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**File: ■ Ashwagandha (*Withania somnifera*)**
**■ Male Infertility**
**■ Semen**

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## RE: Ashwagandha Improves Multiple Parameters Affecting Semen Quality in Infertile Men

Ahmad MK, Mahdi AA, Shukla KK, et al. *Withania somnifera* improves semen quality by regulating reproductive hormone levels and oxidative stress in seminal plasma of infertile males. *Fertil Steril*. Jun 5, 2009. [Epub ahead of print]

Human semen contains antioxidants to counter the oxidative effects of reactive oxygen species (ROS) produced by sperm cell metabolism. Excessive production of ROS causes seminal oxidative stress that is linked to idiopathic male infertility. Ashwagandha (*Withania somnifera*) is traditionally used as an aphrodisiac, and it inhibits lipid peroxidation in animals under stress. In vivo studies have shown that it enhances reproductive functions in mature and immature male rats. This clinical study was designed to assess the effects of ashwagandha on the semen profile, oxidative biomarkers, and reproductive hormone levels of infertile men.

The researchers obtained ashwagandha roots from the Central Council for Research in Unani Medicine in New Delhi, India. The roots were shade-dried and ground into a fine powder. The study was conducted between February 2007 and August 2008 at the Chhatrapati Shahuji Maharaj Medical University in Lucknow, India. The authors recruited 75 infertile men aged 25-40 years. They were aged-matched to the control group (n=75), which included healthy men who had initiated at least 1 pregnancy and had a normal semen profile (sperm concentration>20 x $10^6$/ml, motility>40%, >40% normal morphology). The 3 treatment groups included 25 infertile men with normal semen profiles (normozoospermic group), 25 men with low sperm concentrations (<20 x $10^6$/ml, oligozoospermic group), and 25 men with low sperm motility (<40%, asthenozoospermic group). The treatment groups took 5 g/day ashwagandha root powder with milk for 3 months. They provided semen samples following 3-4 days of abstinence before and after treatment. The control group provided 1 semen sample. The samples were used to assess semen profile following the World Health Organization (WHO) procedures. Seminal plasma obtained as supernatant after repeated centrifugation was used to assess biochemical parameters, and venous blood samples were taken to measure hormone levels.

After treatment, sperm concentration and motility were significantly increased compared to baseline levels in all 3 treatment groups (P<0.01 for all). The sperm motility was still "less than optimal" in the asthenozoospermic treatment group (24.44%). Following treatment, semen volume increased significantly compared to baseline levels in the normozoospermic and oligozoospermic treatment groups (P<0.01 for both), but not in the asthenozoospermic treatment group.

The levels of lipid peroxides (LPO) and protein carbonyl groups were significantly higher compared to the control group in all 3 treatment groups at baseline (P<0.01 for all). After treatment, levels of LPOs and protein carbonyl groups were significantly lower compared to baseline levels in all 3 treatment groups (P<0.01). Seminal plasma superoxide dismutase (SOD) activity was significantly lower than that of the control group in the 3 treatment groups before supplementation (P<0.01). Pre-treatment catalase activity was also significantly lower compared to the control group in all 3 treatment groups (normozoospermic and oligozoospermic groups: P<0.05, asthenozoospermic: P<0.01). Similarly, glutathione activity was significantly lower in the 3 treatment groups compared to the control group at baseline (P<0.01 for all). Following treatment, SOD, catalase, and glutathione activities all increased significantly compared to baseline levels in all 3 treatment groups (P<0.01 for all).

Pre-treatment levels of vitamins A, E, and C and fructose were all significantly lower in the seminal plasma of the treatment groups compared to the control group (P<0.01 for all). After treatment, the levels of vitamins A, E, and C had significantly improved compared to baseline levels in the 3 treatment groups (P<0.01 for all). Fructose levels were also significantly improved in all 3 groups compared to baseline levels (P<0.05). Before treatment, the serum testosterone and luteinizing hormone (LH) levels of the 3 groups were significantly lower than those of the control group (P<0.01 for both). Following treatment, testosterone and LH levels were both significantly improved compared to pre-treatment levels in the 3 treatment groups (P<0.01 for all). LH stimulates the production of testosterone, which stimulates spermatogenesis (sperm production). Pre-treatment serum levels of follicle stimulating hormone (FSH) and prolactin were significantly higher in the asthenozoospermic and oligozoospermic groups compared to the control group (P<0.01-0.05). Following treatment, the asthenozoospermic and oligozoospermic groups' serum FSH and prolactin levels were significantly lower compared to baseline levels (P<0.01-0.05). FSH was significantly lower after treatment than at baseline for the normozoospermic group (P<0.05).

The authors conclude that low levels of LH and testosterone were "very good indicators of infertility," while high levels of FSH and prolactin were good but less accurate infertility markers. The authors also conclude that treatment with ashwagandha increased sperm counts and motility and seminal levels of antioxidants, while decreasing oxidants and improving the serum hormone profiles of infertile men. More research is needed to determine the mechanism of action and active constituents responsible for these effects.

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