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Effect of Abutilon indicum extract on Female Libido in Rats

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Abstract: Female sexual dysfunction (FSD) is a prevalent, yet largely unrecognized, disorder. Approximately 30–50% of women report sexual complaints, though the number that are distressed about sexual dysfunction and would seek treatment is a smaller proportion. FSD has historically been considered a primarily psychological disorder, though it is now clear that it can also occur secondarily to other organic medical problems. Several conventional medicines are available at present but they are associated with various untoward effects and are less efficacious. This has diverted the researchers towards the potential of medicinal plants and its polyherbal formulations claimed in the traditional systems of medicines like Ayurveda. These therapies can be successfully integrated with conventional therapy to provide maximal benefits to patients. *Abutilon indicum,* one of the plants from Ayurvedic system of medicine has been traditionally claimed to enhance the libido but has not been scientifically documented so in the present investigation methanolic extract of areal parts of *Abutilon indicum* was investigated for the libido enhancement activity at doses 100, 200 and 400 mg/kg using automated runway methodology and coupulatory behavior models. The results revealed that the extract significantly improved the runway parameters and coupulatory behavior exhibiting its effectiveness in enhancing the female libido.
Key words: *Abutilon indicum*, libido, runway apparatus, coupulatory behaviour.

INTRODUCTION:

Libido refers to a fluctuating state of sexual motivation in all organisms (Pfaus and Scepkowski, 2005) wherein there exist constant fluctuations in sexual arousal, desire and inhibition[1]. A decrease in sex drive (libido) is something that affects millions of women of all ages worldwide, although the largest decrease is seen in menopausal aged women[2]. Female sexual dysfunction (FSD) is considered as a significant age-related, progressive and highly prevalent problem that affects a substantial number of women[3]. The National Health and Social Life Survey reported that 43% of women experienced sexual problems as compared to 31% of men suggesting that sexual dysfunction is more commonly related to women than men[4].

Over the past few years, great progress has been made in both the recognition of female sexual dysfunction as a genuine medical disorder and its treatments to address it. Several drugs of the current treatment strategies target the central control of sexual function through the dopamine, serotonin, and melanocortin transmitter systems, with the aim of modifying desire and subjective arousal. Despite significant advances in sexual medicine over the past 15 years, attraction to natural remedies appears to continue. Because some herbal medicines are also promoted as general health supplements, users may not only view them as a more natural way of dealing with their problems, but they may also perceive them as providing health benefits beyond those specifically related to sexual performance[5]. The majority of FSD patients are

currently poorly treated and so the arrival of these novel treatments in the market place is eagerly awaited[6].

Abutilon indicum (Indian Abutilon, Indian Mallow; syn. Sida indica L.), a traditionally claimed medicinal plant, belongs to the family Malvaceae. It is found distributed throughout the warmer parts of India, especially eastern part of Maharashtra[7], often dominant on disturbed land.

The plant is widely claimed in Ayurveda and Siddha medicines. In fact, the root, bark, flowers, leaves and seeds are all used for medicinal purposes which the Tamils knew from Time immemorial.

Dried whole plant is used as laxative and demulcent[8], febrifuge, anthelmintic, diuretic, anti–inflammatory especially in urinary and uterine discharges, piles, lumbago[9]. The demulcent action of herbs coupled with its ability to reduce excessive gastric acid gives relief to acid dyspepsia[10]. The folk practitioners also used the whole plant to control severe dysentery, fever and allergy. The areal parts of the plant are traditionally claimed as an aphrodisiac, to promote the libido and to relieve menorrhagia and also recommended to increase semen in men[10,11,12] not yet documented scientifically. In the present investigation, the methanolic extract of Abutilon *indicum* (AI) was evaluated for the libido improvement using various animal models of Libido.

MATERIALS AND METHODS:

Plant material:

Aerial parts of *Abutilon indicum* (AI) were purchased from local market and authenticated.

Preparation of extract:

Powdered material of aerial parts of AI was charged into soxhlet apparatus and extraction was carried out using petroleum ether, diethyl ether, chloroform, ethyl acetate and methanol. For water a simple decoction was prepared.

Equipments used

Automated runway apparatus (VJ Instruments, India) and Copulatory arena zone apparatus with video output (VJ Instruments, India).

Chemicals and drugs:

Methotrexate tablets (Neotrexate), Indomethacin Capsule (Indocap), Complete Freund's Adjuvant. Sigma-Aldrich USA, Ketamine injection (Hypnoket), Framycetin cream (Soframycin), Sesame oil, propylene glycol, Cotton thread, Diazepam injections, Geriforte tablets, Ashwagandha powder (Himalaya drugs) 43 mg/kg were purchased from the local market. Estradiol benzoate AR and progesterone AR were purchased from the Rajesh Chemicals, Mumbai. Ethylenediamine tetra acetic acid (EDTA) (1 mM), $FeCl_3$(10 mM), H_2O_2 (10 mM), deoxyribose (10 mM), phosphate buffer (50 mM, pH 7.4), ascorbic acid (1 mM), Trichloroacetic acid, 0.5% thiobarbituric acid (TBA) (in 0.025M NaOH containing 0.025% butylated hydroxyanisole BHA), phosphate buffer (0.2 M, pH 6.6), potassium ferricyanide (1%), Ferric chloride (0.1%) was purchased from local approved vendor.

Preparation of drug solution:

Accurately weighed quantities of both the powdered extracts were dissolved in distilled water to prepare the appropriate stock solution of the drug from which the different doses were administered by selecting the appropriate concentration of the stock solution**.**

Animals:

Wistar albino rats of both sex (120-150 gm) and adult male albino mice (20-30gm) were used. They were maintained at 25 ± 2° C and relative humidity of 45 to 55% and under standard environmental conditions (12 h light: 12 h dark cycle). The animals had free access to food (Amrut feed, Chakan oil mills, India) and water *ad libitum* throughout study. Institutional Animal Ethical Committee approved the protocol. All the experiments were carried out between 9:00- 16:00 hour.

All mice were free of any toxicity as per acceptable range given by the OECD guidelines up to the dose of 2000 mg/kg. From this data and pilot study reports; three different doses 100, 200 and 400 mg/kg were selected for this study.

Automated run way methodology performance:

Effect of AI extract on automated run way methodology performance of female rats in estrous (EB+P) state.

Runtime

Runtimes in the estrous state for various goal box targets like empty, male and female was as 15.26 ± 1.70, 8.85 ± 0.78, 9.82 ± 1.24 respectively. 11 days and 21 days pretreatment with AI 400 significantly lowered runtime for male target ($p<0.05$, $p<0.01$). Moreover, AI significantly lowered the run times for female target at the dose 400 mg/kg. AI 200 significant reduced the runtime for male target only after 11 days, whereas AI-100 did not show any significant activity for any of the targets.

Table 1: Effect of AI extract on run time of estrous females for three goalbox targets.

Treatment (mg/kg)		Run time (seconds)		
		Empty target	**Male target**	**Female target**
After 11 days treatment	Control (10ml/kg)	15.26±1.70	8.85±0.78	9.82±1.24
	AI-100	9.06±1.38	6.7±0.79	9.28±2.09
	AI -200	8.78±1.04	5.48±0.70*	5.33±1.00
	AI -400	8.86±1.26	5.13±0.43*	3.95±0.67*
After 21 days treatment	Control (10ml/kg)	15.10±1.91	08.99±0.80	9.90±1.05
	AI -100	9.5±1.11	5.03±0.69*	9.5±0.90
	AI -200	9.26±1.63	5.16±0.53*	5.23±1.6
	AI -400	8.83±1.46	4.43±0.49**	4.63±0.79*

Results are expressed as mean ± SEM (n=6). Data was analysed by one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p<0.01.

Proximity Time

No significant effect was observed by any of pretreatment of AI on proximity time for any of the goal box target.

Core Proximity Time

Pretreatment with AI 100, 200 and 400 significantly improved the core proximity time only for male target (p<0.01) as compared to control rats. There was no significant change in core proximity time till entire 21 days treatment schedule for female and empty target (except in case of 400 mg/kg).

Table 2: Effect of AI extract on Proximity Time of estrous females for three goalbox targets.

Treatment (mg/kg)		Proximity time (seconds)		
		Empty target	**Male target**	**Female target**
After 11 days treatment	Control (10ml/kg)	5.02±0.89	1.99±0.34	3.69±0.57
	AI-100	4.56±0.71	2.36±0.33	3.05±1.04
	AI -200	6.05±0.41	2.75±0.40	4.15±0.74
	AI -400	7.06±1.1	1.68±0.36	4.55±1.84
After 21 days treatment	Control (10ml/kg)	5.10±0.90	2.05±0.42	3.75±0.66
	AI -100	3.16±0.58	2.48±0.41	3.31±0.74
	AI -200	5.38±2.15	2.91±0.43	4.58±0.72
	AI -400	4.33±1.67	1.91±0.53	4.26±0.89

Results are expressed as mean ± SEM. (n=6). Data was analysed by one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p<0.01.

Table 3: Effect of AI extract on Core Proximity Time of estrous females for three goalbox targets.

Treatment (mg/kg)		Core Proximity time (seconds)		
		Empty target	**Male target**	**Female target**
After 11 days treatment	Control (10ml/kg)	59.61±5.20	61.16±3.76	60.88±3.47
	AI-100	56.1±4.98	90.83±3.84**	61.45±5
	AI -200	53.6±11.77	90.51±4.44**	67.1±4.09
	AI -400	63.21±13.41	97.78±5.37**	60.53±7.02
After 21 days treatment	Control (10ml/kg)	61.10±4.48	58.30±5.01	62.28±4.59
	AI -100	57.71±3.86	94.6±5.72**	65.58±3.77
	AI -200	86.85±12.57	94.88±5.19**	64.03±7.01
	AI -400	92.66±14.14*	108.68±7.57**	57.35±7.08

Results are expressed as mean ± SEM. (n=6). Data was analysed by one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p<0.01.

Reentries
No significant change was seen in the reentries for any of the targets by any of the dose of AI.

Table 4: Effect of AI extract on Reentries of estrous females for three goalbox targets.

Treatment (mg/kg)		Reentries (seconds)		
		Empty target	**Male target**	**Female target**
After 11 days treatment	Control (10ml/kg)	14.83±1.15	10.33±0.79	14.05±1.11
	AI-100	13.83±1.10	9.5±0.92	09.50±1.17
	AI -200	17.16±3.22	8.5±1.23	11.66±2.41
	AI -400	11.66±1.30	8.66±0.98	10.66±1.14
After 21 days treatment	Control (10ml/kg)	14.50±1.22	10.10±0.83	13.95±1.76
	AI -100	12.83±1.62	9.16±0.94	12.00±1.91
	AI -200	13.33±1.85	10±1.52	12.16±2.46
	AI -400	13.16±2.38	8.33±1.28	12.16±1.97

Results are expressed as mean ± SEM. (n=6). Data was analysed by one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p<0.01.

Copulatory test:

Female rat Copulatory signs:

Proceptive Parameters

The 11 days pretreatment with AI 400 mg/kg showed significant equipotent increase in hops, darts and solicitation (p<0.05) and thereby exhibited proceptive behavior. While 21 days pretreatment with AI-200 and 400 mg/kg showed significant increase in hops, darts, Ear wig, and solicitation. AI- 400mg/kg was found to be more significant than AI-200mg/kg. AI-100 was ineffective on both these days.

Receptive Parameters:

The major receptive behavior i.e., lordosis and the lordosis quotient was not significantly improved by any of the doses of the female libido formula irrespective of the treatment period.

Table 5: Effect of AI extract (After 11 days of treatment) on Female proceptive parameters

Parameters	Control	AI-100	AI-200	AI-400
Hops	18.5±0.99	18.16±1.07	19±0.57	22±0.57*
Darts	17.5±0.428	20.33±1.11	20.5±0.99	21±0.73*
Ear wig.	17.66±1.08	18.5±0.76	18.16±0.87	18±0.96
Solicitation	9±0.816	10±0.894	10.33±0.954	12.16±0.792*
Rejection	0.66±0.210	0.66±0.210	0.33±0.210	0.5±0.210

Results are expressed as mean ± SEM. (n = 6) Data was analysed by one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p<0.01.

Table 6: Effect of AI extract (After 21 days of treatment) on Female proceptive parameters

Parameters	Control	AI-100	AI-200	AI-400
Hops	17.70±1.08	21.33±0.88	22.66±1.05*	22.66±1.28*
Darts	17.32±0.56	22±1.06*	22.16±1.49*	25.16±1.09**
Ear wig.	17.03±1.09	21.16±0.79*	21.5±0.42*	25.16±0.87**
Solicitation	10.02±0.76	11.16±0.47	12.66±0.49**	12.50±0.76**
Rejection	0.73±0.29	0.5±0.233	0.5±0.223	0.5±0.223

Results are expressed as mean ± SEM. (n = 6) Data was analysed by one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p<0.01.

Table 7: Effect of AI extract (After 11 days of treatment) on Female receptive parameters

Parameters	Control	AI-100	AI-200	AI-400
Lordosis	16.66±0.66	16.16±0.792	15.66±1.02	18±0.57
LQ (%)	87.82±3.11	86.82±3.17	91.15±2.13	96.55±1.09

Results are expressed as mean ± SEM. (n = 6) Data was analysed by one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p<0.01.

Table 8: Effect of AI extract (After 21 days of treatment) on Female receptive parameters

Parameters	Control	AI-100	AI-200	AI-400
Lordosis	15.94±0.54	16.33±1.563	14.83±0.872	19±0.774
LQ (%)	85.50±3.19	87.05±2.688	77.72±4.863	91.39±2.745

Results are expressed as mean ± SEM. (n = 6) Data was analysed by one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p<0.01.

Male rat Copulatory signs

Mount Latency (ML) and Mount Frequency (MF)

The mount latency of male rats paired with AI treated female rats showed significant (p<0.01) reduction at the doses of 200 and 400 mg/kg after 21 days of treatment. But none of the doses of AI did improve the number of mounts in the period of 30 minutes.

Intromission Latency (IL) and Intromission Frequency (IF)

All the doses of AI significantly reduced the intromission latency after 21 days. AI 200 and 400 were found to be equipotent and more significant (p<0.01) in this regard as compared to AI 100 (p<0.05). In addition, only AI 400 mg/kg significantly (p<0.05) improved the intromission frequency after 21 days of treatment.

Ejaculation Latency (EL) and Ejaculation Frequency (EF)

No change was observed in the ejaculation latency of the male rats after the AI treatment, irrespective of the treatment period. However, AI 400 was found to be significant (p<0.01) after 11 days. AI-200mg/kg and 400mg/kg significantly increased (p<0.05) the ejaculation frequency after 21 days also.

Post Ejaculatory Interval (PEI) and Hit Rate (HR)

AI 200 and 400 mg/kg significantly showed lowering in post ejaculatory interval after 11 days (p<0.01) and 21 day days (p<0.05).

No significant change in hit rate (i.e, copulatory efficiency of male rats) was seen with AI treated females on 11th day of treatment. Only the dose of 400 mg/kg significantly increased (p<0.01) the HR after 21 days.

Table 9: Effect of AI extract (After 11 days of treatment) on male copulatory parameters

Parameters	Control	AI-100	AI-200	AI-400
ML (min)	3.65±0.656	2.89±0.437	2.46±0.325	2.66±0.442
IL (min)	4.26±0.583	3.40±0.425	2.91±0.409	3.23±0.438
EL (min)	1.55±0.309	1.36±0.358	1.50±0.302	1.71±0.453
PEI (min)	3.01±0.519	1.91±0.2	1.17±0.247**	0.85±0182**
MF	19.16±1.27	18.66±0.843	16.83±1.07	18.66±0.71
IF	15.16±1.01	14.66±0.88	15.33±0.88	16.66±0.76
EF	10.66±0.666	13±0.96	13.33±0.66	14.83±0.703**
HR	0.793±0.027	0.790±0.046	0.908±0.008	0.894±0.034

Results are expressed as mean ± SEM. (n = 6) Data was analysed by one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p<0.01.

Table 10: Effect of AI extract (After 21 days of treatment) on Male copulatory parameters

Parameters	Control	AI-100	AI-200	AI-400
ML (min)	3.51±0.63	2.56± 0.278	1.79±0.237**	1.35±0.474**
IL (min)	4.28±0.51	3.01±0.288*	2.01±0.437**	1.72±0.170**
EL (min)	1.43±0.38	1.13±0.23	1.26±0.33	1.27±0.22
PEI (min)	3.03±0.58	1.94±0.222	1.87±0.177*	1.71±0.287*
MF	20.09±1.33	18.66±1.498	19.83±0.600	20.83±0.833
IF	16.16±1.10	15.16±0.302	16.33±0.66	19.33±0.614*
EF	10.10±0.73	12.16±0.600	13.16±0.600*	13.16±0.600*
HR	0.78±0.02	0.89±0.029	0.824±0.031	0.92±0.016**

Results are expressed as mean ± SEM. (n=6). Data was analysed by one way analysis of variance (ANOVA) followed by Dunnett's 't' test. *p<0.05, **p<0.01.

DISCUSSION:

In the present investigation, preliminary phyto - chemical analysis of methanolic extract of aerial parts of *Abutilon indicum* (AI) showed the presence of steroids, glycosides, triterpenoids, alkaloids, saponins, flavonoids, carbohydrates and proteins. The earlier scientific studies have revealed that these phytochemicals are mainly responsible for the pharmacological actions and thereby suggested worth to explore the traditional claims[21]. Toxicity is one of the most important aspects of any medication to govern the extent of therapeutic utility. Since preliminary phytochemical results gave indication of further pharmacological screening, it becomes mandatory to evaluate the extracts for their toxicity profile to confirm its safety[22]. As per the principles of pharmacology any drug shall not only be pharmacologically effective but also free of toxicity. The maintenance of desirable risk and benefit ratio is prerequisite to label any compound as a drug[23,24]. The acute oral toxicity studies of *Abutilon indicum* extracts was found to be safe up to the dose of 2000mg/kg and from these findings the doses three different 100, 200 and 400 mg/kg were selected for the further studies[13].

In the current investigation, the effect was assessed using two different models i.e Run way behavior and Copulatory behavior[15,17,19,20]. The results revealed significant reduction in runtime and increase in core proximity time for the male targets in estrous AI treated females. As per the principles of preclinical pharmacology, the inherent sexual activity in animals is best observed during estrous phase. The above mentioned results indicated possible use of AI extract in females with low initial arousal and motivation[25] as observed in estrous phase. Since, sexual dysfunction is a complex result of physical and/or psychogenic factor and no satisfactory therapy is available in modern medicine[17] making it a serious complaint that needs to be addressed on immediate basis. The female sexual behavior does not complete with initial arousal or motivation rather the successful sexual interplay to satisfy mind and body is required[26]. In this regard, the evaluation of AI extract in copulatory behavior also revealed significant improvement in both proceptive and receptive behaviours and thereby suggesting its possible role in wide variety of sexual dysfunctions especially that of genital and sexual arousal disorders[1,27]. The drug induced improved sexual performance may be troublesome in patients with asthma due to increase in basal metabolic rate[28,29]. The earlier documentation of AI for its anti-asthmatic effect can be a golden advantage in such a situation[30,31].

The sexual performance can also be adversely affected in patients with painful joints and associated inflammation which in turn may lead to psychologic problems such as anxiety, fear and stress making it more and more complicated[26]. In addition to this, recent evidences also showed that patients of rheumatoid arthritis prescribed with certain drugs like Methotrexate that may also affect sexual dysfunction[32]. At this junction, the dual role of AI i.e. in sexual dysfunction and rheumatoid arthritis can be emerged as a golden option. The significant improvement in inflammatory condition of RA may favor natural sexual act, and during this sexual activity the freeze joint will be more relaxed giving better relief**.** This interdependent dramatic relief may drastically reduce the dependency of patients on modern symptomatic drug. This reduced drug requirement will in turn automatically reduce the dose and duration dependent side-effects[26].

CONCLUSION:

In summary, the present study provides evidence that the methanolic extract of *Abutilon indicum* is a potent stimulator of sexual behavior, particularly of sexual arousal in female rats. On this basis, this extract can be considered to possess libido enhancing properties.

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