECG was also done. At the end of the study, subject's global evaluation for overall improvement and investigator's global evaluation for overall improvement was done. Tolerability of the trial drug was assessed by investigator and by subject at the end of the study. All subjects were closely monitored for any AE/ADR starting from baseline visit till the end of the study visit. All the subjects were advised to stop consumption of trial medicine and to take advice of investigator for further treatment. All the activities and findings were documented in the CRF.

**9. Statistical Analysis**

Consultant statistician performed the analysis of the data using statistical software SPSS 10.0. Data describing quantitative measures are expressed as median or mean ± SD or SE or the mean with range. Qualitative variables are presented as counts and percentage. All p-values are reported based on two-sided significance test and all the statistical tests are interpreted at 5% level of significance.

**RESULTS**

The study was completed in thirty one subjects. The mean age of subjects in the study was 39.06 ±7.80 years. There were 4 (12.9%) subjects in the age group of 21 to 30 years, 14 (45.16%) subjects in the age group of 31 to 40 years and 13 (41.49%) subjects in the age group of 41 to 50 years. There were 9 (29.03%) subjects of *Vata-Pitta Prakruti*, 1 (3.23%) subject each of *Vata-Kapha Prakruti* and *Kapha-Vata Prakruti*, 5 (16.13%) subjects of *Pitta-Vata Prakruti*, 8 (25.8%) subjects of *Pitta-Kapha Prakruti* while 7 (22.58%) subjects of *Kapha-Pitta Prakruti*.

**Assessment of erectile function of penis on erectile function subscale of IIEF Questionnaire**

The International Index of Erectile Function (IIEF) Questionnaire is a validated, 5-dimensional, self-administered investigation that has been found useful in the clinical assessment of erectile dysfunction and treatment outcomes in clinical trials. A score of 0-5 is awarded to each of the 15 questions that examine the 5 dimensions i.e. erectile function, orgasmic function, sexual desire, intercourse satisfaction and overall satisfaction. Each dimension possesses 6, 2, 2, 3, 2 items (questions) respectively.

**Assessment of sexual functions (erectile function)**
On baseline visit, the average erectile function score was 15.96 ± 3.06 which improved significantly to 21.83 ± 3.02 at the end of study (day 30). The details are given in table 2 and figure 1.

**Assessment of sexual functions (orgasmic function)**
On baseline visit, the mean orgasmic score was 6.41 ± 1.47 which improved significantly to 7.80 ± 0.90 at the end of study (day 30). The details are given in table 3 and figure 2.

**Assessment of sexual functions (sexual desire)**
On baseline visit, the mean score of sexual desire was 6.90 ± 1.10 which improved significantly to 8.06 ± 0.85 at the end of study (day 30). The details are given in table 4 and figure 3.

**Assessment of sexual functions (Intercourse Satisfaction)**
The mean intercourse satisfaction score on baseline visit was 7.80 ± 1.62, which improved significantly to 10.64 ± 1.37 at the end of study (day 30). The details are given in table 5 and figure 4.

**Assessment of sexual functions (overall satisfaction)**
On baseline visit, the mean overall satisfaction was 4.96 ± 1.01, which improved to 7.19 ± 1.10 at the end of study (day 30). The difference observed between the score was statistically significant. The details are given in table 6 and figure 5.

**Hardness of penis on Erection Hardness Score (EHS)**
The Erection Hardness Score (EHS) is a single-item Likert scale that can be a helpful tool to evaluate erectile dysfunction (ED). The tool asks to the person to consider the question "How would you rate the hardness of your erection?" and select one of the following options such as 0 – penis does not enlarge; 1 – penis is larger, but not hard; 2 – penis is hard, but not hard enough for penetration; 3 – penis is hard enough for penetration, but not completely hard; and 4 – penis is completely hard and fully rigid. It was observed that at the baseline visit the EHS score was observed to be 2.56 ± 0.4. The score increased to 3.25 ± 0.39 at the end of the study. This improvement was found to be statistically significant.

**Male sexual health on erectile dysfunction inventory of treatment satisfaction (EDITS) questionnaire (patient & partner version)**
EDITS is a single dimensional (i.e. treatment satisfaction) questionnaire, which has been used to assess the male sexual health. EDITS questionnaire has two versions i.e. patient version and partner version. The patient version of EDITS questionnaire is composed of 11 investigating items. The partner version of EDITS questionnaire is composed of 5 investigating items. Higher score on EDITS shows higher treatment benefits. The responses given to questions of patient version of EDITS questionnaire are given below.

**Overall, how satisfied are you with this treatment?**
The response was recorded on the basis of answers as very satisfied, somewhat satisfied, neither satisfied nor dissatisfied, somewhat dissatisfied, and very dissatisfied. It was observed that 22.58% of subjects were very satisfied; 64.52% subjects were somewhat satisfied; 9.68% of subjects were neither satisfied nor dissatisfied while only 3.22% of subjects were somewhat dissatisfied with the treatment. None of the subject was very dissatisfied. The details are presented in table no. 8.

**During the past four weeks, to what degree has the treatment met your expectations?**
The response was recorded on the basis of answers as completely, considerably, half way, a little and not at all. It was observed that 3.22% of subjects mentioned that their expectation was completely met with this treatment; while 64.52% of subjects mentioned that their expectations were considerably met. 12.90% of subjects mentioned that that their expectations were met half way. 12.90% of subjects mentioned that that their expectations were met a little. Also 6.46% of subjects mentioned that the treatment did not meet their expectations at all. The details are presented in table no. 9.

**How likely are you to continue using this treatment?**
Response to question "How likely are you to continue using this treatment was recorded on the basis of answers as very likely, moderately likely, neither likely nor unlikely, moderately unlikely, and very unlikely. It was observed that 45.16% of subjects mentioned that they are very likely to continue this treatment. 35.48% of subjects mentioned that they are moderately likely to continue this treatment. 19.36% subjects mentioned that there are neither likely nor unlikely to continue the treatment, while none of the subjects mentioned that they are unlikely to continue this treatment. The details are presented in table no. 10.

**During the past four weeks, how easy was it for you to use this treatment?**
Response to question "How easy was it for you to use this treatment was recorded on the basis of answers as very easy, moderately easy, neither easy nor difficult, moderately difficult and very difficult. It was observed that 64.51% of subjects felt that it was either very easy of moderately easy to use this treatment, while 25.80% of subjects felt it was neither easy nor difficult. 9.67% subjects found the treatment to be moderately difficult to take, while none of the subject felt it to be very difficult. The details are presented in table no. 11.

**During the past four weeks, how satisfied have you been with how quickly the treatment works?**
Response to question "How satisfied have they been with how quickly the treatment was recorded on the basis of answers as very satisfied, somewhat satisfied, neither satisfied nor dissatisfied, somewhat dissatisfied, and very dissatisfied. It was observed that 80.64% of subjects felt that they were satisfied (either very or somewhat) that

the treatment works quickly; 12.90% subjects were neither satisfied nor dissatisfied with the quick response to the treatment; 6.46% of subjects were somewhat dissatisfied while none of the subjects were very dissatisfied with the quick response to the treatment. The details are presented in table no. 12.

**During the past four weeks, how satisfied have you been with how long the treatment lasts?**

Response to question "How satisfied have they been with how long the treatment was recorded on the basis of answers as very satisfied, somewhat satisfied, neither satisfied nor dissatisfied, somewhat dissatisfied, and very dissatisfied. It was observed that 9.67% subjects were very satisfied that the treatment lasts long. 70.97% subjects felt that they were somewhat satisfied with the long lasting effect of the treatment. 12.90% were neither satisfied nor dissatisfied with the long lasting effect of the treatment, while 6.46% of subjects were somewhat dissatisfied with the long lasting effect of the treatment. The details are presented in table no. 13.

**How confident has this treatment made you feel about your ability to engage in sexual activity?**

Response to question "How confident has this treatment made them feel about their ability to engage in sexual activity" was recorded on the basis of answers as very confident, somewhat confident, it has had no impact, somewhat less confident and very much less confident. It was observed that 9.67% of subjects were very confident and 77.42% subjects were somewhat confident that this treatment increased their ability to engage in sexual activity. 12.90% of subjects mentioned that the treatment did not have any impact on their sexual ability and none of the subjects were less confident or very much less confident on the treatment's ability to improve their sexual ability. The details are presented in table no. 14.

**Overall, how satisfied do you believe your partner is with the effects of this treatment?**

Response to question "Overall, how satisfied do you believe your partner is with the effects of this treatment was recorded on the basis of answers as very satisfied, somewhat satisfied, neither satisfied nor dissatisfied, somewhat dissatisfied, and very dissatisfied. It was observed that 9.67% of subjects were very satisfied with the treatment; 70.97% were somewhat satisfied; 16.12% of subjects were neither satisfied nor dissatisfied while 3.23% of subjects were somewhat dissatisfied. None of the subjects were very dissatisfied with the treatment. The details are presented in table no. 15.

**How does your partner feel about your continuing to use this treatment?**

Response to question "How does your partner feel about your continuing to use this treatment?" was recorded. It was observed that 41.94% of subjects mentioned that their partner wanted them to absolutely continue the treatment; 38.71% of subjects mentioned that they generally prefer them to continue; 19.35% of subjects mentioned that their partner did not have opinion while none of the subject's partner wanted them to stop the treatment. The details are presented in table no. 16.

**How natural did the process of achieving an erection feel when you used this treatment over the past four weeks?**

Response to question "How natural did the process of achieving an erection feel when you used this treatment over the past four weeks?" was recorded on the basis of answers as very natural, somewhat natural, neither natural nor unnatural, somewhat unnatural and very unnatural. It was observed that 45.16% of subjects mentioned that the process of achieving erection was very natural; 48.39% of subjects mentioned that it was somewhat natural, while 6.45% of subjects felt that the process was neither natural nor unnatural. None of the subjects mentioned that process of achieving erection was very unnatural. The details are presented in table no. 17.

**Compared to before you had an erection problem how would you rate naturalness of your erection when you used this treatment over past 4 weeks in terms of hardness?**

Response to question "Compared to before you had an erection problem how would you rate naturalness of your erection when you used this treatment over past 4 weeks in terms of hardness? was recorded. It was observed that 19.35% of subjects mentioned that as compared to before they achieved a lot harder erection. 54.84% subjects mentioned that as compared to before they achieved somewhat harder erection. 12.90% of subjects mentioned that they did not find any change in the hardness. 9.68% subjects mentioned that they achieved somewhat less hard erection than before. 3.23% subjects mentioned that they achieved a lot less hard erection than before. The details are presented in table no. 18.

**Assessment of Male Sexual Health based on Questions (Partner Version)**

Assessment of sexual health was also done by evaluating the response of the partners of subjects. This was done based on five questions asked to the female partners and were recorded in the Diary. Below are the illustrative responses. The responses given to questions of partner version of EDITS questionnaire are given below.

**Overall, how satisfied are you with this treatment for your husband's or partner's erection problem?**

Response to question "Overall, how satisfied are you with this treatment for your husband's or partner's erection problem?" was recorded on the basis of answers as very satisfied, somewhat satisfied, neither satisfied nor dissatisfied, somewhat dissatisfied, and very dissatisfied. It was observed that 6.45% partners were very satisfied with the treatment. 70.96% of partners were somewhat satisfied with the subject's treatment. 19.35% of the partners were neither satisfied nor dissatisfied with the treatment, while 3.23% of the partners were somewhat

dissatisfied with the treatment. None of the partners were very dissatisfied with the subject's treatment. The details are presented in table no. 19.

**During the past four weeks, to what degree has the treatment met your expectations?**

Response to question "During the past four weeks, to what degree has the treatment met your expectations?" was recorded on the basis of answers as completely, considerably, half way, a little, and not at all. 3.23% partners mentioned that they completely met the treatment expectations. 64.52% of partners mentioned that the treatment has considerably met their expectations; 9.68% of partners mentioned that their expectations have been met halfway while 16.12% of subjects mentioned that their expectations have been met a little. Two subjects (6.45%) mentioned that their expectations have not been met at all. The details are presented in table no. 20.

**Over the past four weeks, how has this treatment affected your sense of being sexually desirable?**

Response to question "Over the past four weeks, how has this treatment affected your sense of being sexually desirable?" was recorded. It was observed that 9.68% of partners mentioned that the treatment made them feel much more sexually desirable. 58.06% partners mentioned that the treatment made them feel somewhat more sexually desirable, 32.26% of subjects felt that the treatment has had no impact on their sense of being sexually desirable. None of the partners felt to be somewhat less or less sexually desirable. The details are presented in table no. 21.

**Over the past four weeks, how satisfied have you been with how long this treatment enhances your husband's or partner's ability to achieve an erection?**

Response to question "Over the past four weeks, how satisfied have you been with how long this treatment enhances your husband's or partner's ability to achieve an erection?" was recorded on the basis of answers as very satisfied, somewhat satisfied, neither satisfied nor dissatisfied, somewhat dissatisfied and very dissatisfied. It was observed that 12.90% of partners were very satisfied; 67.74% of subjects were somewhat satisfied; 19.35% of partners were neither satisfied nor dissatisfied while none of the partner was somewhat dissatisfied or very dissatisfied on this question. The details are presented in table no. 22.

**How do you think your husband or partner feels about continuing this treatment?**

Response to question "How do you think your husband or partner feels about continuing this treatment?" was recorded. It was observed that 45.16% partners mentioned that they think their partner very much wants to continue using treatment. 38.70% of partners mentioned that they think their partner somewhat wants to continue using treatment; 16.13% of subjects were neutral in their opinion about continuing the treatment while none of the partner mentioned of thinking discontinuing the treatment. The details are presented in table no. 23.

**Quality of sexual life on sexual quality of life questionnaire (SQoL-M)**

Subject's quality of sexual life was assessed as per the sexual quality of life questionnaire (SQoL). SQoL questionnaire has 11 questions. It was observed that the mean scores on SQoL questionnaire showed significant improvement from baseline to day 15 which continued till the end of the study (day 30). The table no. 24 illustrates response to questions on sexual quality of life.

**Changes in serum testosterone level**

The mean testosterone level at baseline level was 656.96 ± 203.30 ng/dl which decreased at the end of the study (day 30) to 637.92 ± 233.34 ng/dl. No significant change was observed in the testosterone levels from baseline values to end of the study.

**Global assessment for overall improvement by the investigator and by the patient at the end of the study treatment**

As per the global assessment for overall improvement done by the investigator, 6.45% of subjects showed excellent improvement, 90.32% of subjects showed good to fair improvement while 3.23% of subjects showed poor improvement in their condition. As per the global assessment for overall improvement done by the subject, 90.32% of subjects showed good to fair improvement, 6.45% of subjects showed excellent improvement while 3.23% of subjects reported of poor improvement in their condition.

**Safety assessment**

Almost all subjects showed excellent tolerability to the study drug as per the assessment of tolerability of study drug done by physician and by subject. No statistically significant changes were observed in lab parameters (CBC, lipid profile, liver profile, renal profile and urine routine microscopic) and ECG from baseline visit to the end of the study. Lab parameters remained in the normal range, which showed excellent safety of study drug on these parameters. No significant change from baseline to end of therapy values in any of the vital signs (pulse rate, body temperature, respiratory rate, systolic and diastolic BP) sleep, appetite and bowel movements was observed. Also, no subject had any adverse event or adverse drug reaction during the study period.

**Table 1: Composition of Ayuvigo (Forte) capsule**

| Sr. No. | Ingredients | Scientific Name | Quantity |
|---|---|---|---|
| 1 | Kapikacchu Extract | *Mucuna pruriens* | 75 mg |
| 2 | Ashvagandha Extract | *Withania somnifera* | 75 mg |
| 3 | Gokshura Extract | *Tribulus terrestris* | 75 mg |
| 4 | Bala | *Sida cordifolia* | 120 mg |
| 5 | Shilajit | Asphaltum | 75 mg |

**Table 2: Assessment of sexual functions (erectile function)**

| Erectile Function Baseline | Erectile Function Day 30 |
|---|---|
| Mean 15.96 SD ±3.06 | Mean 21.83 SD ±3.02 p <0.0001 |

**Table 3: Assessment of sexual functions (orgasmic function)**

| Orgasmic Function Baseline | Orgasmic Function Day 30 |
|---|---|
| Mean 6.41 SD ±1.47 | Mean 7.80 SD ±0.90 p < 0.0001 |

**Table 4: Assessment of sexual functions (sexual desire)**

| Sexual Desire Baseline | Sexual Desire Day 30 |
|---|---|
| Mean 6.90 SD ±1.1 | Mean 8.06 SD ± 0.85 p < 0.0001 |

**Table 5: Assessment of sexual functions (Intercourse Satisfaction)**

| Intercourse Satisfaction Baseline | Intercourse Satisfaction Day 30 |
|---|---|
| Mean 7.80 SD ±1.62 | Mean 10.64 SD ± 1.37 p < 0.0001 |

**Table 6: Assessment of sexual functions (overall satisfaction)**

| Overall Satisfaction Baseline | Overall Satisfaction Day 30 |
|---|---|
| Mean 4.96 SD ±1.01 | Mean 7.19 SD ±1.1 p < 0.0001 |

**Table 7: Assessment of Erection Hardness Score.**

| EHS Score - Baseline | EHS Score Day 30 |
|---|---|
| Mean 2.56 SD ±0.45 | Mean 3.25 SD ±0.39 p < 0.05 |

**Table 8: Response to Question 'Overall, how satisfied are you with this treatment'**

| Question 1 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| **Overall, how satisfied are you with this treatment?** | Very satisfied | 7 | 22.58% |
| | Somewhat satisfied | 20 | 64.52% |
| | Neither satisfied nor dissatisfied | 3 | 9.68 % |
| | Somewhat dissatisfied | 1 | 3.22% |
| | Very dissatisfied | 0 | 0 |

**Table 9: Response to the question 'During the past four weeks, to what degree has the treatment met your expectations'**

| Question 2 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| **During the past four weeks, to what degree has the treatment met your expectations?** | Completely | 1 | 3.22% |
| | Considerably | 20 | 64.52% |
| | Half Way | 4 | 12.90% |
| | A little | 4 | 12.90% |
| | Not at all | 2 | 6.46% |

**Table 10: Response to the question "How likely are you to continue using this treatment"?**

| Question 3 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| **How likely are you to continue using this treatment?** | Very likely | 14 | 45.16% |
| | Moderately likely | 11 | 35.48% |
| | Neither likely nor unlikely | 6 | 19.36% |
| | Moderately unlikely | 0 | 0 |
| | Very unlikely | 0 | 0 |

**Table 11: Response to the question "During the past four weeks, how easy was it for you to use this treatment"?**

| Question 4 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| During the past four weeks, how easy was it for you to use this treatment? | Very easy | 8 | 25.80% |
| | Moderately easy | 12 | 38.71 |
| | Neither easy nor difficult | 8 | 25.80% |
| | Moderately difficult | 3 | 9.67% |
| | Very difficult | 0 | 0 |

**Table 12: Response to the question 'During the past four weeks, how satisfied have you been with how quickly the treatment works'?**

| Question 5 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| During the past four weeks, how satisfied have you been with how quickly the treatment works? | Very satisfied | 4 | 12.90% |
| | Somewhat satisfied | 21 | 67.74% |
| | Neither satisfied nor dissatisfied | 4 | 12.90% |
| | Somewhat dissatisfied | 2 | 6.46% |
| | Very dissatisfied | 0 | 0 |

**Table 13: Response to the question "During the past four weeks, how satisfied have you been with how long the treatment lasts"?**

| Question 6 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| During the past four weeks, how satisfied have you been with how long the treatment lasts? | Very satisfied | 3 | 9.67% |
| | Somewhat satisfied | 22 | 70.97% |
| | Neither satisfied nor dissatisfied | 4 | 12.90% |
| | Somewhat dissatisfied | 2 | 6.46% |
| | Very dissatisfied | 0 | 0 |

**Table 14: Response to the question 'How confident has this treatment made you feel about your ability to engage in sexual activity'?**

| Question 7 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| How confident has this treatment made you feel about your ability to engage in sexual activity? | Very confident | 3 | 9.67% |
| | Somewhat confident | 24 | 77.42% |
| | It has had no impact | 4 | 12.90% |
| | Somewhat less confident | 0 | 0 |
| | Very much less confident | 0 | 0 |

**Table 15: Response to the question "Overall, how satisfied do you believe your partner is with the effects of this treatment"?**

| Question 8 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| Overall, how satisfied do you believe your partner is with the effects of this treatment? | Very satisfied | 3 | 9.67% |
| | Somewhat satisfied | 22 | 70.97% |
| | Neither satisfied nor dissatisfied | 5 | 16.12% |
| | Somewhat dissatisfied | 1 | 3.23% |
| | Very dissatisfied | 0 | 0 |

**Table 16: Response to the question "How does your partner feel about your continuing to use this treatment"?**

| Question 9 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| How does your partner feel about your continuing to use this treatment? | My partner absolutely wants me to continue | 13 | 41.94% |
| | My partner generally prefers me to continue | 12 | 38.71% |
| | My partner has no opinion | 6 | 19.35% |
| | My partner generally prefers me to stop | 0 | 0 |
| | My partner absolutely wants me to stop | 0 | 0 |

**Table17: Response to the question 'How natural did the process of achieving an erection feel when you used this treatment over the past four weeks'?**

| Question 10 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| How natural did the process of achieving an | Very natural | 14 | 45.16% |
| | Somewhat natural | 15 | 48.39% |

| | | | |
|---|---|---|---|
| **erection feel when you used this treatment over the past four weeks?** | Neither natural nor unnatural | 2 | 6.45% |
| | Somewhat unnatural | 0 | 0 |
| | Very unnatural | 0 | 0 |

**Table 18: Response to the question 'Compared to before you had an erection problem how you would rate naturalness of your erection when you used this treatment over past 4 weeks in terms of hardness'?**

| Question 11 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| **Compared to before you had an erection problem how would you rate naturalness of your erection when you used this treatment over past 4 weeks in terms of hardness?** | A lot harder than before I had an erection problem | 6 | 19.35% |
| | Somewhat harder than before I had an erection problem | 17 | 54.84% |
| | The same hardness as before I had an erection problem | 4 | 12.90% |
| | Somewhat less hard than before I had an erection problem | 3 | 9.68% |
| | A lot less hard than before I had an erection problem | 1 | 3.23% |

**Table 19: Response to question "Overall, how satisfied are you with this treatment for your husband's or partner's erection problem?"**

| Question 1 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| **Overall, how satisfied are you with this treatment for your husband's or partner's erection problem?** | Very satisfied | 2 | 6.45% |
| | Somewhat satisfied | 22 | 70.96% |
| | Neither satisfied nor dissatisfied | 6 | 19.35% |
| | Somewhat dissatisfied | 1 | 3.23% |
| | Very dissatisfied | 0 | 0 |

**Table 20: Response to question "During the past four weeks, to what degree has the treatment met your expectations?"**

| Question 2 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| **During the past four weeks, to what degree has the treatment met your expectations?** | Completely | 1 | 3.23% |
| | Considerably | 20 | 64.52% |
| | Half Way | 3 | 9.68% |
| | A little | 5 | 16.12% |
| | Not at all | 2 | 6.45% |

**Table 21: Response to question 'Over the past four weeks, how has this treatment affected your sense of being sexually desirable'?**

| Question 3 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| **Over the past four weeks, how has this treatment affected your sense of being sexually desirable?** | It has made me feel much more sexually desirable | 3 | 9.68% |
| | It has made me feel somewhat more sexually desirable | 18 | 58.06% |
| | It has had no impact on my sense of being sexually desirable | 10 | 32.26% |
| | It has made me feel somewhat less sexually desirable | 0 | 0 |
| | It has made me feel less sexually desirable | 0 | 0 |

**Table 22: Response to question 'Over the past four weeks, how satisfied have you been with how long this treatment enhances your husband's or partner's ability to achieve an erection?**

| Question 4 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| **Over the past four weeks, how satisfied have you been with how long this treatment enhances your husband's or partner's ability to achieve an erection?** | Very satisfied | 4 | 12.90% |
| | Somewhat satisfied | 21 | 67.74% |
| | Neither satisfied nor dissatisfied | 6 | 19.35% |
| | Somewhat dissatisfied | 0 | 0 |
| | Very dissatisfied | 0 | 0 |

**Table 23: Response to question 'How do you think your husband or partner feels about continuing this treatment?**

| Question 5 | Observation | No of Subjects at Day 30 | Percentage |
|---|---|---|---|
| **How do you think your husband or partner feels about continuing this treatment?** | I think that he very much wants to continue using treatment | 14 | 45.16% |
| | I think that he somewhat wants to continue using treatment | 12 | 38.70% |
| | I think my partner feels neutral about continuing to use treatment | 5 | 16.13% |
| | I think that he somewhat wants to discontinue using this treatment | 0 | 0 |
| | I think that he very much wants to discontinue using this treatment | 0 | 0 |

**Table 24: Assessment of Sexual Quality of life (Questions)**

| Q. No. | Question | Mean ±SD Baseline Score | Mean Score Day 15 | Mean Score Day 30 |
|---|---|---|---|---|
| 1 | When I think about my sexual life I feel frustrated? | 2.32±0.7 | 2.96±0.54 p<0.0001 | 3.83±0.77 p <0.0001 |
| 2 | When I think about my sexual life I feel frustrated? | 2.54±0.8 | 3.03±0.65 p - 0.012 | 3.87±0.71 p <0.0001 |
| 3 | When I think about my sexual life I feel less like a man? | 2.83±0.77 | 3.22±0.66 p-0.0399 | 3.96± 0.7 p <0.0001 |
| 4 | I have lost confidence in myself as a sexual partner. | 2.51± 0.72 | 3±0.57 p -0.0050 | 3.83±0.73 p <0.0001 |
| 5 | When I think about my sexual life I feel anxious? | 2.54±0.62 | 3.25±0.68 p < 0.0001 | 4±0.77 p < 0.0001 |
| 6 | When I think about my sexual life I feel angry? | 3±1.09 | 3.29±0.73 p -0.22 | 4.03±0.75 p < 0.0001 |
| 7 | I worry about the future of my sexual life | 2.41±0.92 | 2.96±0.87 p - 0.019 | 3.74±0.63 p < 0.0001 |
| 8 | When I think about my sexual life I feel embarrassed? | 2.58±0.84 | 3.03±0.75 p -0.030 | 3.74±0.72 p < 0.0001 |
| 9 | When I think about my sexual life I feel guilty? | 2.48±0.76 | 3±0.63 p 0.005 | 3.83±0.73 p < 0.0001 |
| 10 | When I think about my sexual life I worry that my partner feels hurt or rejected? | 2.64±0.75 | 3.03±0.65 p -0.035 | 3.83±0.63 p < 0.0001 |
| 11 | When I think about my sexual life I feel I have lost something? | 2.29±0.9 | 2.74±0.72 p <0.05 | 3.51±0.72 p < 0.0001 |

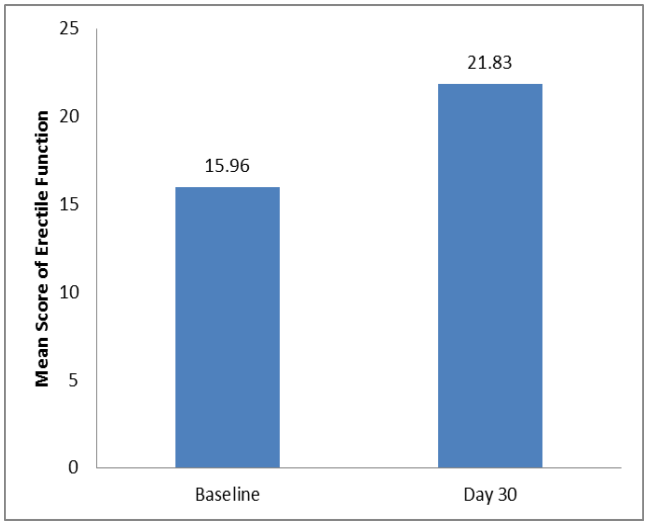


**Figure 1: Assessment of sexual functions (erectile function)**

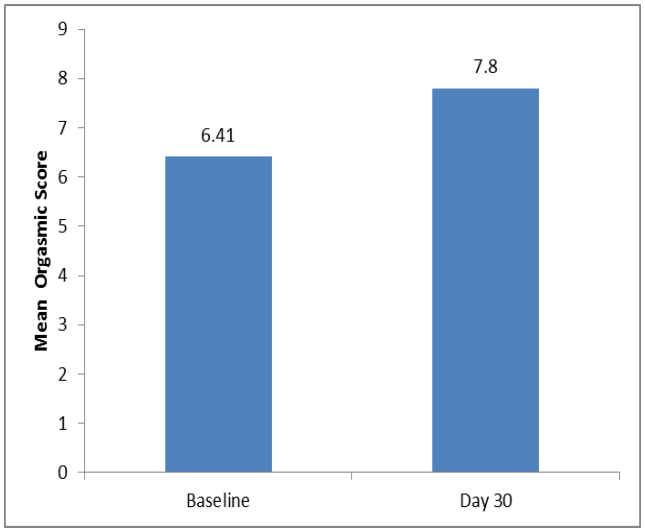


**Figure 2: Assessment of sexual functions (orgasmic function)**

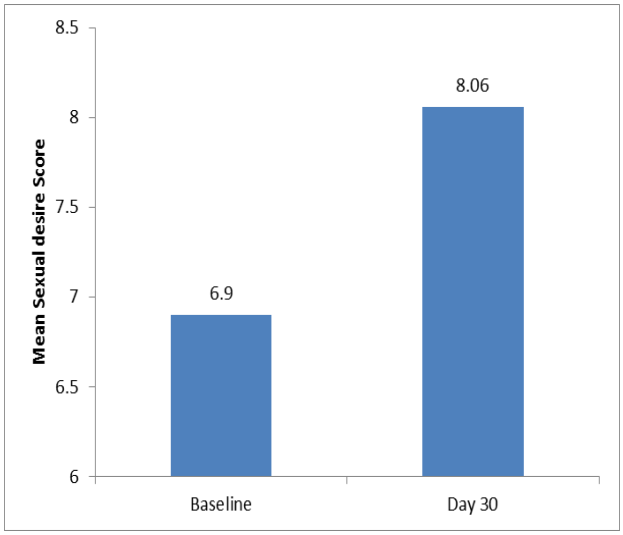


**Figure 3: Assessment of sexual functions (sexual desire)**

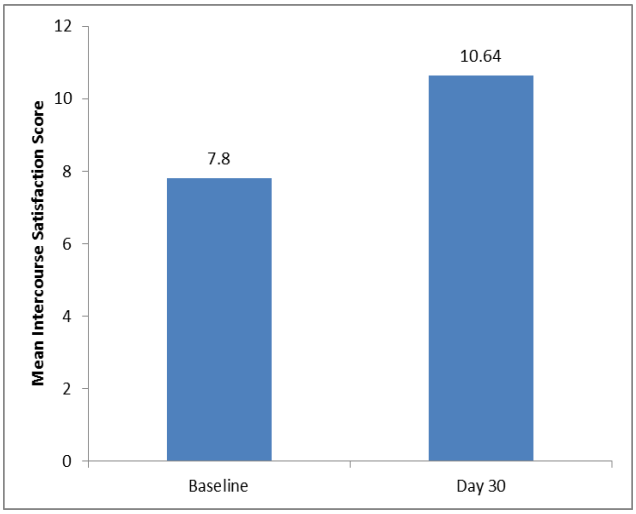


**Figure 4: Assessment of sexual functions (intercourse satisfaction)**

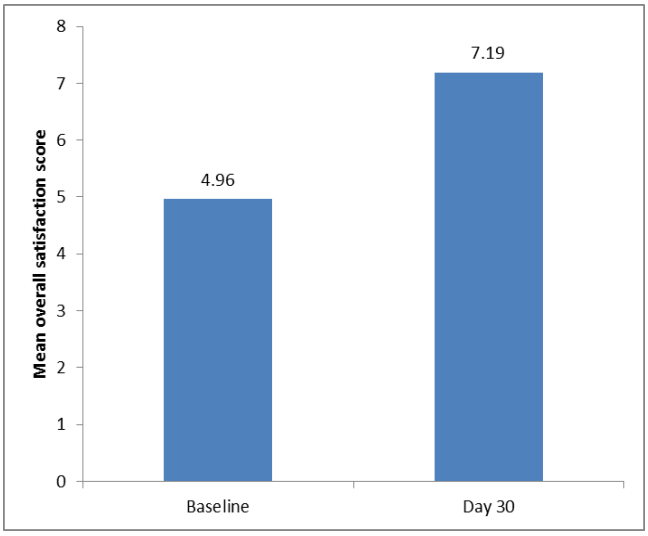


**Figure 5: Assessment of sexual functions (overall satisfaction)**

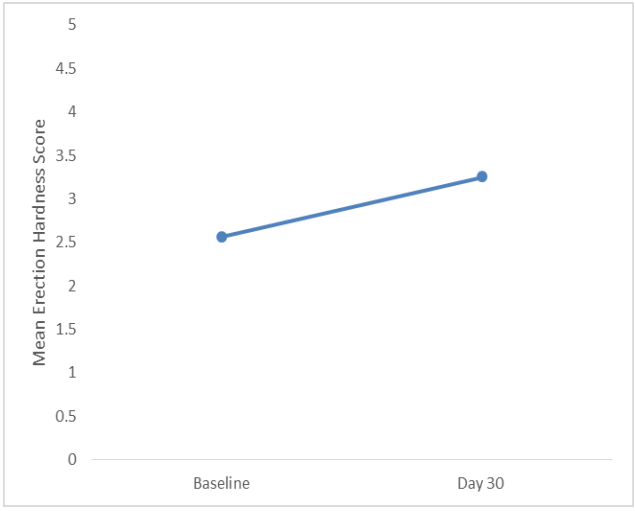


**Figure 6: Assessment of erection hardness score (EHS)**

## DISCUSSION

The present study was carried out to evaluate the efficacy and safety of Ayuvigo Forte capsule in patients suffering from mild to moderate erectile dysfunction. All the subjects were received two Ayuvigo Forte capsule thrice daily orally after meals with water for 30 days. During entire study period excellent compliance to the study drug was observed.

It has been observed that consumption of Ayuvigo Forte capsules in subjects suffering from mild to moderate erectile dysfunction significantly improves the condition as observed on various parameters. Evaluation of erectile function of penis as per erectile function subscale of IIEF Questionnaire showed a significant improvement over a period of 30 days. Evaluation of male sexual health on EDITS questionnaire (patient & partner version) also showed a significant improvement at the end of the study period. Quality of sexual life on sexual quality of life questionnaire (SQoL-M) showed a significant improvement as evaluated by various questions. There was no significant change in the testosterone level. As per the global assessment for overall improvement by investigator and by patient at the end of the study treatment, it showed that a majority of subjects had good response to the treatment. The study drug was found to be safe as no adverse drug reactions were observed. The vital parameters like pulse, respiration rate etc. and laboratory investigations like renal profile, liver profile, lipid profile and CBC were found to be non-significantly changed.

The results of this clinical study on Ayuvigo Forte Capsules are in line with the results of the earlier clinical studies conducted on Ayurvedic proprietary medicines (with respect to the ingredients used in the formulation) for erectile dysfunction.[30-31] The formulation Ayuvigo Forte capsule was developed by Welex Laboratories Private Limited, which contains a unique combination of 5 ingredients such as Kapikacchu (*Mucuna pruriens*), Ashvagandha (*Withania somnifera*), Gokshura (*Tribulus terrestris*), Bala (*Sida cordifolia*), and Shilajit (asphaltum). Since ages, these ingredients have been used in Ayurveda for the treatment of erectile dysfunction and loss of libido. Ingredients of Ayuvigo Forte capsule have aphrodisiac, rejuvenator and libido enhancer activities. Most of these ingredients help to increase androgen levels, sexual desire and performance in males. Also, these ingredients are useful to promote stamina, a sense of well-being vigor, semen, and sperm count.[9-29] It was observed from results of this clinical study that the synergistic effect of the herbs present in the formulation has beneficial effects in loss of libido and mild to moderate erectile dysfunction of patients. Hence, it has been said that Ayuvigo Forte capsule is a safe and effective medicine for the treatment of loss of libido and mild to moderate cases of erectile dysfunction. However, further study should be planned with larger number of study population to establish the efficacy and safety of the herbal Ayurvedic formulations.

## CONCLUSION

The study concluded that Ayuvigo Forte capsule is a safe and effective medicine for the treatment of loss of libido and mild to moderate cases of erectile dysfunction.

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