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ORIGINAL ARTICLE

Evaluation of Aphrodisiac Activity of AHPL/AYCAP/0114 Capsule in Sexually Sluggish Male Rats

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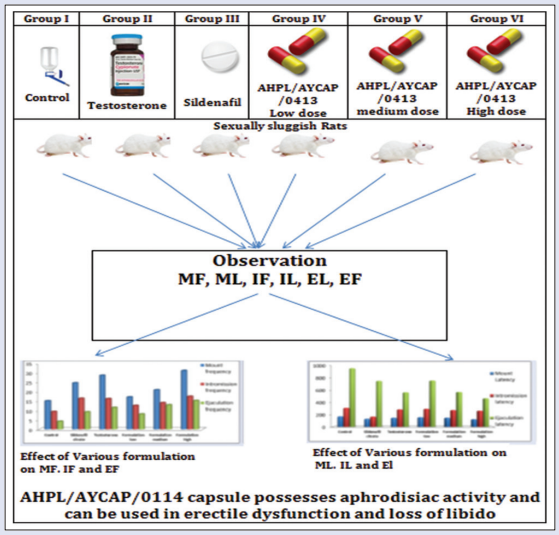
ABSTRACT

Background: Male sexual dysfunction includes a wide range of problems such as erectile dysfunction and premature ejaculation, for which medical help is sought. The conventional use of various pharmacological and nonpharmacological measures are associated with multiple adverse events. Hence, a polyherbal formulation AHPL/AYCAP/0114 capsule was developed to provide safe and effective therapeutic option. **Objectives:** The aim of this study was to evaluate the aphrodisiac potential of AHPL/AYCAP/0114 capsule by assessing sexual behavior parameters such as mount frequency (MF), mount latency (ML), intromission frequency (IF), intromission latency (IL), ejaculation latency (EL), and ejaculation frequency (EF) in sexually sluggish male rats. **Materials and Methods:** Male Wistar rats were divided into six groups (n = 6) and treated with testosterone (30 mg/kg), sildenafil citrate (0.5 mg/kg), and AHPL/AYCAP/0114 capsule (110, 220, and 440 mg/kg) as Group II, Group III, and Group IV, V, and VI, respectively, for 28 days. Group I animals served as control. Then, they were introduced to sexually active female rats and their sexual behavior was recorded. **Results:** A significant increase in MF, IF, and EF was observed in all the AHPL/AYCAP/0114 capsule groups as compared to control group. A significant decrease in ML, IL, and EL was observed in all the AHPL/AYCAP/0114 capsule groups as compared to control group. AHPL/AYCAP/0114 capsule was well tolerated by rats. **Discussion:** Increase in MF, IF, and EF and reduction in ML, IL, and EL are indicative of increased sexual motivation and arousal and prolonged duration of coitus. This suggests enhanced sexual performance in sexually sluggish animals treated with AHPL/AYCAP/0114 capsule. **Conclusion:** It can be concluded that AHPL/AYCAP/0114 capsule possesses aphrodisiac activity and can be used in erectile dysfunction and loss of libido.

Key words: AHPL/AYCAP/0114 capsule, aphrodisiac, erectile dysfunction, loss of libido, premature ejaculation

SUMMARY

- Aphrodisiac Activity of AHPL/AYCAP/0114 Capsule
- A polyherbal formulation AHPL/AYCAP/0114 capsule was developed by Ari Healthcare Pvt. Ltd. Intended to be used in erectile dysfunction and loss of libido. The aphrodisiac potential of AHPL/AYCAP/0114 capsule was assessed by testing sexual behavior parameters such as mount frequency (MF), mount latency (ML), intromission frequency (IF), intromission latency (IL), ejaculation latency (EL), and ejaculation frequency (EF) in sexually sluggish male rats. Male Wistar rats were used for the study. A significant increase in MF, IF, and EF was observed in all the AHPL/AYCAP/0114 capsule groups as (low, medium and high dose) compared to control group. A significant decrease in ML, IL, and EL was observed in all the AHPL/AYCAP/0114 capsule groups as compared to control group. Increase in MF, IF, and EF and reduction in ML, IL, and EL are indicative of increased sexual motivation and arousal and prolonged duration of coitus. It can be concluded that AHPL/AYCAP/0114 capsule possesses aphrodisiac activity and can be used in erectile dysfunction and loss of libido.



Abbreviations used: (MF): Mount frequency; (ML): Mount latency; (IF): Intromission frequency; (IL): Intromission latency; (EL): Ejaculation latency; (EF): Ejaculation frequency; (ED): Erectile dysfunction; CPCSEA: Committee for the Purpose of Control And Supervision of Experiments on Animals.

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INTRODUCTION

Until a decade ago, research and development in the field of male sexual dysfunction was on back foot. A lot of attention was focused on the development of drugs to improve the sexual potency in men only after the outburst of Viagra onto the scene.[1] According to the National Health and Social Life Survey of the USA, the prevalence of sexual dysfunction in males was 31%.[3] The male sexual dysfunction comprises primarily two disorders, namely, erectile dysfunction (ED) and

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premature ejaculation (PE)[2] In Asia, the prevalence of ED is estimated to be 9%–73% and that of PE was estimated to be 20%–32.7%.[1] In accordance with the above data it is found that, among these two types, ED is so much common that, many times, term male sexual dysfunction is used synonymously with ED. However, it is believed that such surveys probably provide underestimates of the current situation, and the incidence of the male sexual dysfunction could be much higher considering the tendency of feeling of embarrassment in seeking help for such problems.

Erectile dysfunction is a persistent inability to attain and maintain erection sufficient for satisfactory sexual performance. It is a vascular phenomenon under hormonal control and shares common risk factors with cardiovascular diseases. Besides lifestyle modification, first-line therapy for ED includes the use of PDE5 inhibitors that cause smooth muscle relaxation and increased arterial blood flow leading to penile erection. Drug-free noninvasive treatment options such as use of vacuum erection devices, shockwave therapy are also employed in suitable cases. Other available therapeutic options include intracavernous injections of alprostadil and papaverine and use of penile prostheses.[2]

However, the use of above-mentioned modalities of treatment is limited because of associated adverse events right from headache to increased risk of myocardial infarction. Further patients are usually reluctant to make use of invasive treatment methods. Hence, there is obvious increased need for safe but effective, satisfactory, and noninvasive treatment for ED.[2]

AHPL/AYCAP/0114 capsule is conceptualized and developed by Ari Healthcare Pvt. Ltd. AHPL/AYCAP/0114 capsule is a polyherbal formulation containing *Gokshura extract (Tribulus terrestris),*[12-15] *Ashvagandha extract (Withania somnifera),*[16-22] *Shwet musali extract (Asparagus adscendens),*[23-26] *Kapikacchu extract (Mucuna pruriens),*[27-31] *Nagavalli extract (Piper betle),*[32,33] *Jatiphala extract (Myristica fragrans),*[34] *Lavanga extract (Syzygium aromaticum),*[37] *and Kesara powder (Crocus sativus).*[38-40] In Ayurveda, all these herbs have been used for aphrodisiac (*Vajikara, Vrishya*) and spermatogenic (*Shukrala*) activity since thousands of years. They have also been experimentally evaluated for these activities and displayed satisfactory results. Therefore, the present study was conducted to evaluate aphrodisiac potential of AHPL/AYCAP/0114 capsule in sexually sluggish rats in comparison with standard drugs, i.e., sildenafil and testosterone.

MATERIALS AND METHODS[3-6]

Rats of Wistar strain weighing 200–250 g were housed in group of seven under standard laboratory conditions of temperature and 12 h/dark cycle with free access to standard pellet diet and water. Laboratory animal handling and experimental procedures were performed in accordance with the CPCSEA guidelines (198/99/CPCSEA) and study protocol.

Pharmacological evaluation of aphrodisiac activity[41]

Female rats were ovariectomized under ether anesthesia and after full recovery brought them into estrous state by the sequential subcutaneous administration of 10 μg/kg body weight of estradiol benzoate and 500 μg/kg body weight of progesterone at 48 and 4 h before copulatory studies, respectively. Sexually active adult males (different from the ones used in the study) showing copulatory behavior, i.e., solicitation and lordosis in response to mounting in the study were rejected. Preliminary screening was carried out to identify the sexually sluggish males. Briefly, the male rats were placed singly with sexually receptive females for 30 min at seven different occasions, with a gap of 5 days between each exposure. Male Wistar rats that failed to achieve ejaculation during any of the past three exposures considered to be sexually sluggish and used for further study. Sexually sluggish male Wistar rats were divided into six groups (n = 6) and placed in separate cages. Animals belonging to Group I served as control and received 2 ml/kg vehicle (1% gum acacia) and animals belonging to Group II and III served as standard and received sildenafil citrate at the dose 30 mg/kg and testosterone at the dose of 0.5 mg/kg IM, respectively. Animals belonging to Group IV, V, and VI served as test and received formulation, i.e., AHPL/AYCAP/0114 capsule at a dose of 110, 220, and 440 mg/kg as low, medium, and high-dose levels, respectively.

Dosage and routes of administration

1. Control: Gum acacia (1%, 2 ml/kg p. o.) in saline water (10 ml)
2. Sildenafil citrate: Sildenafil citrate (30 mg/kg, p. o.) + saline water (10 ml)
3. Testosterone: Testosterone (0.5 mg/kg, i. m.) + saline water (10 ml)
4. Formulation low: AHPL/AYCAP/0114 capsule (110 mg/kg, p. o.) + saline water (10 ml)
5. Formulation medium: AHPL/AYCAP/0114 capsule (220 mg/kg, p. o.) + saline water (10 ml)
6. Formulation high: AHPL/AYCAP/0114 capsule (440 mg/kg, p. o.) + saline water (10 ml).

The drugs were administered for 28 days. On day 28, 50 min after the drug treatment, the animals were placed in a glass cage (40 cm × 50 cm × 40 cm). After an adaption period of 10 min, sexually receptive females were presented to the male by dropping into the cage. Sexual behavior parameters such as mount frequency (MF), mount latency (ML), intromission frequency (IF), intromission latency (IL), ejaculation frequency (EF), and ejaculation latency (EL) were assessed for 30 min by direct observation by the investigators.

MF is the number of mounts from the time of introduction of the female until ejaculation. IF is the number of intromissions from the time of introduction of the female until ejaculation, and ML is the time interval between the introduction of the female and the first mount by the male. Other parameters were IL, which was the time interval between the introduction of the female and the intromission by the male, EF, which is the number of ejaculations from the time of introduction of the female rats to the male within a given time interval (30 min), and ejaculatory latency (EL) which is the time interval between the first intromission and ejaculation.[7]

The percentage of mounting, intromission, and ejaculation was calculated by the following formulae:

Percentage of MF = (number of mounted/number paired) ×100

Percentage of intromission = (number of intromissions/number paired) ×100

Percentage of ejaculation = (number of ejaculations/Number paired) ×100

Statistical analysis

Recorded values were expressed as mean ± standard error of mean. Statistical analysis was performed using ANOVA followed by Dunnett's test. The values were considered to be statistically significant if $P < 0.01$.

RESULTS AND DISCUSSION

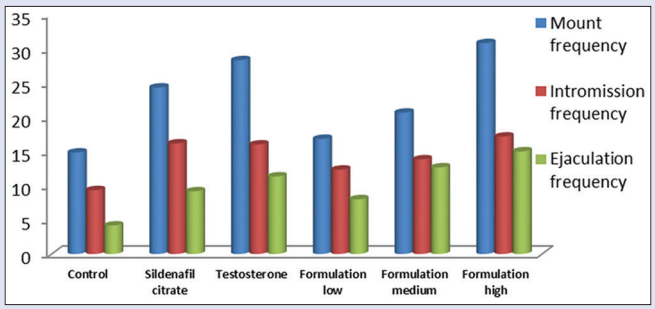
The present study was conducted to establish efficacy and safety of AHPL/AYCAP/0114 capsule in sexually sluggish male rats. Aphrodisiac potential of three dosages (low, medium, and high) of AHPL/AYCAP/0114 capsule was assessed in sexually sluggish male rats in comparison with standard drugs, i.e., sildenafil and testosterone.

Various behavioral patterns were observed in the study to assess the overall sexual activity of the animals. The number of mount (MF) reflects sexual

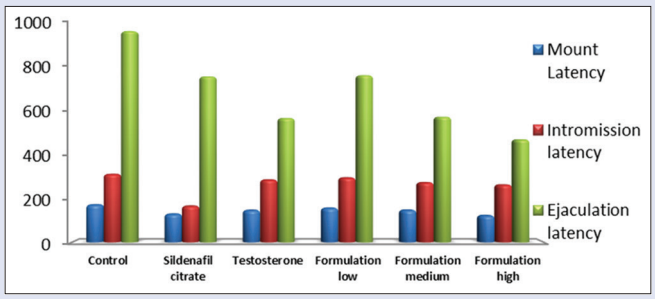
Table 1: Effect of various formulations on mount frequency, intromission frequency, ejaculation frequency, mount percentage, intromission percentage, and ejaculation percentage

Group	MF	IF	EF	ML	EL	IL	Percentage of mounted	Percentage of intromission	Percentage of ejaculation
Control	14.83±0.47	9.33±0.33	4.16±0.30	170.83±1.02	964.83±3.40	310.83±48.10	61.79	38.87	17.33
Sildenafil citrate	24.33±0.49**	16.16±0.40**	9.16±0.47**	128.33±1.14**	757.5±2.23**	165±36.35**	97.32**	64.64**	36.64**
Testosterone	28.33±0.42**	16±0.51**	11.33±0.42**	145.5±1.17**	567.33±1.87**	285.5±38.88**	97.68**	55.17**	39.06**
AHPL/AYCAP/0114 capsule low dose	16.83±0.30**	12.33±0.42**	8±0.36**	155.5±1.05**	763.33±2.23**	295±43.90**	84.15**	61.65**	40**
AHPL/AYCAP/0114 capsule medium dose	20.66±0.42**	13.83±0.47**	12.66±0.49**	146.33±0.84**	573±1.65**	273±39.44**	93.90**	62.86**	57.54**
AHPL/AYCAP/0114 capsule high dose	30.83±0.30**	17.16±0.30**	15±0.36**	121.5±1.05**	469.5±0.95**	262.5±34.15**	96.34**	68.64**	60**

Data are expressed as mean±SEM (n=6), one-way ANOVA followed by Dunnett's test, **P<0.01 (all groups were compared with sildenafil and testosterone).
MF: Mount frequency; IF: Intromission frequency; EF: Ejaculation frequency; ML: Mount latency; EL: Ejaculation latency; IL: Intromission latency; SEM: Standard error of mean



Graph 1: Effect of various formulations on mount frequency, intromission frequency, and ejaculation frequency



Graph 2: Effect of various formulations on mount latency, intromission latency, and ejaculation latency

motivation whereas increase in the number of intromission (IF) shows the efficiency of penile erection, penile orientation, and the ease by which ejaculatory reflexes are activated.[7] After the treatment with formulations for 28 days, it was observed that MF, IF, and ejaculatory frequency (EF) significantly increased in all the treatment groups when compared to control group [Table 1 and Graph 1]. The increase in MF and IF observed after administration of AHPL/AYCAP/0114 capsule in sexually sluggish male rats suggests improved libido/sexual vigor, improved erection, and sustenance of erection than normal control group. When compared between the treatment groups, no statistically significant difference was observed. However, the high-dose formulation of AHPL/AYCAP/0114 capsule proved to be the most effective treatment in terms of increasing MF, IF, and EF. Although high dose is better than other formulations tested, medium dose of AHPL/AYCAP/0114 capsule is equally effective and can be administered in human beings with the greatest level of safety. The increase in EF observed with the administration of treatment is an indication of enhanced aphrodisiac effect of the formulation.[7]

ML and IL are considered as indicators of sexual motivation.[8] Both parameters are inversely proportional to sexual motivation. In the present study, significant reduction in time intervals, namely ML, IL, and EL was observed in all treatment groups when compared to normal control group. This is suggestive of increase in the sexual motivation and arousal. The result supports the sexual arousal and motivation improvement effect of AHPL/AYCAP/0114 capsule. The difference between the treatment groups was not statistically significant [Table 1 and Graph 2]. The percentage of mounting, intromission, and ejaculation when calculated was found highest in high-dose formulation group as compared to rest of the groups [Table 1].

Increased MF and IF indicate uninhibited copulatory efficiency, increased libido, sexual vigor, and improved sexual performance. The increase in EF in all the groups treated with AHPL/AYCAP/0114 capsule and standard drug(s) in this study indicated enhanced sexual performance as evident from prolonged duration of coitus and increased sexual motivation.

Enhancement of the libido, sexual motivation, and sexual performance is believed to be linked with the increased concentration of anterior pituitary hormones and serum testosterone. These, in turn, increase the synthesis of dopamine receptor which is a key neurotransmitter in the control of locomotor activity essential for the display of copulatory and sexual behavior.[9-11]

Almost all ingredients of AHPL/AYCAP/0114 capsule possess aphrodisiac activity. Herbs such as *Gokshura,*[12-15] *Ashvagandha,*[16-22] and *Kapikacchu*[27-31] help to improve androgen levels; exert testosterone-like effect, and thereby increase libido and sexual motivation. The locomotor behavior required for copulatory activity is under the control of dopamine. Since *M. pruriens* has direct dopamine-enhancing effect, it helps to improve sexual behavior[9-11] *Gokshura*[12] improves the erectile function probably by release of nitric oxide.[14,15] *Ashvagandha, Kapikachhu, Nutmeg,*[34-36] *Shwet musali,*[23-25] and *Kesar*[38-40] possess proven antidepressant action which helps to relieve anxiety and depression related to sexual dysfunction. *Nagavalli*[32,33] and *Lavang*[37] possess aphrodisiac property. *Jatiphala*[34] helps in delaying the ejaculation, thereby sustaining the erection. Most of the herbs also help to improve spermatopoiesis.

Thus, herbs present in AHPL/AYCAP/0114 capsule act on various pathways and help in enhancing libido, androgen levels, eliminating psychological element involved in sexual dysfunction, delaying the ejaculation time, and thus sustaining the erection during the intercourse. Thus, AHPL/AYCAP/0114 capsule can be effectively used in loss of libido and erectile dysfunction.

CONCLUSION

It is revealed from the results of the study that AHPL/AYCAP/0114 capsule significantly enhanced sexual behavior in sexually sluggish male rats. Thus, AHPL/AYCAP/0114 capsule possesses aphrodisiac activity and can be used for the management of loss of libido, erectile dysfunction, premature ejaculation, and impotency.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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