



EFFECT OF *Mucuna pruriens* ON SPERM PARAMETERS WITH IDIOPATHIC INFERTILITY: A SYSTEMATIC REVIEW

Deepthika S. H. K¹, Karunagoda K. P. K. R²

¹Lecturer- Department of Kaumarabhritya and Stree Roga, Gampaha Wickramarachchi Ayurveda Institute, University of Kelaniya, Yakkala, Sri Lanka

²Senior Lecturer - Academic Unit of Prasutitantra Kaumarabhritya, Institute of Indigenous Medicine, University of Colombo, Rajagiriya, Sri Lanka

Corresponding Author: krishanish@yahoo.com

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ABSTRACT

In Ayurveda *Mucuna pruriens* (*M. pruriens*) is considered as a medicine for male subfertility. There are in vitro, in vivo and literature reviews to demonstrate beneficial medicinal effects of *M. pruriens* in worldwide. This study aims to systematically review the scientific literature and provide a comprehensive summary on the effect of *M. pruriens* on sperm parameters with idiopathic infertility. A comprehensive systematic review was conducted in the following databases: PubMed, Google scholar and Cochrane library for research articles published in between 2000 and 2020. The keywords that were used in combination to search for articles included, "*Mucuna pruriens*", "idiopathic infertility" and "sperm parameters". The literature search done by using keywords and identified following number of articles in the respective databases; PubMed (n=13), Google scholar (n= 116), and Cochrane library (n=4). After removing duplications, the total number of articles included in the present review is 124. 114 studies were omitted due to exclusion criteria and use of combine *M. pruriens* with other medicinal herbs, due to the impossibility of determining the net effect of *M. pruriens*. Included articles were screened in the final stage by reading the full article. There were 10 different studies evaluating the in vitro effect of *M. pruriens* on sperm parameters with idiopathic infertility. The results of this study showed that consumption of *M. pruriens* significantly improves

sperm count and motility. According to studies (n=2) *M. pruriens* can improve morphological defects of sperms to some extents and none of those studies recorded any adverse effects.

Keywords: *Mucuna pruriens*, Sperm parameters, Idiopathic infertility, Motility, Morphology

INTRODUCTION

According to the World health Organization, Infertility defined as no conception after at least 12 months of unprotected intercourse¹. According to previously obtained data, infertility affects 10% to 15% of couples in the world, and its prevalence is increasing; thus, it has become a social concern². Male factor has been observed in at least about 50% of infertility cases³. Idiopathic male infertility is known as idiopathic oligoasthenoteratozoospermia, which indicates that the men have an unexplained reduction of semen quantity and quality⁴. According to WHO normal values of seminal analysis are: semen volume, 1.5 ml (1.4–1.7); total sperm number, 39 million per ejaculate (33–46); sperm concentration, 15 million per ml (12 –16); vitality, 58% live (55 –63); progressive motility, 32% (31 –34); total (progressive + nonprogressive) motility, 40% (38 –42); morphologically normal forms, 4.0% (3.0 –4.0)⁵. World health organization further identified some congenital abnormalities, immunological causes, systemic causes, varicoceles, acquired testicular damages, obstructive causes, accessory gland infections and idiopathic causes as etiological factors for seminal fluid defects⁶.

At present several treatment methods such as orally administrative drugs and surgeries are available for male factor infertility⁷. Most drugs do not have clear benefit on the treatment of male infertility⁸. Additionally, these procedures are associated with adverse effects and are not affordable to all. Several medicinal herbs have shown significant effects on the semen parameters⁹. Therefore, finding new treatment modalities for improve sperm parameters are a must. According to WHO traditional medicine strategy, both developed countries and also developing countries have been widely used traditional methods due to because of cultural acceptability and a better fit with the body, fewer side effects, is a non-invasive, less financial and emotional burden, accessibility and affordability¹⁰.

Mucuna pruriens, which belong to the family fabaceae, is a famous herb in traditional medicine, commonly found in Sri Lanka, in dry and intermediate regions and it is rather common in India. It also known as "Cow-hage" in English, "Wanduru-me" in Sinhala and "Dusparsha, Kapikachhu" etc. in Sanskrit. *Mucuna pruriens*, is a semi-woody twining climber with slender branches clothed with short white deflexed hairs; leaves alternate, stipulate, 3 foliate with stipels, rachis 7.5-12.5 cm long, sparingly deflexed hairy, leaflets 7.5-10 cm long, 5-7.5 cm broad, on short, thick, hairy stalks, terminal one smallest and rhomboid oval, lateral ones very unequal with the lower half greatly dilated, all acute, mucronate, pubescent above, densely covered with shining silvery adpressed hairs beneath, stipules linear, setaceous, hairy; flowers irregular, bisexual, dull dark purple with a yellowish green keel, numerous, 3.7-4.3 cm long, on short pubescent pedicels, usually 2 or 3 together at intervals on a slender, pubescent raceme, 15-30 cm long, bracts 1.2 cm long, lanceolate, hairy, deciduous; sepals 5, fused into a campanulate calyx, densely silky, two upper segments completely connate, lowest much the longest; petals 5, exserted, very unequal, wings twice as long as the standard, keel rather than wings, curved into a stiff beak at apex; stamens 10, diadelphous; ovary superior, surrounded at base by a small crenulate disc, unilocular with marginal ovulens, style beardless, stigma capitate; fruit legume 6.2-7.5 cm long, 1.2 cm broad, linear, blunt, falcately curved at both ends with a longitudinal rib along the whole length of each valve but without wings, densely covered with close rather weak orange-brown irritant bristles pointing backwards and readily detached, 4-6 seeded with partitions between them; seed ovoid, 0.6 cm long, compressed, brownish, mottled with black, hilum oblong¹¹. *Mucuna pruriens* can be identified as anti cholesterol, antiparkinson, antidiabetic, aphrodisiac, anti-

inflammatory and antimicrobial drug. The plant exhibits wide array of phytoconstituents like alkaloids, flavonoids, tannins and phenolic compounds which are responsible for varied potent physiological and pharmacological activities¹². *M. pruriens* seeds contain high concentrations of L-DOPA, an unusual non protein amino acid and a direct precursor to the neurotransmitter dopamine, an important brain chemical involved in mood, sexuality and movement. Besides, it also contains some other amino acids, glutathione, lecithin, gallic acid and beta sitosterol. The mature seeds of the plant contain about 3.1 to 6.1% L-DOPA, with trace amounts of 5-hydroxy tryptamine (serotonin), nicotine, dimethyl tryptamine (DMT), bufotenine, 5-MeO-DMT and beta-carboline. The leaves contain about 0.5% L-DOPA, 0.006% dimethyl tryptamine and 0.0025% 5-MeO-DMT^{12, 13}. Aim of this study is to review the existing in vivo studies on the effect of *Mucuna pruriens* on sperm parameters in men with idiopathic infertility.

METHOD

In the present study, all the articles including the clinical studies, animal studies and literature reviews were collected. A comprehensive search of the literature was conducted in the following databases: PubMed, Cochrane library and Google scholar for studies published between 2000 and 2020. The keywords that were used in combination to search for articles included, "*Mucuna pruriens*", "idiopathic infertility" and "sperm parameters". Results were limited to full research articles which were published in English. Conference proceedings, commentaries, articles which did not contain adequate details and articles written in other languages were excluded. In the second stage the total articles obtained from searching the above databases using above keywords were pooled together and duplicate articles were removed. The remaining articles were primarily screened by reading the "abstracts". In the present study, published all in-vitro articles written in English



Fig: 01 *Mucuna pruriens*
Flowers, Leaves and seed pods
(Henry.M, Mucuna pruriens dosage for testosterone,Sport nutrition expert,2020)

language which investigated the effect of *Mucuna pruriens* on sperm parameters in idiopathic infertility were studied. Men suffer infertility due to congenital abnormalities, immunological causes, systemic causes, varicoceles, acquired testicular damages, Obstructive causes, accessory gland infections were excluded and research articles, combine *Mucuna pruriens* with other medicinal herbs were also excluded, due to the impossibility of determining the net effect of *Mucuna pruriens*. Included articles were screened in the final stage by reading the full article and those not matching with inclusion criteria were further excluded.

RESULTS

Literature search

The literature search done by using keywords and identified following number of articles in the respective databases; PubMed (n=13), Google scholar (n= 116), and Cochrane library (n=4). After removing duplications, the total number of articles included in the present review is 124. 114 studies were omitted due to exclusion criteria of the study. The search strategy is summarized in figure 02.

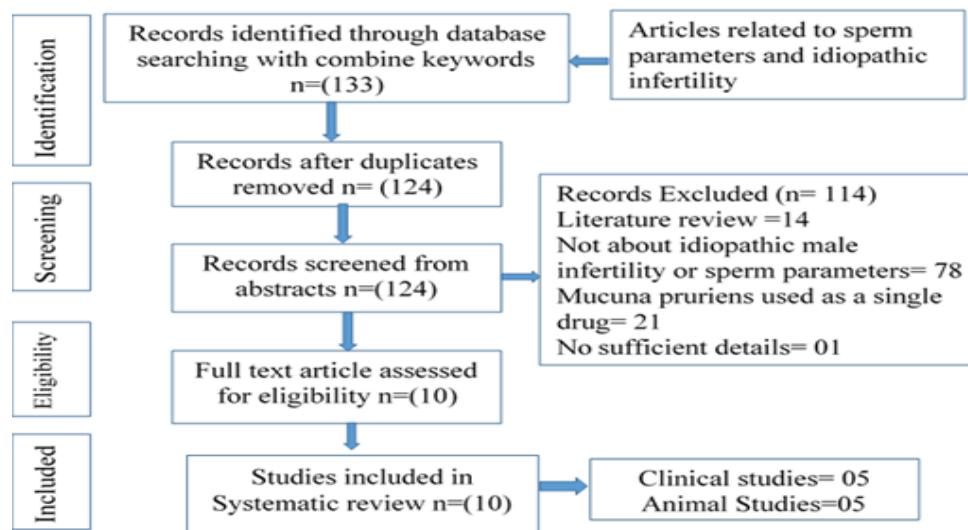


Fig: 02 Summarized search strategy

Table 1: Summary of clinical Studies regarding effect of *Mucuna pruriens* on sperm parameters with idiopathic infertility

	Main outcomes	Sample size	Age	Duration	Intervention	Study type	References
01.	<i>M. pruriens</i> improved the sperm concentration and motility significantly	120	30-38 years	3 months	<i>M. pruriens</i> seed powder (5 g/day orally with milk)	RCT*	Shukla, K.K. et al (2007)
02.	<i>M. pruriens</i> Significantly improved the sperm concentration and motility	60	30-40 years	3 months	<i>M. pruriens</i> seed powder (5 g/day orally with milk)	RCT*	Ahmad, K.M. (2008)
03.	<i>M. pruriens</i> improved the sperm concentration and motility significantly	150	25-40 years	3 months	<i>M. pruriens</i> seed powder (5 g/day orally with milk)	RCT*	Shukla, K.K. et al (2009)
04.	<i>M. pruriens</i> significantly improved the sperm concentration and motility	200	20-40 years	3 months	<i>M. pruriens</i> seed powder (5 g/day) and <i>Withania somnifera</i> root powder (5 g/day) orally with milk.	RCT*	Ahmad, K. M. (2009)
05.	Both types of seeds of <i>Kapikacchu</i> (Black and white) have increased the erectile function, sexual desire and overall satisfaction significantly and orgasmic function marginally. Both types of seeds of <i>Kapikacchu</i> have increased semen volume, pH of Semen, total Sperm count, Rapid linear progressive sperm and decreased Non progressive and Immotile sperm significantly. Black seeds of <i>Kapikacchu</i> . On percentage of relief it can be said that black seeds of <i>Kapikacchu</i> have given more results as compared to white seeds, but it is not significant.	30	20-60 years	30 days	<i>M. Pruriens</i> black seed powder 5 gm twice/day and <i>M. Pruriens</i> white seed powder 5 gm twice/day orally with milk.	RCT*	Sharma, T. et al (2017)

* RCT= Randomized Clinical trial

Table 2: Animal Studies regarding effect of *Mucuna pruriens* on sperm parameters with idiopathic infertility

	Main outcomes	Sample size	Intervention	Animal Used	References
01.	<i>Mucuna pruriens</i> increase sperm motility, sperm count	30	<i>Mucuna pruriens</i> seed powder+ ethanol suspension	Male albino rats	Suresh, S., Prithiviraj, E. & Prakash, S. (2009)
02.	<i>Mucuna pruriens</i> helped a highly significant and fast recovery of both sperm count and motility.	84	<i>Mucuna pruriens</i> seed powder	Male Sprague Dawley (SD) rats	Singh, A. P. et al (2013)
03.	<i>Mucuna pruriens</i> significantly improve sperm concentration and sperm motility. Further it maintained sperm abnormality at a low level.	20	<i>Mucuna pruriens</i> seed powder	West Africa Dwarf buck	Daramola, J. O. et al (2015)
04.	<i>Mucuna pruriens</i> improved testosterone levels and significantly recovered sperm count and motility.	35	<i>Mucuna pruriens</i> seed powder extracted with an ethanol-water mixture	Sprague-Dawley male rats	Sahin, K. et al (2016)
05.	<i>Mucuna pruriens</i> significantly increase sperm motility and sperm concentration. Further it decreased major anomalies of the sperm.	24	<i>Mucuna pruriens</i> seed powder	rabbit bucks (<i>Oryctolagus cuniculus</i>)	Mutwedu, V. B. et al (2019)

DISCUSSION

There were 10 different studies evaluating the in-vitro effect of *Mucuna pruriens* on sperm parameters with idiopathic infertility. Five of them were clinical studies and other five were animal studies. Table 1 summarizes the findings of the clinical effect of *Mucuna pruriens* on sperm parameters with idiopathic infertility and animal studies regarding above are summarized in Table 2. Clinical trials that have investigated the effect of *Mucuna pruriens* on sperm parameters in idiopathic infertile men are as follows:

According to Ahmad, M. K.'s comparative clinical study which done using infertile male patients with *M. pruriens* for three months, significantly improved the sperm concentration and motility. The study population included control group (n = 100) and infertile patients (n = 100), aged 20-40 years, The patients were further categorized in four groups according to semen parameters; normozoospermic infertile men (n = 25), had normal semen profile (defined below as in the control group) and infertility of unknown etiology, oligozoospermic infertile men (n = 25) and asthenozoospermic infertile men and azoospermic (n = 25). The control group comprised of age-matched healthy men who had previously initiated at least one pregnancy and exhibited normal semen profile. The subjects were prescribed *Mucuna pruriens* seed powder (5 g/day) and *Withania somnifera* root powder (5 g/day) orally for 3

months with milk. Efficacy of *M. pruriens* in improving male factor fertility was found more in comparison to *Withania somnifera*¹⁴.

Shukla, K.K. et al, done a prospective control study to understand the mechanism of action of *Mucuna pruriens* in the treatment of male infertile. Study included four parallel groups of subjects, three patient groups which consist with 25 patients in each on the basis of semen profile: normazoospermic, oligozoospermic and asthenozoospermic. The control group comprised 75 age matched healthy men. Infertile men were prescribing *M. pruriens* seed powder 5g/d orally in a single dose with milk for 3 months and it was found that treatment with *M. pruriens* regulates steroidogenesis (improve sperm concentration) and improves semen quality by improving motility¹⁵.

Ahmad, M.K. et al investigated the impact of *Mucuna pruriens* seeds on semen profiles and biochemical levels in seminal plasma of infertile men. The study included two groups of 60 subjects each; the control group and study group (consisting of 20 subjects each in their subgroups: normospermic, oligospermic and asthenospermic). The control group comprised age matched healthy men, who had previously initiated at least one pregnancy and exhibited a normal semen profile. Treatment with *M. pruriens* seed powder 5g/day

orally for 3 months with milk significantly inhibited lipid peroxidation, elevated spermatogenesis and improved sperm motility¹⁶.

Shukla, K.K. et al proved the role of *Mucuna pruriens* in infertile men who were under psychological stress. Study included 60 subjects who were undergoing infertility screening and were found to be suffering from psychological stress, assessed on the basis of a questionnaire and elevated serum cortisol levels. Study subjects were further divided into three subgroups on the basis of semen profiles and in each subgroup a minimum of 20 patients were included. These groups were (i) normozoospermic infertile men (ii), oligozoospermic infertile men and (iii) asthenozoospermic infertile men. Age-matched 60 healthy men having normal semen parameters and who had previously initiated at least one pregnancy were included as controls. Infertile subjects were administered with *M. pruriens* seed powder (5g per day) orally. According to the results, it may be concluded that *M. pruriens* not only reactivates the antioxidant defense system of infertile men but it also helps in the management of stress and improves sperm concentration and motility¹⁷.

As proven by Sharma, T. et al the black seeds of *M. pruriens* comparatively give more percentage improve on all subjective parameters i.e. Erectile function, orgasmic function, Sexual desire, Intercourse satisfaction; as well as objective parameters i.e. semen volume, total sperm count, rapid linear progressive, non-progressive and immotile sperms. A randomized comparative clinical trial done on 30 male sexual dysfunction patients and they were divided randomly into 2 groups, each group having 15 patients. In group-A was treated with *M. pruriens* black seed powder and in another group-B treated with white seed powder, in the dose of 5 gm twice/day with lukewarm milk for 30 days¹⁸.

Of the 5 articles, only one comparative study reported without control arm. All other 4 studies were control studies and they test the same dosage as 5g per day with milk. One study compares the *Mucuna pruriens* with another herb named *Withania somnifera* and it was proved that *M. Pruriens* is more effective than *M. somnifera*. Another study compares the effect of two varieties of *Mucuna pruriens* and that study showed, black

seed variety effective than white seed variety. According to all these clinical studies give evidence of ability to improve sperm count and motility of *M. pruriens*.

Animal Studies that have investigated the effect of *Mucuna pruriens* on sperm parameters in idiopathic infertility are as follows:

Singh, A. P. et al carried out a randomized control study to demonstrating spermatogenic restorative efficacy of *Mucuna pruriens* (MP) and its major constituent L-DOPA (LD), and finding the possible mechanism of action in a rat model. On this study, the Group I represented control animals (N=14) receiving 0.5% carboxymethylcellulose (CMC), group II (N=7) III (N=21) IV (N=21) and V (N=21) were administered Ethinyl estradiol (EE) (in 0.5% CMC) at 3 mg/kg BW/day for 14 days to compromise spermatogenesis. After 14th day, group II and 7 animals from group I were sacrificed. Group III was left for auto recovery for 56 days, receiving only 0.5% CMC during this period. Group IV and V were administered 300 mg/kg BW *M. pruriens* (in 0.5% CMC) and 20 mg/kg BW of L-DOPA (in 0.5% CMC), respectively, for 56 consecutive days on daily basis and the results were compared with an auto-recovery group. *M. pruriens* efficiently recovers the spermatogenic loss induced due to EE administration. The recovery is mediated by reduction in reactive oxygen species level, restoration of mitochondrial membrane potential, regulation of apoptosis and eventual increase in the number of germ cells and regulation of apoptosis. Further recovered the hypothalamic-pituitary-gonadal axis and ultimately leading to increased sperm count and motility¹⁹.

The study done by Daramola, J. O. et al, were carried out to investigate the potential effect of *Mucuna pruriens* seed powder on spermograms of West African Dwarf bucks (WAD). The animals were divided into 5 groups of 4 animals each and each group was randomly assigned to one of experimental treatments consisting of 0, 25, 50, 75, 100mg/BW of *Mucuna pruriens* seed powder administered via oral route to the animals for 30 days consecutively. The results showed that bucks treated with *Mucuna pruriens* seed powder had higher sperm motility compared to the control and the im-

provement was much pronounced in bucks that received both 75mg and 100mg of *Mucuna pruriens* seed powder ($P<0.05$). Treatment also led to maintenance of sperm abnormality at low level particularly at 75mg levels of inclusion. Higher ($P<0.05$) sperm concentration was observed in 100mg inclusion of *Mucuna pruriens* seed powder compared to other treatments. The results showed a decline ($P<0.05$) in the level of testosterone with increasing level of *Mucuna pruriens* seed powder administration²⁰.

Study of Sahin, K et al aimed to compare the effects of *Mucuna*, *Ashwagandha*, and *Tribulus* complexes on sexual function in rats. Thirty-five male rats were divided into five groups: the control group, sildenafil-treated group (5 mg/kg/d), *Mucuna*, *Tribulus* and *Ashwagandha* groups. The extract groups were treated orally either with *Mucuna*, *Tribulus* or *Ashwagandha* (300 mg/kg b.w.) for 8 weeks. Rats that were supplemented with *Mucuna* and *Tribulus* showed higher mean value for sperm motility, while *Mucuna*, *Tribulus*, and *Ashwagandha* supplementation produced a significant increase in sperm counts compared to the control group²¹.

Mutwedu, V. B et al, in their study, aim to investigate the effects of *Mucuna pruriens* seed meal (MSM) on sexual behavior, semen, and biochemical parameters in rabbit bucks. Animals were randomly assigned to three groups of 8 animals each with comparable weight. The three groups were allocated to the three dietary treatments (0, 1.5, or 3% inclusion of MSM) throughout the 12-week experimentation period. Supplementation of rabbit bucks with MSM increased significantly ($P<0.05$) the sperm motility, sperm concentration and decreased major anomalies²².

Suresh, S., Prithiviraj, E. and Prakash, S., revealed an increase in sperm count and motility by the ethanolic extracts of *Mucuna pruriens* Linn. seed. Female and male albino rats of wistar strain were used for the study. Animals were randomly divided in to five groups with six animals per group. Group I represented the negative control group, animals in group II, III, and IV were given oral suspension of ethanolic extract of *Mucuna pruriens* for 45 days at dose of 150, 200 and 250mg/kg respectively and group V rats received sildenafil citrate

5mg/kg as a positive control. Sperm parameters revealed an increase in the number of spermatozoa and motility in all the experimental groups and they mentioned that enhances the spermatogenic potential as the action may be in the hormonal level²³.

All animal studies were randomized control studies. Three of studies used *M. pruriens* powder as it is and other two were used as ethanolic extract suspension. According to all animal studies it was confirmed that *M. pruriens* improves sperm count and motility and two of them given evidence for decreasing of sperm abnormality.

Idiopathic male infertility is identified by reduction of spermatogenesis and defective sperm function. There are reports that abnormalities in sex hormone biosynthesis may impair spermatogenesis. Testosterone is essential for promoting spermatogenesis and secreted by the Leydig cells under LH stimulation. Prolactin acts on the Leydig cells of the testis to increase their responsiveness to LH. FSH has an important role in the development of testis. The failure of the pituitary to maintain proportionate levels of FSH, LH, and PRL may lead to disruption of testicular function, leading to infertility²⁴. Dopamine also play an important role in mediating male sexual behavior and function. An increased level of dopamine in brain results in increased libido and a decreased may reduce male sexual function²⁵. It was found that treatment with *M. pruriens* significantly improved Testosterone, LH, dopamine, adrenaline, and noradrenaline levels in infertile men and reduced levels of FSH and PRL¹⁵.

Also, the beneficial effect may be attributed to its anti-oxidant and neurostimulator properties. *Mucuna pruriens* is reported to contain many bioactive constituents, including alkaloids, coumarins, flavonoids, and alkylamines, which may play an important role in increasing the antioxidant capacity of treated men. There are also reports that the methanol extract of *M. pruriens* seeds has strong antioxidant activity, because it inhibits 1,1-diphenyl-2-picryl-hydrazyl and hydroxyl radical, and that it also has nitric oxide and superoxide anion scavenging and hydrogen peroxide decomposing and reducing power^{14,26}. It also proved that *M. pruriens* not only reactivates the anti-oxidant defense system of infertile

men but it also helps in the management of stress and improves semen quality¹⁷. Furthermore, *M. pruriens* seeds contain magnesium and zinc (8.74–19.38 mg and 0.25–0.54 mg per 5 g seed flour, respectively), which are important for spermatogenesis²⁷.

CONCLUSION

The results of this study showed that consumption of *Mucuna pruriens* significantly improves sperm count and motility. According to studies (n=2) *M. pruriens* can improve morphological defects of sperms to some extents and none of those studies recorded any adverse effects. As a study, it can be said that black seeds of *Mucuna pruriens* have given more results as compared to white seeds, but it is not significant. *Mucuna pruriens* seed powder orally used in all clinical studies and four studies among five prescribed 5g of seed powder with milk per day for 3 months duration while other one prescribes 5g seed powder with milk twice daily for the one-month duration. Therefore, it can be concluded as the powder of *Mucuna pruriens* 5g per day as minimal sufficient dosage for humans to improve sperm count and motility.

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