



## Impact of stress on female reproductive health disorders: Possible beneficial effects of shatavari (*Asparagus racemosus*)



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### ARTICLE INFO

#### Keywords:

Stress  
ROS  
Oxidative stress  
Oocyte quality  
Female reproductive health  
Shatavari

### ABSTRACT

Stress is deeply rooted in the society and women are frequently exposed to psychological, physical and physiological stressors. Psychological stress disturbs reproductive health by inducing generation of reactive oxygen species (ROS) and thereby oxidative stress (OS). The increased OS may affect physiology of ovary, oocyte quality and cause female reproductive health disorders. To overcome stress-mediated reproductive health disorders in women, shatavari (*Asparagus racemosus*) is frequently recommended in Ayurvedic system of medicine. Although shatavari is one of the major health tonics and most popular rasayana drugs to treat reproductive ailments of women, underlying mechanism of shatavari action at the level of ovary remains poorly understood. Based on the existing studies, we propose that shatavari may improve female reproductive health complications including hormonal imbalance, polycystic ovarian syndrome (PCOS), follicular growth and development, oocyte quality and infertility possibly by reducing OS level and increasing antioxidants level in the body. Further studies are required to elucidate the mechanism of shatavari actions at the level of ovary and oocyte that directly impacts the reproductive health of women.

### 1. Introduction

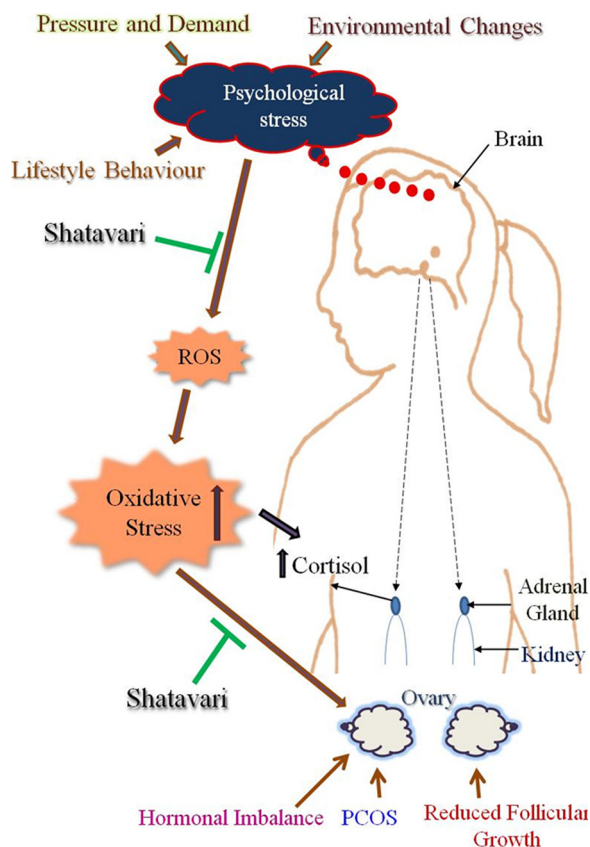
Nowadays, stress is noticed at each level in society due to environmental changes, pressure and demand, limited resources and lifestyle behaviors in human [1]. Girls and women in their reproductive age are more frequently exposed to psychological, physical and physiological stressors that increase reproductive health problems [2]. Chronic psychological stress leads to poor in vitro fertilization (IVF) outcome possibly due to its negative impact at the level of ovary and oocytes [3,4]. Negative life events induce generation of reactive oxygen species (ROS; Fig. 1) as well as the release of cortisol that inhibits estradiol-17 $\beta$  biosynthesis in the ovary resulting in reduced number and poor quality oocytes [3,5,6]. As per World Health Organization (WHO), approximately 60–80 million couples have infertility problems worldwide [1].

The reproductive health complications in women are frequently treated by one of the most popular herbal medicines i.e. shatavari (*Asparagus racemosus*) in Ayurveda, which is derived from Sanskrit,

‘ayur’ stands for “life” and ‘ved’ for knowledge. In Ayurvedic system of medicine, practitioners use herbal drugs to correct health disorders with holistic approach [7]. Shatavari belongs to Liliaceae family and is commonly grown in tropical and subtropical parts of India including Himalayas [8]. It is a climber of 1–2 m height and flowering undershrub having number of fleshy tuberous roots [9]. The medicinal utilities of shatavari have been reported in Indian and British Pharmacopoeias and traditional system of medicine [10,11]. Literally, the term shatavari means “able to have one hundred husbands” and ability to strengthen reproductive health so that women can produce healthy ova [12]. Shatavari has also been used to increase vitality and fertility [13].

In Ayurveda, shatavari has been treated as one of the important herbal medicines [7], commonly prescribed to nourish ovary, promote production of reproductive hormones and maintain libido of women [13]. Shatavari is mentioned under six important rasayanas [7]. Rasayanas are herbal medicines, which promote general well being of an individual by increasing cellular vitality and immunity [14]. Shatavari is used to correct pitta and vata dosha of patients. According to

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**Fig. 1.** Schematic diagram showing the negative impact of stress on ovary. Pressure and demand, environmental changes and lifestyle behavior result in psychological stress. The psychological stress increases reactive oxygen species (ROS) and thereby oxidative stress (OS) that negatively impact the physiology of ovary. Shatavari scavenges ROS, reduces OS and prevents stress-mediated negative changes at the level of ovary.

Ayurveda, world is comprised of five elements i.e. air, water, fire, earth and sky [15]. Changes in these five elements may cause various health disorders that have been categorized in Ayurvedic system of medicine as vata, pitta and kapha based on the physiological disturbances in a person [16,17].

Shatavari has more than 50 organic compounds including steroidal saponins, glycosides, alkaloids, polysaccharides, mucilage, racemosol and isoflavones [10]. The steroidal saponins are biological active constituents of shatavari root [9,13]. Flavanoids and glycosides of quercetin such as rutin and hyperoside are present in flowers and fruits, whereas quercetin 3-glucuronide is found in leaves of shatavari [18]. Several other bioactive ingredients such as asparagine [19], racemosol and kaempferol are extracted from the ethanolic root extract of shatavari [20,21]. Although evidences are not available to suggest the impact of these bioactive ingredients in the improvement of reproductive health parameters, based on the existing studies we propose that shatavari may improve stress-mediated reproductive health complications due to its antioxidant ability in women.

Shatavari is commonly available in the form of tablets, capsules or powder under the name of shatavari by various manufacturing companies. It improves ovarian physiology, increases estrogen level and uterine weight in rat [22]. Shatavari roots exhibits active constituents in wet as well as dry form [23]. Shatavari is well known to prevent ageing, increase longevity, impart immunity, improve mental function, vigor and add vitality to the body [13]. It is highly effective in female reproductive problems [8,13]. Shatavari has been recommended for the treatment of various diseases such as gonorrhoea, piles, diabetes, rheumatism, cough, diarrhea, gastric troubles and headache [12,24].

The anticancer, antidysenteric, antifungal, antibacterial, anti-inflammatory, antiulcer, antioxidant, antiabortifacient and anticoagulant activities of shatavari have been reported in experimental animals and clinical trials [13,25,26]. In addition, long term administration of shatavari does not show any toxicity or abnormality in the behavior of mouse as well as rat [13,27]. In Ayurvedic system of medicine, shatavari has been extensively used for the treatment of stress-related immune disorders and to improve general state of health [11,13]. Oral administration of alcoholic extract of shatavari rhizome (daily for 15 days) exerts estrogenic effects on the female mammary glands as well as genital organs in adult pregnant female rats [28]. Based on these studies, we hypothesize that shatavari could be used for the management of stress-mediated reproductive health complications in women. This is the first review article of its own kind wherein we have focused on the stress-mediated reproductive health disorders in women and proposed the possible impact of shatavari to overcome such an important health issues in women.

## 2. Possible impact of shatavari on stress-mediated hormonal imbalance

Physical, physiological and other stressors directly as well as indirectly may generate psychological stress that affect female reproductive health possibly by modulating the ovarian physiology and reproductive hormones [3]. These hormones include glucocorticoids, catecholamines, growth hormone and prolactin [29]. Increase of stress hormone such as cortisol may reduce estradiol-17 $\beta$  biosynthesis in the ovary [3,5]. The androgen as well as estrogen levels are impaired in women having reproductive health problems [30]. The high level of stress for a longer time may result in complete impairment of reproductive functions [31]. For instance, stress may result in amenorrhea, anovulation and menstrual irregularities in females [32].

Shatavari can be effectively used to correct the hormonal imbalance due to its phytoestrogenic properties [21]. The phytoestrogens of shatavari could regulate estrous or ovarian cycle in mammals [33] and reduce adverse menopausal symptoms [22]. Shatavari has been reported to correct pre-menstrual syndrome (PMS) and dysmenorrhoea (painful menstruation) in a study of 40 patients for 3 months [34]. Shatavari corrects pituitary gland functions and promotes growth, differentiation and physiological functions of the female genital tract [33]. Drugs that contain shatavari ‘U-3107’ or EveCare (containing 32 mg shatavari extract per 5 ml syrup, Himalaya Drug Co., Bangalore) increase uterine weight as well as estrogen levels without altering progesterone level in experimental rats [35]. Several clinical studies carried out using shatavari treatment suggests that it improves dysfunctional uterine bleeding (DUB) in women during their reproductive age (20–45 years) [36,37].

## 3. Possible impact of shatavari on stress-induced PCOS

The poly cystic ovarian syndrome (PCOS) is a most common anovulatory reproductive health problems affecting 4–12% of women leading to female infertility [38]. The increase of ROS [30] and OS induce the onset of PCOS [39]. Shatavari treatment is mainly focused to overcome the PCOS problem and to normalize the physiology of ovary (Fig. 2) [21]. Shatavari is found much effective to reduce PCOS, improve follicular growth, development and ovulation in clinical subjects [40]. It is suggested that PCOS-mediated subfertility could be managed successfully by using oral administration of Ayurvedic treatment regimen of shatavari (10 mg/day) along with shatapushpa and guduchi for 105 days and thereafter 1000 mg/day of Rasayana Kalpa, combination of shatavari along with guduchi, jatamansi and amla for 60 days [40].

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