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File: ■ *Shatavari* (*Asparagus racemosus*, Asparagaceae)
■ Infertility
■ Women's Reproductive Health

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RE: *Shatavari* May Improve Reproductive Health Outcomes in Stressed Women: A Non-systematic Review

Pandey AK, Gupta A, Tiwari M, et al. Impact of stress on female reproductive health disorders: Possible beneficial effects of shatavari (*Asparagus racemosus*). *Biomed Pharmacother*. July 2018;103:46-49. doi: 10.1016/j.biopha.2018.04.003.

Women of reproductive age are frequently exposed to psychological, physical, and physiological stressors that may affect reproductive health. Chronic psychological stress is associated with higher rates of in vitro fertilization failure, possibly due to its negative effects on ovaries and oocytes. Stress induces generation of reactive oxygen species (ROS) and release of cortisol, which in turn inhibits estradiol-17β biosynthesis in ovaries, resulting in reduced oocyte quantity and quality. It is estimated that ~ 60-80 million women worldwide have problems with infertility.

In Ayurvedic medicine, women's reproductive health issues are often treated with *shatavari* (asparagus; *Asparagus racemosus*, Asparagaceae). "Shatavari" means "able to have 100 husbands" in Sanskrit. *Shatavari* boosts overall vitality, nourishes ovaries, promotes production of reproductive hormones, and maintains libido in women. It is used in six important *rasayanas*, or Ayurvedic formulas that promote general well-being by increasing cellular vitality and immunity. The herb is extensively used in stress-related immune disorders, and is reputed to slow aging, increase longevity, and improve mental function. Commonly administered in tablets, capsules, or powders, *shatavari* has been used in disorders including gonorrhea, hemorrhoids, diabetes, rheumatism, cough, diarrhea, gastric problems, and headache. Steroidal saponins, glycosides, alkaloids, polysaccharides, mucilage, and isoflavones are among its > 50 compounds. Flavonoids and glycosides of quercetin (e.g., rutin, hyperoside) are seen in flowers and fruits; quercetin 3-glucuronide, in leaves of this climbing plant. Kaempferol, asparagamine, and racemosol are found in ethanolic root extracts. In vivo, two *shatavari*-containing medicines improved ovarian physiology, estrogen production and uterine weight without altering progesterone levels. An alcoholic extract of *shatavari* rhizome had estrogenic effects on mammary glands and genitalia of pregnant female rats. Its anticancer, anti-dysenteric, antifungal, antibacterial, anti-inflammatory, anti-ulcer, antioxidant, anti-abortifacient, and anticoagulant effects have been reported in vivo and/or in clinical trials. The authors propose that *shatavari* would benefit stress-mediated reproductive health disorders in women and review potential mechanisms of action.

Female reproductive hormones include glucocorticoids, catecholamines, growth hormone, and prolactin. Both androgen and estrogen levels are impaired in women's reproductive health problems. High levels of stress, with release of stress hormones like cortisol, over extended periods may seriously impair reproductive function, causing amenorrhea, anovulation, and menstrual irregularity. *Shatavari*'s phytoestrogens may regulate the ovarian cycle. It corrects pituitary gland function, promoting growth, differentiation, and physiological function of the female genital tract. The herb was reported to relieve premenstrual syndrome and dysmenorrhea in 40 women over three months' use. Other clinical studies report that *shatavari* reduced dysfunctional uterine bleeding.

Polycystic ovarian syndrome (PCOS), a common anovulatory disorder, affects 4-12% of women of reproductive age and often leads to infertility. Increased oxidative stress (OS) and ROS induce PCOS onset. *Shatavari* is reported to effectively reduce PCOS by improving follicular growth and ovulation in clinical studies. A regimen of 100 mg/d *shatavari* combined with *shatapushpa* (fennel, *Foeniculum vulgare*, Apiaceae) and *guduchi* (balloon plant; *Cardiospermum halicacabum*, Sapindaceae) for 105 days followed by 1000 mg/d *Rasayana Kalpa*, combining *shatavari*, *guduchi*, *jatamansi* (spikenard; *Nardostachys jatamansi*, Capifoliaceae), and amla (*Phyllanthus emblica*, Phyllanthaceae) for 60 days may help manage PCOS-mediated subfertility.

Chronic psychological stress negatively impacts ovaries and oocytes, impairing follicular development, growth, and ovulation by inducing apoptosis. Oocyte apoptosis may deplete ovarian germ cells and reduce oocyte quality after ovulation, directly affecting reproductive outcomes. While *shatavari* nourishes and rejuvenates ovarian function and development and regulates menstruation, it was not superior to clomiphene citrate in one clinical trial. This may have been due to insufficient dosage and length of treatment in the *shatavari* group. Antioxidant effects of *shatavari* include ROS scavenging, reduced OS level, greater antioxidant capacity, and improved ovarian and endometrial physiology. In vivo studies report increased production of several antioxidant compounds with various *shatavari* extracts. Its isoflavones, racemofuran, asparagamine A, and racemosol, are credited with its antioxidant effects. At time of publication, no evidence yet supported the authors' proposal that benefits of *shatavari* in stress-mediated reproductive disorders such as PCOS may be due in part to its elevation of antioxidant enzymes in ovaries. *Shatavari*'s steroidal saponins may also enhance female fertility by blocking oxytocin-induced uterine contractions, as seen in several mammal models.

While molecular mechanisms of its benefits in treating infertility need more elucidation, existing studies support its use to protect against stress-related negative reproductive health outcomes in women. No mention is made of *shatavari*'s safety profile in this brief non-systematic review.

—Mariann Garner-Wizard