Mucuna pruriens improves male fertility by its action on the hypothalamus–pituitary–gonadal axis

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Objective: To understand the mechanism of action of *Mucuna pruriens* in the treatment of male infertility.
Design: Prospective study.
Setting: Departments of Biochemistry, Urology, and Obstetrics and Gynecology, C.S.M. Medical University, Lucknow, India.
Patient(s): Seventy-five normal healthy fertile men (controls) and 75 men undergoing infertility screening.
Intervention(s): High-performance liquid chromatography assay for quantitation of dopa, adrenaline, and noradrenaline in seminal plasma and blood. Estimation by RIA of hormonal parameters in blood plasma, namely T, LH, FSH, and PRL.
Main Outcome Measure(s): Before and after treatment, serum T, LH, FSH, PRL, dopamine, adrenaline, and noradrenaline in seminal and blood plasma were measured.
Result(s): Decreased sperm count and motility were seen in infertile subjects. Serum T and LH levels, as well as seminal plasma and blood levels of dopamine, adrenaline, and noradrenaline were also decreased in all groups of infertile men. This was accompanied by significantly increased serum FSH and PRL levels in oligozoospermic subjects. Treatment with *M. pruriens* significantly improved T, LH, dopamine, adrenaline, and noradrenaline levels in infertile men and reduced levels of FSH and PRL. Sperm count and motility were significantly recovered in infertile men after treatment.
Conclusion(s): Treatment with *M. pruriens* regulates steroidogenesis and improves semen quality in infertile men. (Fertil Steril® 2009;92:1934–40. ©2009 by American Society for Reproductive Medicine.)

Key Words: Male infertility, testosterone, *Mucuna pruriens*, dopamine, catecholamines, follicle-stimulating hormone

Infertility can be defined as a lack of pregnancy after 1 year of unprotected intercourse, and it is the manifestation of one or more pathologic conditions of male or female origin. Reduced spermatogenesis and defective sperm function are the most prevalent causes of idiopathic male infertility. Many environmental, physiologic, endocrine, and genetic factors have been reported as underlying poor sperm function and male factor infertility (1). A meta-analysis of 61 studies worldwide reported a downward trend in sperm count and semen volume over the past 50 years (2, 3). Given its etiologic heterogeneity, successful treatment of male infertility is quite cumbersome (4).

Testosterone is secreted by the Leydig cells under LH stimulation and is essential for promoting spermatogenesis, whereas FSH has a role in the development of testes. An increased FSH level in men has been correlated with damage to the seminiferous tubules (5). Testosterone, E_2, and inhibin control the secretion of gonadotropins and also autoregulate their plasma concentrations by acting on the hypothalamic–pituitary axis (6). There are reports that abnormalities in sex hormone biosynthesis may impair spermatogenesis. The failure of the pituitary to maintain proportionate levels of FSH, LH, and PRL may lead to disruption of testicular function, leading to infertility (7).

Prolactin secretion from pituitary lactotrophs is under the inhibitory control of dopamine secreted from the hypothalamus, and hyperprolactinemia arises either from interference with the action of dopamine or from a lactotroph adenoma (8). Dopamine plays an important role in mediating male sexual behavior and function; an increase of dopamine in the brain results in increased libido (9). A decrease in catecholamine content, especially of dopamine in the brain, may reduce male sexual function (10). It has been reported that low serum T levels with raised gonadotropin (FSH) levels cause damage to Leydig cells and seminiferous tubules (11). A better understanding of the hormonal requirements of spermatogenesis is desirable for the improvement of treatment for male infertility (12).

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In the ancient Indian Ayurvedic and Unani medicine systems, numerous plants and their products have been recommended for endurance against stress, general resistance against infection, retardation of the aging process, and eventual improvement of male sexual function, alleviating disorders like psychogenic impotence and unexplained infertility (13). However, the scientific rationale behind the use of these products remains unexplored to date. Recently we reported that *Mucuna pruriens* seed powder helps fight stress-mediated poor semen quality and acts as a restorative and invigorator tonic or aphrodisiac in infertile subjects (14, 15). The study reported successful treatment of 70% of infertile individuals (14). We proposed a possible mechanism of action of *M. pruriens*; however, experimental evidence in support of the hypothesis was lacking. In view of the above considerations, the present study was planned to investigate the possible effects of *M. pruriens* on seminal plasma and blood levels of dopamine and sex hormones and on semen quality.

MATERIALS AND METHODS

Plant Material

The seeds of *M. pruriens* were purchased from an authorized dealer in Lucknow, India. These were identified and authenticated by Dr. M.M.A.A Khan, Senior Lecturer, Department of Botany, Shia P.G. College, Lucknow, India (Herbarium No. M-113, dated October 17, 2005). The seeds were dried under shade and ground to a fine powder with a laboratory mill.

Study Protocol

The study protocol was approved by the Institutional Review Board and Ethics Committee of the Chhatrapati Sahuji Maharaj (C.S.M.) Medical University, Lucknow, India. Before enrolment in the study, written informed consent from each subject was obtained in response to a full written and verbal explanation of the nature of study. The potential participants with infertility persisting longer than 1 year were clinically examined before being included in the study. A complete medical history of the subjects and their female partners was also recorded. Subjects with diabetes, hypertension, arthritis, malignancy, tuberculosis, HIV infection, other infections, or other endocrine disorders and those taking drugs or with conditions known to influence fertility were excluded from this study.

Subjects

One hundred fifty men, aged 25–40 years, were selected from the couples attending the Infertility Clinic of the Department of Obstetrics and Gynecology and the Outpatient Department of Urology, C.S.M. Medical University. Semen samples were collected from the subjects after 3 to 4 days of sexual abstinence. Semen analysis was carried out according to the World Health Organization guidelines (16). Venous blood samples were also withdrawn and serum separated for assessment of hormone levels.

The prospective study included four parallel groups of subjects: three patient groups and one control group. The patient group comprised 75 subjects and was further divided into three subgroups of 25 patients each on the basis of semen profiles: [1] normozoospermic infertile men (sperm count $>20 \times 10^6$/mL, >40% motility, and >40% normal morphology), [2] oligozoospermic infertile men (sperm count $<20 \times 10^6$/mL, motility >40%, and >40% normal morphology), and [3] asthenozoospermic infertile men (sperm count $>20 \times 10^6$/mL, <40% motility, and >40% normal morphology). The control group comprised 75 age-matched healthy men who had previously initiated at least one pregnancy and had a normal semen profile (sperm count $>20 \times 10^6$/mL, >40% motility, and >40% normal morphology). All subjects were instructed not to take any nutritional supplement or vitamins and not to change their dietary habits during the course of treatment. This study was undertaken between January 2005 and January 2007.

Treatment

The infertile men were prescribed *M. pruriens* seed powder (5 g/d), orally, in a single dose with milk for 3 months (17). Semen and blood samples were collected before administration of the medicine and after 3 months of treatment.

Preparation of Seminal Plasma and Serum

Semen samples were collected by masturbation after 3 to 4 days of abstinence into sterile plastic containers for analyses. The semen volume was recorded, and an aliquot was taken to assess sperm motility after allowing 30 minutes for liquefaction. Semen samples were centrifuged at $1,200 \times g$ at 4°C for 20 minutes for separation of seminal plasma. The supernatant (seminal plasma) was again centrifuged at $10,000 \times g$ at 4°C for 30 minutes to eliminate all possible contaminating cells and stored at −20°C until analysis. All blood samples were drawn between 8 AM and 10 AM and centrifuged at $3,000 \times g$ at 4°C for 10 minutes to collect supernatant.

Chemicals

All chemicals and RIA kits for LH, FSH, T, and PRL were of analytic grade and were purchased from Sigma Chemical (St. Louis, MO).

Hormonal Assay

Serum T, LH, FSH, and PRL were measured by a double antibody RIA method using Gamma Counter (Stratec Biomedical Systems, Birkenfeld, Germany) (18).

Estimation of Catecholamines

Seminal plasma or blood plasma (250 μL) from normal fertile and infertile men was deproteinized by precipitation with 250 μL perchloric acid and centrifugation at $10,000 \times g$. The clear supernatant was placed in a fresh tube and combined with 25 μL of 2,3-dihydroxybenzoic acid, 0.625 ng as

internal standard in 3 M Tris buffer (pH 8.6), containing 5% ethylenediaminetetraacetic acid disodium salt to a final volume of 1.0 mL. To this reaction mixture, 500 mg of neutral alumina was added. The tubes were stoppered, shaken vigorously for 10 minutes, and centrifuged at 10,000 × *g* for 20 minutes at room temperature. The supernatant was drained out. Alumina was washed with water and eluted with 0.5 mL of 0.1 M perchloric acid and estimated for catecholamines content, using the method of DeVitro and Wagner (19). The filtered eleunt was injected manually through a 20-μL loop over the ODS-C18 column coupled with a high-performance liquid chromatography/electrochemical detector (Waters Corporation, Milford, MA) for separation and quantification. The mobile phase consisted of 0.1 M potassium phosphate (pH 4.0), 10% methanol, and 1.0 mM heptane sulfonic acid. Samples were separated on a C18 column using a low flow rate of 1.0 mL/min. The concentrations of dopamine, adrenaline, and noradrenaline were calculated using a standard curve generated by determining the ratio between the known amounts of dopamine, adrenaline, and noradrenaline (5 ng of each) and a constant amount of internal standard by Millennium software (Waters Corporation) and reported as nanograms per milliliter (19).

Statistical Analysis

Normal healthy fertile men and infertile men were compared by one-way analysis of variance; the significant mean difference of the normal healthy fertile group (control) from the infertile groups was calculated by Dunnett's posttest. Similarly, two related groups (before and after treatment) of infertile subjects were compared by paired *t*-test. A *P* value of $<.05$ was considered statistically significant. Statistical analysis was performed with Instat 3.0 (GraphPad Software, San Diego, CA).

RESULTS

Semen Profile

General semen characteristics of the different subject groups before and after treatment are depicted in Table 1. In normal healthy fertile men (control group) the mean sperm concentration was 58.07 ± 7.61 × 10^6/mL, with motility at 56.75% ± 5.05%, and liquefaction time was 20.85 ± 2.22 minutes. The sperm concentration and motility in the infertile groups was statistically significantly less as compared with controls. The sperm concentration in the oligozoospermic group (86%; $P<.001$) and motility in the asthenozoospermic group (77%; $P<.001$) were statistically significantly less as compared with controls. Treatment with *M. pruriens* for 3 months showed significant reversal of the above parameters. Sperm concentration was most significantly improved in oligozoospermic patients (576%; $P<.001$), and sperm motility was significantly improved in asthenozoospermic patients (41%; $P<.05$).

TABLE 1

Clinical parameters of patients before and after treatment with *M. pruriens*.

Physiologic parameters	Control	Normozoospermic		Oligozoospermic		Asthenozoospermic	
		Pretreatment	Posttreatment	Pretreatment	Posttreatment	Pretreatment	Posttreatment
Semen volume (mL)	2.70 ± 0.32	2.56 ± 0.47 (−5)	2.78 ± 0.61 (+8)	2.65 ± 0.35 (−2)	2.72 ± 0.43 (+3)	2.18 ± 0.40 (−19)	2.29 ± 0.19 (+5)
Liquefaction time (min)	20.85 ± 2.22	25.10 ± 2.92[a] (+20)	19.40 ± 2.16[b] (−23)	24.15 ± 1.79 (+16)	18.75 ± 2.49[b] (−22)	58.10 ± 6.38[c] (+179)	35.80 ± 4.96[b] (−38)
Motility (%)	56.75 ± 5.05	62.50 ± 6.44[d] (+10)	67.15 ± 6.27 (+7)	68.00 ± 9.60 (+20)	70.80 ±15.45 (+ 4)	12.85 ± 2.39[c] (−77)	18.10 ± 2.86[b] (+41)
Sperm concentration ($\times 10^6$/mL)	58.07 ± 7.61	56.10 ± 7.31[d] (−3)	70.65 ± 7.17[b] (+26)	8.31 ± 2.82[c] (−86)	56.20 ± 6.69[b] (+576)	54.55 ± 6.37 (−6)	57.70 ± 9.16 (+6)

Note: Results are expressed as mean ± SD. Values in parentheses indicate percentage change (pretreatment groups vs. control and posttreatment groups vs. respective pretreatment groups).

[a] $P<.05$ vs. control group.

[b] $P<.001$ vs. pretreatment group.

[c] $P<.001$ vs. control group.

[d] $P<.01$; vs. control group.

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Hormone Levels

The serum T level in the control group was 5.63 ± 0.81 mg/mL; this level was lower in the normozoospermic (20%; $P<.01$), oligozoospermic (30%; $P<.01$), and asthenozoospermic (52%; $P<.01$) infertile groups as compared with the control group. After treatment with *M. pruriens*, the T level improved significantly in normozoospermic (27%; $P<.5$), oligozoospermic (39%; $P<.01$), and asthenozoospermic (17%; $P<.01$) infertile men (Table 2). Similarly, serum LH levels in normozoospermic (17%; $P<.05$), oligozoospermic (30%; $P<.05$), and asthenozoospermic (43%; $P<.05$) patients were significantly lower when compared with controls. Treatment with *M. pruriens* recovered the levels of LH in normozoospermic (23%; $P<.05$), oligozoospermic (41%; $P<.05$), and asthenozoospermic (40%; $P<.05$) subjects. On the other hand, in oligozoospermic and asthenozoospermic men, FSH and PRL levels were significantly increased (FSH: 33% and 17%, respectively [$P<.001$]; PRL: 61% and 4% [$P<.001$]), and after treatment with *M. pruriens* these levels were significantly reduced. Intra- and interassay coefficients of variation in T, LH, FSH, and PRL were 10.0%, 14.0%, 8.5%, and 12.5%, respectively.

Dopamine levels were decreased in seminal plasma and blood plasma of normozoospermic (45%, 48%; $P<.01$), oligozoospermic (45%, 34%; $P<.01$), and asthenozoospermic (58%, 67%; $P<.01$) infertile men (Tables 3 and 4). Treatment with *M. pruriens* recovered the seminal plasma and blood plasma dopamine levels in normozoospermic (65%, 63%; $P<.01$), oligozoospermic (70%, 19%; $P<.05$), and asthenozoospermic (72%, 75%; $P<.01$) men, as compared with pretreatment levels. Similarly, seminal plasma and blood levels of adrenaline in normozoospermic (58%, 51%; $P<.05$), oligozoospermic (62%, 41%; $P<.05$), and asthenozoospermic (64%, 61%; $P<.05$) infertile subjects were decreased as compared with the control group. Treatment with *M. pruriens* recovered the seminal plasma and blood plasma levels of adrenaline in normozoospermic (76%, 84%; $P<.05$), oligozoospermic (37%, 64%; $P<.05$), and asthenozoospermic (58%, 73%; $P<.05$) infertile men. Noradrenaline levels in seminal plasma and blood plasma were decreased in normozoospermic (41%, 48%; $P<.05$), oligozoospermic (55%, 63%; $P<.001$), and asthenozoospermic (63%, 64%; $P<.001$) men; after treatment with *M. pruriens* these levels were significantly recovered in normozoospermic (46%, 53%; $P<.05$), oligozoospermic (43%, 34%; $P<.01$), and asthenozoospermic (44%, 53%; $P<.001$) men.

DISCUSSION

Recently we reported that *M. pruriens* increases semen volume, improves sperm quality, and regresses unspecific generation of reactive oxygen species in infertile subjects (14, 15). In continuation of these findings, the present study explored the possible mode of action of *M. pruriens* against infertility; treatment with this natural product for 3 months significantly regulated the levels of PRL and other male sex hormones, as well as sperm motility and concentration in infertile men.

TABLE 2

Hormonal parameters of patients before and after treatment with *M. pruriens*.

Hormonal parameters	Control	Normozoospermic		Oligozoospermic		Asthenozoospermic	
		Pretreatment	Posttreatment	Pretreatment	Posttreatment	Pretreatment	Posttreatment
LH (mIU/mL)	7.35 ± 0.52	6.08 ± 0.93[a] (−17)	7.50 ± 0.96[b] (+23)	5.15 ± 0.97[c] (−30)	7.28 ± 0.92[b] (+41)	4.14 ± 1.35[c] (−43)	5.79 ± 0.97[b] (+40)
FSH (mIU/mL)	6.22 ± 1.71	7.11 ± 1.30[a] (+14)	6.28 ± 1.94[b] (−11)	8.30 ± 1.06[c] (+33%)	6.32 ± 1.46[b] (−24)	7.28 ± 2.05[c] (+17)	6.67 ± 1.29[b] (−8)
T (ng/mL)	5.63 ± 0.81	4.49 ± 0.53[a] (−20)	5.72 ± 0.36[b] (+27)	3.89 ± 0.95[c] (−30)	5.40 ± 0.48[b] (+39)	2.65 ± 0.73[c] (−52)	3.66 ± 0.39[b] (+17)
PRL (ng/mL)	6.68 ± 2.03	6.75 ± 1.13[a] (+1)	5.45 ± 0.66[b] (−19)	10.76 ± 2.94[c] (+61)	7.28 ± 1.66[b] (−32)	6.92 ± 1.53[c] (+4)	6.16 ± 1.74[b] (−11)

Note: Results are expressed as mean ± SD. Values in parentheses indicate percentage change (pretreatment groups vs. control and posttreatment groups vs. respective pretreatment groups).

[a] $P<.05$ vs. control group.

[b] $P<.01$ vs. pretreatment group.

[c] $P<.01$ vs. control group.

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As a measure of biochemical factors correlating with male infertility, we observed that dopamine, noradrenaline, and adrenaline levels were decreased in the seminal plasma as well as serum of infertile men. The decreased levels of dopamine were associated with decrease in serum levels of T and LH in all three infertile groups (normozoospermic, oligozoospermic, and asthenozoospermic) and with a significant increase in PRL and FSH in the oligozoospermic infertile men. However, after treatment with *M. pruriens* there was significant improvement in the levels of dopamine, noradrenaline, and adrenaline, as well as in T and LH levels. Furthermore, PRL and FSH levels were decreased in infertile men after treatment.

Hyperprolactinemia is less common in men; however, it is associated with hypogonadism with absolute or relative impotence and loss of sexual behavior (20). There is mounting evidence that PRL acts on the Leydig cells, germ cells, prostate, vas deferens, and other regions of the male reproductive tract, but the role of these actions in infertile men remains to be clearly defined (21). It is reported that plasma PRL levels in men increase immediately after orgasm and that they have a role in inhibiting sexual drive and behavior (22).

Prolactin is unique among the anterior pituitary hormones because its secretion is affected by a large variety of stimuli called PRL-releasing factors, such as thyrotropin-releasing hormone, oxytocin, and neurotensin; the most important psychological stimuli that elevate pituitary PRL secretion are suckling stress in women and psychological stress in men (23). In mammals the control exerted by the hypothalamus over pituitary PRL secretion is largely inhibitory. The known PRL-inhibiting factors are dopamine, somatostatin, and γ-aminobutyric acid; however, it is mostly inhibited by dopamine (24). Our observation of increased PRL levels in infertile men and its decreased content in treated men may be an effect of treatment and it establishes the inhibitory effect of PRL on spermatogenesis.

There are hardly any reports that infertile men have increased levels of PRL-releasing factors, but generally because of psychological stress these levels may be elevated (25, 26). In the present study we observed decreased amounts of PRL-inhibiting factors, namely dopamine, adrenaline, and noradrenaline, in the seminal plasma as well as blood plasma of infertile patients. This may be the reason for increased levels of PRL in infertile men. However, after treatment with *M. pruriens*, PRL levels were reduced, perhaps because *M. pruriens* seeds are rich in L-3, 4 dihydroxy phenyl alaline (L-DOPA) and its metabolites, which include dopamine, epinephrine, and norepinephrine (27). Therefore, it is suggested that dopamine may inhibit the release of PRL from the anterior lobe of the pituitary gland, and this stimulates the hypothalamus and forebrain to secrete GnRH, which in turn may activate the anterior pituitary gland to secrete FSH and LH, causing increased synthesis of T by Leydig cells of the testis in infertile subjects (28). Moreover, LH controls steroid production by binding with the receptors on the Leydig cells, thereby inducing the synthesis of cyclic adenosine

TABLE 3

Catecholamine parameters in seminal plasma of patients before and after treatment with *M. pruriens*.

Catecholamine	Control	Normozoospermic		Oligozoospermic		Asthenozoospermic	
		Pretreatment	Posttreatment	Pretreatment	Posttreatment	Pretreatment	Posttreatment
Dopamine (ng/mL)	4.34 ± 0.95	2.36 ± 0.55[a] (−45)	3.89 ± 0.82[b] (+65)	2.36 ± 0.24[a] (−45)	4.03 ± 0.34[b] (+70)	1.82 ± 0.82[a] (−58)	3.14 ± 0.88[b] (+72)
Adrenaline (ng/mL)	7.60 ± 1.04	3.12 ± 1.12[a] (−58)	5.45 ± 0.88[b] (+76)	2. 85 ± 0.65[a] (−62)	4.67 ± 0.67[b] (+37)	2.71 ± 0.96[a] (−64)	4.28 ± 1.12[b] (+58)
Noradrenaline (ng/mL)	9.29 ± 1.02	5.41 ± 0.82[a] (−41)	7.93 ± 1.51[b] (+46)	4.12 ± 1.73[a] (−55)	5.92 ± 0.65[b] (+43)	3.44 ± 0.96[a] (−63)	4.97 ± 0.37[b] (+44)

Note: Results are expressed as mean ± SD. Values in parentheses indicate percentage change (pretreatment groups vs. control and posttreatment groups vs. respective pretreatment groups).

[a] $P < .01$ vs. control group.

[b] $P < .001$ vs. pretreatment group.

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TABLE 4

Catecholamine parameters in blood plasma of patients before and after treatment with *M. pruriens*.

Catecholamine	Control	Normozoospermic		Oligozoospermic		Asthenozoospermic	
		Pretreatment	Posttreatment	Pretreatment	Posttreatment	Pretreatment	Posttreatment
Dopamine (ng/mL)	2.29 ± 0.59	1.17 ± 0.40[a] (−48)	1.91 ± 0.05[b] (+63)	1.52 ± 0.34[a] (−34)	1.80 ± 0.44[b] (+19)	0.93 ± 0.06[a] (−67)	1.63 ± 0.59[b] (+75)
Adrenaline (ng/mL)	3.61 ± 0.86	1.75 ± 0.51[a] (−51)	3.23 ± 0.43[b] (+84)	2.14 ± 0.68[a] (−41)	2.94 ± 0.12[b] (+64)	1.40 ± 0.58[a] (−61)	2.43± 0.31[b] (+73)
Noradrenaline (ng/mL)	5.63 ± 1.00	2.89 ± 0.65[a] (−48)	4.44 ± 0.91[b] (+53)	2.07 ± 0.57[a] (−63)	2.78 ± 0.55[b] (+34)	2.04 ± 0.39[a] (−64)	2.66 ± 0.20[b] (+53)

Note: Results are expressed as mean ± SD. Values in parentheses indicate percentage change (pretreatment groups vs. control and posttreatment groups vs. respective pretreatment groups).

[a] $P<.01$ vs. control group.

[b] $P<.001$ vs. pretreatment group.

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monophosphate (cAMP) from adenosine triphosphate, and increased levels of cAMP are largely responsible for the up-regulation of steroidogenesis (15, 29–31).

Seminal vesicles and vas deferens, including testis and epididymides, are also rich sources of adrenaline and noradrenaline in human semen (32). These catecholamines have been shown to enhance sperm motility, transport, capacitation, and acrosome reaction (33), and they are also involved in contraction of the seminal vesicles and inhibition of lipid peroxidation in spermatozoa (34). Our study also states that *M. pruriens* regulates the level of these catecholamines to facilitate proper functioning of the genitourinary system in infertile subjects.

In brief, it may be stated that *M. pruriens* helps in some central mechanism to increase secretion of semen, decrease spermatorrhea, and act as a restorative invigorating tonic and aphrodisiac in disorders characterized by weakness or loss of sexual power (35, 36). Although the exact chemical composition of *M. pruriens* seeds remains to be explored, their ability to enhance the secretion of semen, affect sex hormones including T, and improve performance and sexual drive has been well established. The present study was carried out to asses the effect of *M. pruriens* on the hypothalamic–pituitary–gonadal axis. Our study demonstrated the positive impact of *M. pruriens* not only on dopamine levels but also on other biochemical constitutes, such as adrenaline and noradrenaline, in the reproductive tract. Therefore, in conclusion, *M. pruriens* seems to influence fertility by its action on the central nervous system through dopamine and the reproductive tract through adrenaline and noradrenaline. More in-depth studies are needed to unravel the positive impact of this "wonder herb."

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REFERENCES

1. Mahdi AA, Bano F, Singh R, Singh RK, Siddiqui MS, Hasan M. Seminal plasma superoxide dismutase and catalase activities in infertile men. Med Sci Res 1999;27:201–3.
2. Bano F, Singh RK, Singh R, Siddiqui MS, Mahdi AA. Seminal plasma lipid peroxide levels in infertile men. J Endocrinol Reprod 1999;3:20–8.
3. Sikka SC. Relative impact of oxidative stress on male reproductive function. Curr Med Chem 2001;8:851–62.
4. Madhukar D, Singh R. Hormonal treatment of male infertility: pitfalls and promises. J Androl. In press.
5. Weinbauer GF, Nieschlag E. Gonadotrophin control of testicular germ cell development. Adv Exp Med Biol 1995;377:55–65.
6. Horita H, Sato Y, Adachi H, Suzuki N, Kato R, Hisasue S, et al. Effects of levodopa on nocturnal penile tumescence: a preliminary study. J Androl 1998;19:619–24.
7. Dashistani HI, Dayem MA. Hyperprolactinemia and hypergonadotropins in infertile men with sever oligospermia and azoospermia. Int J Endocrinol 2007;3:3–8.
8. Thorner MO. Disorders of prolactin secretion. J Clin Pathol 1976;7: 36–41.
9. Bachelot A, Binart N. Reproductive role of prolactin. Reproduction 2007;133:361–9.

10. Orth AB, Royse DJ, Tien M. Ubiquity of lignin-degrading peroxidases among various wood-degrading fungi. Appl Environ Microbiol 1993;59:4017–23.
11. Foresta C, Bewttel A, Spolaore D, Metico M, Rossata M, Ferlin A. Suppression of the high endogenous levels of plasma FSH in infertile men are associated with improved Sertoli cell function as reflected by elevated levels of plasma inhibin B. Hum Reprod 2004;19:1431–7.
12. Dahanukar SA, Hazra A. Ayurveda unravelled. In: Dahanukar SA, ed. Heal with herbs: publications and information directorate. New Delhi, India: Council of Scientific and Industrial Research, 1995:53–74.
13. Tripathi YB, Upadhyay AK. Antioxidant property of Mucuna pruriens. Curr Sci 2001;80:1377–8.
14. Shukla KK, Mahdi AA, Ahmad MK, Shankwar SN, Jaiswar SP, Tiwari SC. Mucuna pruriens reduces stress and improves the quality of semen in infertile males. eCAM. Online 18 Dec, 2007.
15. Ahmad MK, Mahdi AA, Shukla KK, Islam N, Jaiswar SP, Ahmad S. Effect of Mucuna pruriens on semen profile and biochemical parameters in seminal plasma of infertile men. Fertil Steril 2008;90:627–35.
16. World Health Organization. Laboratory manual for the examination of human semen and sperm cervical mucus interaction. 4th ed. New York: Cambridge University Press, 1999.
17. Singh D. Konch (Kiwach). In: Singh D, ed. Unani dravvyagunadarsh, Vol II. Varanasi, India: Jivan Shiksha Mudralay Limited, Lucknow, India; 1974:101–2.
18. Medgely AR. Radioimmunoassay for human follicle stimulating hormone. J Clin Endocrinol Metab 1967;27:295–9.
19. DeVitro MJ, Wagner GC. Methamphetamine induced neural damage: a role for free radicals. Neuropharma 1989;28:1145–50.
20. De Roas M, Zarrilli S, Di Sarno A, Milano N, Gaccione M, Bogia B, et al. Hyperprolactinemia in men: clinical and biochemical features and response to treatment. Endocrine 2003;1:75–82.
21. Bartke A. Prolactin in the male: 25 years later. J Androl 2004;25:661–6.
22. Krüger THC, Haake P, Haverkamp J, Krämer M, Exton MS, Saller B, et al. Effects of acute prolactin manipulation on sexual drive and function in males. Endocrinol 2003;179:357–65.
23. Daughaday WH. The anterior pituitary. In: Wilson JD, Foster DW, eds. Williams textbook of endocrinology. 7th ed. Philadelphia: Saunders, 1985: 568–13.
24. MacLeod RM. Regulation of prolactin secretion. In: Martini L, Ganong WF, eds. Frontiers in neuroendocrinology. Vol 4. New York: Raven Press, 1976:169–94.
25. Neill JD. Prolactin secretion and its control. In: Knobil E, Neill JD, eds. The physiology of reproduction. New York: Raven Press, 1988: 1379–90.
26. Fait G, Pauzner D, Gull I, Lessing JB, Jaffa AJ, Wolman I. Effect of 1 week of oral hydration on the amniotic fluid index. J Reprod Med 2003;48:187–90.
27. Misra L, Wagner H. Extraction of bioactive principle from Mucuna pruriens seeds. Ind J Biochem Biophys 2007;44:56–60.
28. Islam N, Trainer PJ. The hormonal assessment of the infertile male. Br J Urol 1998;82:69–75.
29. Payne AH, Hales DB. Overview of steroidogenic enzymes in the pathway from cholesterol to active steroid hormones. Endocr Rev 2004;25: 947–70.
30. Haider SG. Cell biology of Leydig cells in the testis. Int Rev Cytol 2004;233:181–241.
31. Shukla KK, Mahdi AA, Shankwar SN, Ahmad MK. Effect of Mucuna pruriens on hormonal status and semen quality in infertile males. Contraception 2008;78:194.
32. Chang A, Shin SH. Dopamine agonists both stimulate and inhibit prolactin release in GH4ZR7 cells. Eur J Endcrinol 1999;141:387–95.
33. Nira BJ, Robert H. Dopamine as a prolactin (PRL) inhibitor. Endocr Rev 2001;22:724–63.
34. Bavister BD, Chen AF, Fu PC. Catecholamine requirement for hamster sperm motility in vivo. J Reprod Fertil 1979;56:507–13.
35. Tripathi YB, Upadhyay AK. Effect of the alcohol extract of the seeds of Mucuna pruriens on free radicals and oxidative stress in albino rats. Phytother Res 2002;16:534–8.
36. Kumar KVA, Srinivasan KK, Shanbhag T, Rao SG. Aphrodisiac activity of the seeds of Mucuna pruriens. Ind Drug 1994;31:321–7.