

# SHATAVARI

## *Asparagus racemosus* Willd.

### *Family*

Asparagaceae. The genus *Asparagus* has been recently moved from the subfamily Asparagae, in the family Liliaceae, to the newly created family Asparagaceae.

### *Parts Used*

Root and Rhizome.

### *Description*

The word asparagus originates from the Greek word for stalk or shoot. About 300 species of *Asparagus* are known to occur in the world. A European species, *Asparagus officinalis*, is a popular vegetable consumed in many parts of the world. Out of several species of 'Asparagus' grown in India, *Asparagus*

*racemosus*, *Asparagus gonaclades* and *Asparagus adsendens* are most frequently used in indigenous medicine.<sup>1</sup> *Asparagus racemosus* has been used by tribes in India from primeval time and is commonly mentioned as a rasayana in the Ayurveda. Rasayana refers to plant drugs which promote general wellbeing of an individual by increasing cellular vitality or resistance.<sup>2,3,4</sup>

Shatavari grows throughout the tropical, and subtropical, parts of India and Bangladesh up to an altitude of 1500 metres. It has a spinous under-shrub, with tuberous, short rootstock bearing numerous succulent roots (30 to 100cm long and 1 to 2cm thick), that are silvery white or ash coloured externally, and white internally. The stem is woody, climbing (up to 1 to 3m high), whitish grey or brown coloured, with small spines.<sup>5</sup> The plant flowers during February-March leaving a mild



fragrance in its surroundings, and by the end of April fruits can be seen with attractive red berries. Shatavari is also found in other countries in Asia, Java, Australia, Africa and southern parts of China.<sup>6,7</sup>

Due to its multiple uses, the demand for shatavari is constantly on the rise. The mature plants can be harvested only after flowering, which takes 3 to 4 years, because shatavarins are accumulated in the roots only post flowering. The normal practice of root collection involves uprooting of the whole plant, which usually leads to wastage of 50% of the collected material. Destructive harvesting, combined with habitat destruction in the form of deforestation, has aggravated the problem. The plant is now considered 'endangered' in its natural habitat. Therefore, the need for conservation of this plant is crucial.<sup>8,9,10</sup> This plant has also been recognized as 'vulnerable'.<sup>11,12,13</sup>

### *Traditional Use*

In Western herbal medicine shatavari is often seen as a female reproductive tonic, and shatavari does indeed mean to "possess a hundred husbands" as its tonic and rejuvenative action on the female reproductive organs is said to give the capacity to have one hundred husbands. However, it is equally considered a general tonic.

Withania is sometimes also seen as a "female" tonic by Western herbalists, perhaps due to the fact that it is less stimulating than Korean ginseng (*Panax ginseng*). However, in Ayurvedic medicine, shatavari is the main rejuvenative tonic for the female, while withania is for the male. Nevertheless, shatavari is used for sexual debility and infertility in both sexes. It is also used for menopausal symptoms and to increase lactation.<sup>14,15</sup>

Ancient Ayurvedic literature recommends the root of shatavari in cases of threatened abortion as a uterine tonic/sedative.<sup>16</sup>

Shatavari was used beneficially for female infertility: for increasing libido, curing inflammation and moistening the dry tissues of the sexual organs, enhancing folliculogenesis and ovulation, preparing the womb for conception, preventing miscarriages, acting as a post-partum tonic by increasing lactation and normalizing the uterus and the changing hormones.<sup>17</sup> Shatavari was also used beneficially

in nervous disorders, dyspepsia, hyperacidity, diarrhoea, dysentery, tumours, inflammations, hyperdipsia, neuropathy, hepatopathy,<sup>18</sup> cough, bronchitis and certain infectious diseases.<sup>19</sup>

### *Constituents*

Steroidal saponins (shatavarins VI-X); saponins (shatavarin I [or asparoside B], shatavarin IV [or asparinin B, a glycoside of sarsasapogenin], shatavarin V, immunoside and schidigerasaponin D5 [asparanin A]); isoflavones, including 8-methoxy-5,6,4'-trihydroxyisoflavone 7-O-beta-D-glucopyranoside; phytosterols (0.8%); polyphenols (1.7%); asparagamine (a polycyclic alkaloid); racemosol (a cyclic hydrocarbon: 9,10-dihydrophenanthrene); sterols; terpenes; polysaccharides; proteins; starch; tannin; flavonoids, ascorbic acid.<sup>20,21,22</sup>

### *Actions*

Reproductive tonic, aphrodisiac, oestrogen modulator, adaptogen, immunomodulator, antitussive, cytoprotective, digestive, antiulcerogenic, antidiarrhoeal, antioxytotic, uterine sedative, antispasmodic, hepatoprotective, galactogogue, antioxidant, antibacterial, diuretic, skin lightening, antiaging, neuroprotective and demulcent for the dry and inflamed membranes of the lungs, stomach, kidneys and sexual organs.

### *Pharmacological Activity*

#### **Hormonal Activity**

Oestrogen replacement therapy is recommended primarily for the treatment of menopausal symptoms, and for the prevention of cardiovascular disease and osteoporosis, in postmenopausal women.<sup>23</sup> At the same time, oestrogen therapy is known to increase the risk for endometrial cancer, breast cancer, venous thromboembolic events and gall bladder disease.<sup>24,25</sup> Consequently, the interest in plant-derived oestrogens or 'phyto-oestrogens' has increased due to the realization that hormone replacement therapy is neither as safe nor as effective as previously envisaged.<sup>26</sup>

The high level of steroidal saponins may be responsible for the oestrogenic effect of shatavari

and explain its traditional use as a reproductive tonic. Phyto-oestrogens are defined as any plant compound structurally and/or functionally similar to ovarian and placental oestrogens and their active metabolites.<sup>27</sup> Phyto-oestrogens affect the regulation of ovarian cycles, and oestrous, in female mammals and the promotion of growth, differentiation and physiological functions of the female genital tract, breast, pituitary and several other organs and tissues in both sexes. There are several studies that indicate a lower rate of breast cancer in populations with a high exposure to phyto-oestrogens.<sup>28,29,30</sup> Studies have shown no correlation between phytoestrogens and breast cancer.<sup>31,32</sup>

It has been demonstrated that a chloroform and methanol root extract of shatavari inhibited chemically-induced mammary carcinogenesis in rats. The extract was added in different percentages to the animal feed. Rats fed on a 2% extract diet showed a significant ( $p < .05$ ) decline in both tumour incidence, and mean number of tumours, per tumour bearing animal. The authors concluded that shatavari root extract exerted a mammatropic and/or lactogenic influence on normal, as well as on oestrogen-primed, animals thereby rendering the mammary epithelium refractory to the carcinogen.<sup>33</sup>

Pilot studies in India furthermore suggest that shatavari may be beneficial in the treatment of dysfunctional uterine bleeding (DUB) and premenstrual syndrome (PMS). Seventy women aged 20 to 45 years with DUB were included in the first study. It was found that by the end of the treatment, 63 women had achieved a regular menstrual cycle. The authors attributed this result to the local healing of the endometrium stimulated by endometrial microvascular thrombosis caused by the high doses of phytoestrogens in the preparation ('U-3107' or EveCare® (containing 32mg *Asparagus racemosus* extract per 5mL syrup). In another study, a group of 40 patients suffering from dysmenorrhoea and PMS were found to be symptom free after treatment with shatavari (EveCare capsules). Another product containing about 85% shatavari has been shown to be effective in the treatment of PMS.<sup>34</sup>

A more recent study suggests that shatavari may have oestrogenic effects on breast tissue and genital organs in female rats. An alcoholic extract of the shatavari rhizome was administered orally

to adult pregnant female albino rats at a dose of 30mg/100g body weight, daily for 15 days (days 1 to 15 of gestation). The macroscopic findings revealed a prominence of the mammary glands, a dilated vaginal opening and a transversely situated uterine horn in the treated group of animals. The weight of the uterine horns of the treated group was found to be significantly higher ( $p < .001$ ) but the length was shorter ( $p > 0.01$ ). Microscopic examination of the treated group showed proliferation in the lumen of the duct of mammary gland. It was obliterated due to hypertrophy of ductal and glandular cells. Hyperplasia of the glandular and muscular tissue, and hypertrophy of the glandular cells, were observed in the genital organs. The parenchyma of the genital organs showed abundant glycogen granules, with dilated blood vessels and thickening of the epithelial lining. The oviduct in the treated group showed hypertrophied muscular wall, whereas the ovary revealed no effect of the drug. The results suggest an oestrogenic effect of shatavari on the female mammary gland and genital organs.<sup>35</sup>

The energy source for the female reproductive system is oestrogen-dependent glycogen. Oestrogen increases the glycogen content in the uterus and any decrease in uterine glycogen would directly implicate oestrogen deficiency.<sup>36</sup> Another formulation containing 110mg of shatavari extract per tablet (Menosan®) was found to cause an increase in uterine weight and uterine glycogen, without altering serum oestrogen and progesterone levels in immature rats as against ovariectomised rats used as control.<sup>37</sup> This study indicates that the phytoestrogen performs its function by binding directly to the oestrogen receptor without enhancing the endogenous oestrogen levels. Menosan has also been found beneficial in reducing menopausal symptoms. In a trial comprising 27 women aged 35 to 56 years, significant relief from post-menopausal symptoms such as depression (90% relief), insomnia (83.33% relief), irritability (50% relief), weight gain (50% relief), bone and joint pains (40%), sweating (37.88%) and hot flashes (37.03%) was observed after the use of Menosan.<sup>38</sup>

Interestingly, shatavari is clinically useful as an aphrodisiac in males.<sup>39</sup> At 400mg/kg body weight, shatavari showed significant aphrodisiac activity in rats enhancing sexual behaviour and performance. The parameters observed during the study were mount

frequency, mount latency, intromission frequency, intromission latency, ano-genital sniffing and genital grooming. Another isolated report found that rats fed with shatavari root powder (0.5g/kg rat feed) for 21 consecutive days exhibited significantly high testes weights as compared to untreated controls.<sup>40</sup>

### Galactagogue

Shatavari has galactagogue, and mammogenic, functions through enhancing blood prolactin and cellular division in the mammary glands.<sup>41,22,43</sup>

Early studies have indicated that an ethanol extract increased both the weight of mammary lobulo-aveolar tissue and the milk yield. These effects were attributed to the action of released corticosteroids or an increase in prolactin.<sup>44</sup>

An increase in milk production was observed after administration of shatavari (40mg concentrated root extract per tablet) to women suffering from deficient milk secretion in one study; however Sharma et al did not observe any increase in prolactin levels in females complaining of secondary lactational failure with shatavari suggesting that it has no lactogenic effect. A randomised controlled trial in 53 women who had delivered at term without complications reporting with lactational inadequacy received 100g dose of a polyherbal formula containing 15g shatavari root extract as the main ingredient. Lactation inadequacy was defined as: (i) failure to regain infant's birth weight at 15 days of life, or (ii) infant weight gain of <15g/day, or (iii) mother supplementing >250mL/day of milk for infant feeding after 4 weeks of birth. All mothers included with the diagnosis of lactational inadequacy were motivated to exclusively breastfeed, and advised on position and frequency of feeds, adequate rest and nutrition. If after one week of exclusive breastfeeding the infant's weight gain was <15g/day, the mothers were included in the trial.<sup>45</sup>

The prolactin levels were tested before and four weeks after the trial, which seems questionable as prolactin levels gradually decrease but milk supply is maintained or increased by local feedback mechanisms (autocrine control).<sup>46</sup>

Therefore, an increase in prolactin levels is needed to increase, but not maintain, milk supply. Furthermore, the increase in the infant's weight gain and decrease in supplemental feeds was put down

to "probably a result of improved breastfeeding techniques", see the table for trial outcome<sup>47</sup> (reproduced below for clarity) despite proper counselling on that before the trial was started.

Both prolactin and cortisol are involved in lactogenesis, and in shatavari fed buffaloes, serum levels of prolactin and cortisol were significantly increased ( $p < 0.01$ ) than the control group.<sup>48</sup> The shatavari treated group also produced 10.68% more milk yield. This information validates earlier reports that prolactin and cortisol hormone release is stimulated by shatavari in laboratory animals.<sup>49,50,51</sup>

TABLE II - Comparison of Outcome Variables

Variable	Galactagogue (n=32)	Placebo (n=32)
Maternal PRL levels (ng/mL) (Median, range)		
Before therapy	525 (8-210)	40.5 (7-220)
After therapy	25 (2-200)	38 (7-156)
Infant weight gain velocity (g/d) (Median, range)		
Before therapy	12 (0-35)	10 (0-41)
After therapy	30 (14-52)	25 (10-75)
Volume of supplemental milk (mL/d) (Mean±SD)		
Before therapy	291.9±144	262.6±118
After therapy	163.2±214	210±242.3

Shatavari is a rich source of minerals and trace elements such as calcium, copper, magnesium, iron, manganese, nickel, and zinc. The presence of calcium correlates with the analytical results for galactagogues.<sup>52</sup>

### Antioxytotic Activity

Studies have found that the saponin-rich fraction in shatavari inhibited oxytocin-induced uterine contractions *in vivo*.<sup>53</sup> The antioxytotic effect has been found to be due to shatavarin I, as it was demonstrated that the compound competitively blocked oxytocin-induced contraction of rat, guinea pig and rabbit's uteri, *in vitro*, as well as *in vivo*.<sup>54</sup>

Additionally, shatavari extract was shown to inhibit uterine contraction induced by spasmogens such as acetylcholine, barium chloride and 5-hydroxytryptamine, as well as blocking spontaneous uterine motility; thus can be used as

a uterine sedative. This non-contractile response, decreased motility and antispasmodic activity of shatavari makes it useful in conditions associated with hyper motility of the uterus, for example threatened abortion and dysmenorrhea.<sup>55</sup> Shatavari could well be considered as a substitute for the endangered *Chamaelirium luteum* (False Unicorn Root).

### Adaptogenic Activity

As previously mentioned, shatavari is considered to be a rasayana herb. Rasayana means rejuvenation. Rasayana consists of the Sanskrit word ayana, meaning path, and rasa, which means taste, essence, flavour, juice, or emotion. In the therapeutic process, rasa is concerned with the conservation, transformation, and revitalisation of energy. Rasa nourishes the body, boosts immunity and promotes physical and mental health. They are given to small children as tonics, and are also taken by the middle-aged and elderly to increase longevity. Six of the major rasayana plants from Ayurveda have been studied for adaptogenic activities. The whole, aqueous, standardised extracts of selected plants (*Tinospora cordifolia*, *Asparagus racemosus*, *Embllica officinalis*, *Withania somnifera*, *Piper longum* and *Terminalia chebula*) were administered orally to experimental animals, in a dose extrapolated from the human dose, after which they were exposed to a variety of biological, physical and chemical stressors. The plant extracts were found to protect against the stressors, as measured by markers of stress responses and objective parameters for stress manifestations. Using a model of cisplatin induced alterations in gastrointestinal motility, the ability of the plants to exert a normalizing effect, irrespective of direction of pathological change was tested. All the plants reversed the effects of cisplatin on gastric emptying, while shatavari also normalized cisplatin-induced intestinal hypermotility. All the plant drugs were found to be safe in both acute and subacute toxicity studies. Studies on the mechanisms of action of the plants revealed that they all produced immunostimulation.<sup>56</sup>

Another traditional adaptogenic/rasayana formulation (Siotone) containing *Withania somnifera*, *Ocimum sanctum*, *Asparagus racemosus*, *Tribulus terrestris* and shilajit (a mineral-rich, composted plant exudate scraped off rocks) was found in

animal studies to improve glucose tolerance, libido, depression, cognitive dysfunction and immunosuppression caused by chronic stress.<sup>57</sup>

### Immunological Activity

Shatavari is an immunomodulator. Animal studies found that shatavari is capable of producing leucocytosis with neutrophilia and, furthermore, was able to prevent myelosuppression by reducing cyclophosphamide-induced leucopenia.<sup>58</sup> Shatavari has also been shown to inhibit drug induced mammary carcinogenesis.<sup>59</sup>

The hypothesis that macrophages play a pivotal role in the development of intraperitoneal adhesions and that modulation of macrophage activity may therefore prevent adhesions, was tested in an Indian study.<sup>60</sup> The effect of shatavari was evaluated in an animal model of intraperitoneal adhesions. Shatavari reduced the severity of the adhesions and this correlated with a significant increase in the activity of the macrophages.

Macrophages are involved at all stages of the immune response. They can produce a rapid response before T cell-mediated amplification has taken place. Activated macrophages play a key role in host defence against intracellular parasitic bacteria, pathogenic protozoa, fungi and helminths, as well as against tumours, particularly in metastasising tumours. In addition, macrophages are important killer cells. They also take part in the initiation of T cell activation by processing and presenting antigen. Finally they are central effector and regulatory cells of the inflammatory response. An *in vitro* study found that shatavari increased phagocytic activity of macrophages.<sup>61</sup>

Ochratoxin (OTA) is a mycotoxin, which has been found as a frequent contaminant in various grains and to a lesser extent coffee, milk and foods from animal origin. It is a well-known tumour promoter that contributes to cancer of the kidney. *Asparagus racemosus*, *Tinospora cordifolia*, *Withania somnifera* and *Picrorhiza kurroa* have been shown in an *in vivo* study to inhibit OTA-induced immune-suppression of chemotactic activity and production of interleukin-1 and TNF-alpha by macrophages. The immune enhancing effects were significant for all four herbs with *Withania* producing the strongest chemotactic activity of peritoneal macrophages. In

terms of Interleukin-1 and TNF-alpha production by macrophages, all four herbs had significant effects with shatavari and withania again showing the strongest effects.<sup>62</sup>

The crude saponins obtained from asparagus shoots inhibited the growth of human leukemia HL-60 cells in culture and macromolecular synthesis in a dose and time-dependent manner.<sup>63</sup>

Ethanol extract of shatavari enhanced both humoral and cell mediated immunity of albino mice injected with sheep red blood cells as particulate antigen.<sup>64</sup>

Oral pre-treatment with shatavari (200mg/kg/day) was found to protect against chemical induced gastric damage in rats. Pre-treatment with shatavari has also been shown to reduce drug induced lung fibrosis. Bleomycin increases the hydroxyproline content of lung tissue causing intra-alveolar fibrosis and deranged alveolar architecture. Shatavari significantly decreased ( $p < .001$ ) the bleomycin induced lung fibrosis. These protective effects were associated with a significant increase in alveolar macrophage activity.<sup>65</sup>

Oral administration of an aqueous root extract (100mg/kg per day for 15 days) to animals immunised with diphtheria, tetanus, pertussis (DTP) vaccine resulted in significant increase ( $p = .0052$ ) in antibody titers to *Bordetella pertussis* as compared to untreated (control) animals. Immunised animals (treated and untreated) were challenged with *Bordetella pertussis* and the animals were observed for 14 days. The treated animals showed a significant increase in antibody titers as compared to untreated animals after challenge ( $p = .002$ ). Immunoprotection against intra-cerebral challenge of live *Bordetella pertussis* cells was evaluated based on degree of sickness, paralysis and subsequent death. Reduced mortality, accompanied with overall improved health status, was observed in treated animals after intra-cerebral challenge of *Bordetella pertussis*, indicating that shatavari promoted a protective immune response. There was significant reduction in morbidity score in animals receiving treatment as compared to untreated animals ( $p = .03$ ). Lower morbidity score indicates fewer incidences and lesser severity of paralysis that results in reduced mortality in treatment groups. The mortality incidence also confirmed the same, as reduced mortality was

seen in treatment group (25%) as compared to control (50%). Adjuvants are used to enhance the immune response to a particular antigen of interest. This enhancement results in improving titers, sustained response duration and avidity. Pertussis antibody titers declined with duration (from day 14 to day 28) in untreated groups ( $p = .04$ ). No such decline in antibody titers was observed in treated groups till the end of study. No significant effect on haemoglobin, polymorphs, lymphocyte and WBC counts was observed at end of study period. The study suggests that shatavari extract exhibited three important characteristics - immunostimulation, immunoprotection and adjuvant activity. Shatavari's immunomodulatory activities may be beneficial in reducing morbidity associated with vaccinations.<sup>66</sup>

### Antimicrobial Activity

Shatavari roots are traditionally used in the treatment of dysentery, diarrhoea, tuberculosis, leprosy, gonorrhoea and in various skin diseases and research has shown it to have antimicrobial activities. Different concentrations (50, 100, 150mcg/mL) of the methanol extract of the roots of shatavari showed considerable *in vitro* antibacterial efficacy against *Escherichia coli*, *Shigella dysenteriae*, *Shigella sonnei*, *Shigella flexneri*, *Vibrio cholerae*, *Salmonella typhi*, *Salmonella typhimurium*, *Pseudomonas putida*, *Bacillus subtilis* and *Staphylococcus aureus*. The effects produced by the methanol extract were compared with chloramphenicol.<sup>67</sup> The antimicrobial activity may be due to 9,10-Dihydrophenanthrene.<sup>68</sup>

Also, shatavari showed a high degree of inhibition against six species of candida (*Candida albicans*, *Candida tropicalis*, *Candida krusei*, *Candida guilliermondii*, *Candida parapsilosis* and *Candida stellatoidea*) when compared to any other antibiotic.<sup>69</sup>

### Digestive Activity

Shatavari is used in Ayurveda for dyspepsia (amlapitta or acid regurgitation), Grahani (ulcerative colitis), Parinam shool (peptic ulcer) and Vataj shool (spastic colon).<sup>70</sup> Shatavari also improves digestion by increasing the levels of amylase and lipase.<sup>71</sup>

In Ayurveda, gastric disorders are classified as sula, parinamasula and amlapitta, which are very similar to modern classification of peptic ulcer and functional dyspepsia. In alcohol induced damage to

the gastric mucosa, pre-treatment for seven days caused a 70% reduction in the ulcer index.<sup>72</sup>

A traditional powder formulation containing herbs and minerals (*Shatavari mandur*) with shatavari as the main ingredient has been shown to significantly ( $p < .05$ ) protect against pyloric ligation induced gastric ulcers during the treatment of ulcers with the allopathic drug Ranitidine.<sup>73</sup> Shatavari methanol extract has been shown to have a dose-dependent ulcer protective effect against cold restraint stress- and pyloric ligation induced gastric ulcers, and against cysteamine-induced duodenal ulcers in rats. However, the extract was ineffective against ethanol- and aspirin-induced gastric ulcers. The anomaly in ulcer protective effect may be due to variability of factors affecting ulcerogenesis in different models. In this study, it was concluded that the healing of gastric ulcers could be attributed to the effect of the protective factors, as the effect seems to be more due to enhancement of protective factors, such as increased mucous secretions, rather than a reduction in acid and pepsin secretions.<sup>74</sup>

A later study compared the antiulcer and antisecretory activity of shatavari and withania root extracts with a standard drug, ranitidine, in various models of gastric ulcer in rats. Ulcers were induced by the indomethacin (NSAID) and swim (restraint) stress treatment. Results demonstrated that shatavari, as well as withania methanolic extract (100mg/kg per day), given orally for 15 days, significantly reduced the ulcer index, volume of gastric secretion, free acidity and total acidity. A significant increase in the total carbohydrate and total carbohydrate/protein ratio was also observed. The study also suggests that the herbs increase the antioxidant defence, as indicated by increases in the antioxidant enzymes superoxide dismutase, catalase and ascorbic acid, with a concomitant and significant decrease in lipid peroxidation. Shatavari was more effective in reducing gastric ulcer in indomethacin-treated gastric ulcerative rats, whereas withania was effective in stress-induced gastric ulcer. Results obtained for both herbal drugs were comparable to those of the standard drug Ranitidine.<sup>75</sup>

Diarrhoea has long been recognized as an important health problem faced globally, especially by the population of developing countries. Diarrhoeal

disease is the second leading cause of death in children under five years old, and is responsible for killing 1.5 million children every year.<sup>76</sup> Diarrhoea can last several days, and can leave the body without the water and salts that are necessary for survival. Children who are malnourished or have impaired immunity are most at risk of life-threatening diarrhoea.

Studies have found shatavari to be extremely effective in the treatment of diarrhoea, dysentery and gastritis. Both the ethanol and the aqueous extract have been shown to have significant antidiarrhoeal activity against castor oil induced diarrhoea in rats, demonstrating an activity similar to loperamide.<sup>77</sup> Shatavari extract, 200mg/kg, significantly ( $p < 0.05$ ) inhibited castor oil induced diarrhoea and PGE2 induced enteropooling (excessive secretion of water and electrolytes). The release of ricinoleic acid from castor oil results in inflammation and irritation of the intestinal mucosa, causing the release of prostaglandins, which in turn stimulate motility and hypersecretion. Both extracts also showed significant ( $p < .001$ ) reduction in gastrointestinal motility in a charcoal meal test in rats.<sup>78</sup>

An Indian study with eight healthy male volunteers compared shatavari with the drug metoclopramide, which is used in dyspepsia to reduce gastric emptying time. Metoclopramide and shatavari did not differ significantly in their effects. It was found that shatavari reduced gastric emptying time by 37% ( $p < .001$ ).<sup>79</sup>

### Diuretic and Antilithic Activity

Traditionally shatavari was used as a soothing and antispasmodic diuretic (although the Western *Asparagus* root, *Asparagus officinalis*, is a stronger diuretic). It was used wherever increased flow of urine was desirable, such as fluid retention and urinary infections.<sup>80</sup> The diuretic and cleansing activities of the roots were of use in the treatment of rheumatic pain.

Shatavari has been shown to inhibit antidiuretic hormone (ADH)<sup>81</sup> and to reduce urinary stone formation in rats.<sup>82</sup> An ethanol extract of shatavari was evaluated for its inhibitory potential on lithiasis (stone formation), induced by oral administration of 0.75% ethylene glycolated water to adult male

albino Wistar rats for 28 days. The ionic chemistry of urine was altered by ethylene glycol, which elevated the urinary concentration of calcium, oxalate and phosphate ions, thereby leading to renal stone formation. The ethanol extract, however, significantly ( $p < .05$ ) reduced the elevated level of these ions in urine. Furthermore, shatavari elevated the urinary concentration of magnesium, which is considered to be one of the inhibitors of crystallization. The high serum creatinine level observed in the ethylene glycol-treated rats was also reduced, following treatment with the shatavari extract. The histopathological findings also showed signs of improvement after treatment with the extract.<sup>83</sup>

#### Antitussive Activity

Rural tribal people of the Khatra region of West Bengal in India use the root juice against cough. The methanol extract of shatavari root (200 and 400mg/kg, p.o.) has been shown to have significant antitussive activity on sulphur dioxide-induced cough in mice, the cough inhibition (40.0 and 58.5%, respectively) being comparable to that of 10 to 20mg/kg of codeine phosphate (36.0 and 55.4%, respectively).<sup>84</sup>

Higher doses of the shatavari alcoholic extract have been shown to have a dilatatory effect on bronchial musculature in guinea pigs but failed to antagonise the histamine induced broncho-constriction.<sup>85</sup>

#### Antioxidant, Cytoprotective and Neuroprotective Effects

Membrane damage induced by free radicals generated during gamma-radiation was examined in rat liver mitochondria. An extract of shatavari was shown *in vitro* to have potent antioxidant properties in mitochondrial membranes of the rat liver. Both the crude extract, as well as a polysaccharide-rich fraction, significantly inhibited lipid peroxidation and protein oxidation. Both fractions also partly protected against radiation-induced loss of protein thiols and inactivation of superoxide dismutase.<sup>86</sup>

There is strong evidence that mitochondrial dysfunction and oxidative stress play a causal role in neurodegenerative disease pathogenesis, including the four of the more well-known diseases Alzheimer's, Parkinson's, Huntington's, and Amyotrophic lateral sclerosis.<sup>87</sup> Reactive oxygen

species (ROS) that are generated extracellularly and intracellularly by various mechanisms are among the major risk factors that initiate and promote neurodegeneration. Shatavari has been shown in experimental designs to be protective against kainic acid-induced hippocampal and striatal neuronal damage. The impairment of hippocampus and striatal regions of brain was marked by an increase in lipid peroxidation and protein carbonyl content and decline in glutathione peroxidase activity and reduced glutathione content. Shatavari supplementation improved the glutathione peroxidase activity and glutathione content and reduced the membrane lipid peroxidation and protein carbonyl.<sup>88</sup>

Herbal immunomodulators are often employed as supportive, or adjuvant, therapy to overcome the undesired effects of cytotoxic chemotherapeutic agents. Total extract, polar and non-polar extracts, and their formulations, prepared from *Withania somnifera*, *Tinospora cordifolia*, and shatavari have been shown to have various immunopharmacological activities in cyclophosphamide -treated mouse ascitic sarcoma. Shatavari significantly increased the white cell counts ( $p < .02$ ) and antibody titers ( $p < .04$ ) in tumor-bearing animals treated with cyclophosphamide. However it was accompanied with inflammatory changes, as seen from increased polymorph counts. Significant myeloprotective and immunoprotective, i.e. significantly increased white cell counts ( $p = .004$ ) and antibody titers ( $p < .001$ ), was seen in animals treated with withania (alkaloid free, polar fraction). Similar activity was also seen with a combination of whole extracts of withania and tinospora (ratio 80:20), which also had significant anti-inflammatory activity. Treatment of ascitic sarcoma-bearing mice with a formulation of total extracts of *Withania somnifera* and *Tinospora cordifolia* (80:20) and alkaloid-free polar fraction of *withania somnifera* resulted in protection towards cyclophosphamide -induced myelo- and immunoprotection, as evident by significant increase in white cell counts and hemagglutinating and haemolytic antibody titers. Antitumor activity of cyclophosphamide was not altered by any of the herbal extracts, as was evident from no significant change in tumour mass, compared to the group of tumour-bearing mice treated with cyclophosphamide alone. None of

the herbal extracts showed any significant effect on haemoglobin and red cell count. In this study the combination of whole extracts of withania and tinospora produced the strongest effect.<sup>89</sup>

### Hypocholesterolemic

Hyperlipidemia and hypercholesteremia along with the generation of reactive oxygen species are the major risk factors for the development of coronary artery disease and atherosclerosis. Shatavari root powder has been shown to decrease lipid peroxidation and cause a dose-dependent reduction in lipid profiles.<sup>90</sup> The total lipids, total cholesterol and triglycerides in plasma and liver as well as plasma LDL (low-density lipoprotein) and VLDL (very low-density lipoprotein)-cholesterol decreased by more than 30%. It is thought that the effect is due to a decrease in exogenous cholesterol absorption coupled with an increased conversion of endogenous cholesterol to bile acid.<sup>91</sup> The saponin active constituents from shatavari extract are believed to be responsible for a significant decline in plasma and hepatic lipid profiles *in vivo*.<sup>92,93</sup>

### Hepatoprotective

The alcoholic extract of shatavari significantly reduced elevated levels of alanine transaminase, aspartate transaminase and alkaline phosphatase in CC14-induced hepatic damage in rats, indicating hepatoprotective activity.<sup>94</sup>

### Antidiabetic

Shatavari may be useful in diabetes mellitus. The ethanol extract of shatavari root concentration-dependently stimulated insulin secretion in isolated perfused rat pancreas, isolated rat islet cells and clonal beta-cells. The extract also increased intracellular Ca(2+), which initiates more insulin release from each beta cell.<sup>95</sup> Furthermore, the dried ethanolic extract 250mg/kg body weight and the inorganic parts 90mg pure ash/kg body weight of the root revealed hypoglycemic activity in a single dose effect on the oral glucose tolerance test (GTT) in fasting albino rats.<sup>96</sup>

### Skin Lightening/Antiaging Effects

The skin is our main primary defence system and is the largest organ exposed to reactive

oxygen species (ROS) and ensuing oxidative damage. Ultraviolet radiation from the sunlight damages the composition of the skin by the accumulation of elastic fibres,<sup>97</sup> collagen reduction and degeneration<sup>98</sup> and deposition of glycosaminoglycans.<sup>99</sup> This reduces the elasticity of the skin and the linearity of dermal elastic fibers, inducing wrinkling and sagging, and subsequently, an aging appearance of the skin results.<sup>100</sup>

In addition, the exposure of the skin to ultraviolet radiation induces the secretion of melanin due to rapid proliferation of melanocytes.<sup>101</sup> The abnormal secretion of melanin leads to hyperpigmentation of the skin. Melanin in the epidermal layers of the skin is produced by a pathway called melanogenesis in which tyrosinase is the important rate limiting enzyme. Thus, tyrosinase is the key enzyme to inhibit, in skin lightening agents.<sup>102</sup> Shatavari extract inhibits tyrosinase and protects the skin from free radical toxicity, as measured with 2, 2-diphenyl -1-picryl hydrazyl (DPPH) radical scavenging assay. Therefore shatavari is useful in cosmetic formulations to deliver the skin lightening and antiaging benefits, after the dermal safety is confirmed.<sup>103</sup>

### Indications

- Sexual debility and infertility; insufficient lactation, menopausal symptoms
- Threatened miscarriage
- As an alternative to the endangered false unicorn root
- Stress, fatigue and general weakness
- Inflammatory conditions of the gastrointestinal and urinary tracts including cystitis, gastritis, diarrhoea, dysentery and gastrointestinal ulceration
- Immune debility
- Chronic disease, prevention of adhesions, cancer and rheumatism
- Cough
- Fluid retention
- Prevention of urinary stones

### *Energetics*

Sweet and bitter herb which is said to be particularly balancing to the Pitta Dosha. It is known as the 'Queen of Herbs' in Ayurveda, as it promotes love and loyalty.<sup>104</sup>

### *Use in Pregnancy*

Although shatavari has been used traditionally to promote conception and for threatened miscarriage caution should be exercised in pregnancy until more is known about effects in humans.

Methanolic extract of shatavari roots (1000mg/kg/day for 60 days) showed teratological effects, such as increased resorption of fetuses and gross malformations e.g. swelling in legs, and intrauterine growth retardation, with a small placental size in Charles Foster rats. Pups born to a mother exposed to shatavari roots for the full duration of gestation showed evidence of higher rate of resorption and therefore smaller litter size. The live pup showed significant decrease in body weight and length and delay of various developmental parameters when compared to respective control groups.<sup>105</sup> The dosage used would be equivalent to around 70g, or 70mL, of a 1:1 liquid extract per day for a human adult. This is more than 8 times the recommended dosage. Another study examining the teratogenicity of a formulation containing shatavari did not find any signs of teratogenicity with the dosage used. Rats received 3g/kg of the product once a day orally from day 0 of gestation till day 21 of lactation or just during gestation. No adverse effects were observed on pregnancy and growth of the foetus.<sup>106</sup> The daily dose of the formulation was 3mg/kg, which would be equivalent to 210g for a 70kg human. It is difficult to calculate the amount of shatavari in the formulation but it could be as high as 2-3%, which would equate to about 5g, which is not too dissimilar to the recommended dosage of shatavari 1:1 extract.

### *Contraindications*

Usually an extremely potent phytoestrogenic herb and long term use is not advisable. Take care with sensitive individuals who may be allergic to the *Asparagus* species. May inhibit hydrochloric acid, observation is advised for those with hypochlorhydria.<sup>107,108,109</sup>

### *Drug Interactions*

Caution with lithium. Shatavari may have diuretic effects and may positively affect diuretic drugs such as chlorothiazide (Chlotride). Caution is advised. An additive effect is possible with the drug Metoclopramide as shatavari root was found in animal studies to have similar effects in gastric emptying time as this antiemetic drug.<sup>110</sup>

Improved immunoprotection may be possible in vaccinated humans after possible immunomodulatory activities were demonstrated in animals immunised with DTP.<sup>111</sup>

### *Administration and Dosage*

Liquid Extract:	1:1
Alcohol:	30%
Weekly Dosage:	30 to 60mL

## References

- Rao SB. Saponins (Sapogenins) from Indian Medicinal Plants: Part I Sapogenins from Asparagus. *Indian J Pharmacy* 14 (1952):131-2.
- Bharatiya Vidya Bhavan's Swami Prakashananda. *Ayurveda Research Centre: Selected Medicinal Plants of India*. Bombay, Chemexcil, 1992, pp 43-46.
- Thakur RS, Puri HS, Husain A. Major medicinal plants of India. Central Institute of Medicinal and Aromatic Plants, Lucknow, 1989, pp 78-81.
- Goyal RK, Singh J, Lal H. *Asparagus racemosus*--an update. *Indian J Med Sci* 57.9 (2003):408-414.
- Shiva Rama Prasad, Dr K. Asparagus (Shatavari) as Multi target drug in Women [document on the internet]. Maharashtra: Datta Meghe Institute Of Medical Sciences. Available from [www.technoayurveda.com/Shatavari](http://www.technoayurveda.com/Shatavari).
- Bharatiya Vidya Bhavan's Swami Prakashananda. *Ayurveda Research Centre: Selected Medicinal Plants of India*. Bombay, Chemexcil, 1992, pp 43-46.
- Thakur RS, Puri HS, Husain A. Major medicinal plants of India. Central Institute of Medicinal and Aromatic Plants, Lucknow, 1989, pp 78-81.
- Bopana N, Saxena S. *Asparagus racemosus*-- ethnopharmacological evaluation and conservation needs. *J Ethnopharmacol* 110.1 (2007): 1-15
- Rao SB. Saponins (Sapogenins) from Indian Medicinal Plants: Part I Sapogenins from Asparagus. *Indian J Pharmacy* 14 (1952):131-2.
- India. Ministry of Health and Family Welfare: Department of AYUSH. National Medicinal Plants Board Publication of Medicinal plants: Shatavari. Available from <http://nmpb.nic.in/shatavari.htm>.
- Bharatiya Vidya Bhavan's Swami Prakashananda. *Ayurveda Research Centre: Selected Medicinal Plants of India*. Bombay, Chemexcil, 1992, pp 43-46.
- Thakur RS, Puri HS, Husain A. Major medicinal plants of India. Central Institute of Medicinal and Aromatic Plants, Lucknow, 1989, pp 78-81.
- Warrier PK, Nambiar VPK, Ganapathy PM. Some important medicinal plants of the Western Ghats, India - a profile. New Delhi: International Development Research Centre, 2001, p15.
- Thakur RS, Puri HS, Husain A. Major medicinal plants of India. Central Institute of Medicinal and Aromatic Plants, Lucknow, 1989, pp 78-81.
- Frawley D, Lad V. *The Yoga of Herbs*. Santa Fe: Lotus Press, 1986: 183-184.
- Nadkarni AK. *Indian Materia Medica*. Bombay: Popular Book Depot, 1954, Vol. 1, pp.153-5.
- Komal Sharma et.al. *Asparagus racemosus* (Shatavari): A Versatile Female Tonic, *International Journal of Pharmaceutical & Biological Archives* 2.3 (2011): 855-863.
- Sharma PC, Yelne MB, Dennis TJ. Data base on medicinal plants used in Ayurveda. Delhi: Documentation & publication Division, Central Council for Research in Ayurveda & Siddha, 2000, Vol I, pp. 418-30.
- Bopana N, Saxena S. *Asparagus racemosus*-- ethnopharmacological evaluation and conservation needs. *J Ethnopharmacol* 110.1 (2007): 1-15
- Hayes PY, Jahidin AH, Lehmann R, Penman K, Kitching W, De Voss JJ. Steroidal saponins from the roots of *Asparagus racemosus*. *Phytochemistry* 69.3 (2008): 796-804.
- Saxena VK, Chourasia S. A new isoflavone from the roots of *Asparagus racemosus*. *Fitoterapia* 72.3 (2001): 307-309
- Visavadiya NP, Narasimhacharya A. *Asparagus* root regulates cholesterol metabolism and improves antioxidant status in hypercholesteremic rats. *Indian J Pharmacol* 37.6 (2005): 376-80.
- Glazier, M.G. A review of the evidence for the use of phytoestrogens as a replacement for traditional oestrogen replacement therapy. *Archives of Internal Medicine* 161,(2001): 1161-1172.
- Barrett-Connor, E. Hormone replacement therapy, heart disease, and other considerations. *Annual Review of Public Health* 19 (1998): 55-72.
- Grady, D., Gebretsadik, T., Kerlikowske, K., Ernster, V., Petitti, D. Hormone replacement therapy and endometrial cancer risk: a meta-analysis. *Obstetrics and Gynaecology* 85 (1995): 304-313.
- Cornwell, T., Cohick,W., Raskin, I. Review: dietary phytoestrogens and health. *Phytochemistry* 65 (2004): 995-1016.
- Whitten PL, Patisaul HB. Cross-species and interassay comparisons of phytoestrogen action. *Environ Health Perspect* 109.1(2001): 5-20.
- Beral, V. Breast cancer and hormone replacement therapy in the million women study. *Lancet* 362 (2003): 419-427.
- Dai, Q., Franke, A.A., Jin, F., Shu, X.O., Herbert, J.R., Custer, L.J., Cheng, J., Gao, Y.T., Zheng,W. Urinary excretion of phytoestrogens and risk of breast cancer among Chinese women in Shanghai. *Cancer Epidemiological and Biomarkers Preview* 11 (2002): 815-821.
- Buring, J.E., Bain, C.J., Ehrmann, R.L. Conjugated estrogen use and risk of endometrial cancer. *American Journal of Epidemiology* 124 (1986): 434-441.
- Weinstein, A.L., Mahoney, M.C., Nasca, P.C., Hanson, R.L., Leske, M.C., Varma, A.O. Oestrogen replacement therapy and breast cancer risk. *International Journal of Epidemiology* 22 (1993): 781-789.
- Horn-Ross, P.L., Hoggatt, K.J., West, D.W., Krone, M.R., Stewart, S.L., Anton, H., Bernstein Culver, L., Deapen, D., Peel, D., Pinder, R., Reynolds, P., Ross, R.K., Wright, W., Ziogas, A. Recent diet and breast cancer risk: the California Teachers Study (USA). *Cancer Causes Control* 13 (2002): 407-415.
- Rao AR. Inhibitory action of *Asparagus racemosus* on DMBA-induced mammary carcinogenesis in rats. *Int J Cancer* 28.5 (1981): 607-610.
- Bopana N, Saxena S. *Asparagus racemosus*-- ethnopharmacological evaluation and conservation needs. *J Ethnopharmacol* 110.1 (2007): 1-15
- Pandey SK, Sahay A, Pandey RS, Tripathi YB. Effect of *Asparagus racemosus* rhizome (Shatavari) on mammary gland and genital organs of pregnant rat. *Phytother Res* 19.8 (2005): 721-724.
- Sharma K, Bhatnagar M. *Asparagus racemosus* (Shatavari): A Versatile Female Tonic. *International Journal of Pharmaceutical & Biological Archives* 2.3 (2011): 855-863
- Gopumadhavan S, Venkataranganna M, Mohamed R. Evaluation of the estrogenic effect of Menosan using the rat models of uterotrophic assay. Available from [www.himalayahealthcare.com/pdf\\_files/menosan006.pdf](http://www.himalayahealthcare.com/pdf_files/menosan006.pdf). 2008. 3-7-2008.
- Bopana N, Saxena S. *Asparagus racemosus*-- ethnopharmacological evaluation and conservation needs. *J Ethnopharmacol* 110.1 (2007): 1-15
- Javeed Ahmed Wani, et.al. Phytochemical Screening and Aphrodisiac Activity of *Asparagus racemosus*. *International Journal of Pharmaceutical Sciences and Drug Research* 3.2 (2011): 112-115.
- Ghumare, B.C., Vadlamudi, V.P., Rajurkar, S.R., 2004. Effect of *Asparagus racemosus* on growth and development of testes in wistar rats. *Aryavaidyan* 18 (2004): 45-48.
- Jetmalani, M., Sabnis, P.B. and Gaitonde, B.B. A Study on the pharmacology of various extract of shatavari (*Asparagus racemosus*). *Journal of Research on Indian Medicine* 2 (1967): 1- 9.

42. Sabnis, P.B., Gaitonde, B.B. and Jetmalani, M. Effects of alcoholic extracts of *Asparagus racemosus* on mammary glands of rats. *Indian Journal of Experimental Biology* 6.1 (1968): 55–57.
43. Pandey SK, Sahay A, Pandey RS, Tripathi YB. Effect of *Asparagus racemosus* rhizome (Shatavari) on mammary gland and genital organs of pregnant rat. *Phytother Res* 19.8 (2005): 721-724.
44. Sabnis, P.B., Gaitonde, B.B. and Jetmalani, M. Effects of alcoholic extracts of *Asparagus racemosus* on mammary glands of rats. *Indian Journal of Experimental Biology* 6.1 (1968): 55–57.
45. Sharma S, Ramji S, Kumari S, Bapna JS. Randomized controlled trial of *Asparagus racemosus* (Shatavari) as a lactagogue in lactational inadequacy. *Indian Pediatr* 33 (1996): 675-7.
46. Lawrence, R.A, Lawrence, R.M. Breastfeeding: A Guide for the Medical Profession, 5th edn. St. Louis: Osby, 1999.
47. Joglekar GV, Ahuja RH, Balwani JH. Galactagogue effect of *Asparagus racemosus*. *Indian Med J* 1967;61:165.
48. Jyotsna, P. and Singh, Mahendra., 2010. Effect of bromocryptine on hormones and milk secretion in Murrah buffaloes (*Bubalus bubalis*). *Animal* 4 (2010): 772–776.
49. Jetmalani, M., Sabnis, P.B. and Gaitonde, B.B. A Study on the pharmacology of various extract of shatavari (*Asparagus racemosus*). *Journal of Research on Indian Medicine* 2 (1967): 1–9.
50. Sabnis, P.B., Gaitonde, B.B. and Jetmalani, M. Effects of alcoholic extracts of *Asparagus racemosus* on mammary glands of rats. *Indian Journal of Experimental Biology* 6.1 (1968): 55–57.
51. Pandey SK, Sahay A, Pandey RS, Tripathi YB. Effect of *Asparagus racemosus* rhizome (Shatavari) on mammary gland and genital organs of pregnant rat. *Phytother Res* 19.8 (2005): 721-724.
52. Lohar, D.R., Chaturvedi, D. and Varma, P.N. Mineral elements of a few medicinally important plants. *Indian Drugs* 29 6 (1991): 271-273.
53. Gaitonde BB, Jetmalani MH. Antioxytotic action of saponin isolated from *Asparagus racemosus* Willd (Shatavari) on uterine muscle. *Arch Int Pharmacodyn Ther* 179.1 (1969): 121-129.
54. Dhuley JN. Effect of some Indian herbs on macrophage functions in ochratoxin A treated mice. *J Ethnopharmacol* 58.1 (1997):15-20.
55. Joshi J, Dev S. Chemistry of Ayurvedic crude drugs: Part VIIIa-Shatavari-2: Structure elucidation of bioactive Shatavarin-I & other glycosidesb,c. *Indian J Chem* 27B (1988): 12-6.
56. Rege NN, Thatte UM, Dahanukar SA. Adaptogenic properties of six rasayana herbs used in Ayurvedic medicine. *Phytother Res* 13.4 (1999): 275-291.
57. Bhattacharya SK, Bhattacharya A, Chakrabarti A. Adaptogenic activity of Siotone, a polyherbal formulation of Ayurvedic rasayanas. *Indian J Exp Biol* 38.2 (2000): 119-128.
58. Thatte UM, Dahanukar SA. Comparative study of immunomodulating activity of Indian medicinal plants, lithium carbonate and glucan. *Methods Find Exp Clin Pharmacol* 10.10 (1988): 639-644.
59. Rao AR. Inhibitory action of *Asparagus racemosus* on DMBA-induced mammary carcinogenesis in rats. *Int J Cancer* 28.5 (1981): 607-610.
60. Rege NN, Nazareth HM, Isaac A, Karandikar SM, Dahanukar SA. Immunotherapeutic modulation of intraperitoneal adhesions by *Asparagus racemosus*. *J Postgrad Med* 35.4 (1989): 199-203.
61. Rege NN, Dahanukar SA. Quantitation of microbicidal activity of mononuclear phagocytes: an *in vitro* technique. *J Postgrad Med* 39.1 (1993): 22-25.
62. Dhuley JN. Effect of some Indian herbs on macrophage functions in ochratoxin A treated mice. *J Ethnopharmacol* 58.1 (1997): 15-20.
63. Shao Y, Chin C K, Ho C T, Ma W, Garrison S A, Huang M T. Anti-tumor activity of the crude saponins obtained from *Asparagus*. *Cancer Letters* 104 (1996): 31-36.
64. Muruganadan S, Garg H, Lal J, Chandra S, Kumar D. Studies on the immunostimulant and antihepatotoxic activities of *Asparagus racemosus* root extract. *J Med Aromat Plant Sci* 22 (2000): 49-52.
65. Rege NN, Thatte UM, Dahanukar SA. Adaptogenic properties of six rasayana herbs used in Ayurvedic medicine. *Phytother Res* 1999;13:275-91.
66. Gautam M, Diwanay S, Gairola S, Shinde Y, Patki P, Patwardhan B. Immunoadjuvant potential of *Asparagus racemosus* aqueous extract in experimental system. *J Ethnopharmacol* 91.2-3 (2004): 251-255.
67. Mandal SC, Nandy A, Pal M, Saha BP. Evaluation of antibacterial activity of *Asparagus racemosus* willd. root. *Phytother Res* 14.2 (2000): 118-119.
68. Boger DL, Mitscher LA, Mullican MD, Drake SD, Kitos P. Antimicrobial and cytotoxic properties of 9,10-dihydrophenanthrenes: structure-activity studies on juncusol. *J Med Chem* 28.10 (1985): 1543-1547.
69. Uma B, Prabhakar K, Rajendran S. Anticandidal activity of *Asparagus racemosus*. *Indian Journal of Pharmacy Science* 71 (2009): 342-43.
70. Nanal, B.P., Sharma, B.N., Ranade, S.S., Nande, C.V. Clinical study of Shatavari (*Asparagus racemosus*). *Journal of Research in Indian Medicine* 9 (1974): 23–29.
71. Dange PS, Kanitkar UK, Pendse GS. Amylase and lipase activities in the root of *Asparagus racemosus*. *Planta Med* 17.4 (1969): 393-395.
72. Rege NN, Thatte UM, Dahanukar SA. Adaptogenic properties of six rasayana herbs used in Ayurvedic medicine. *Phytother Res* 1999;13:275-91.
73. Datta GK, Sairam K, Priyambada S, Debnath PK, Goel RK. Antiulcerogenic activity of Shatavari mandur--an Ayurvedic herbo-mineral preparation. *Indian J Exp Biol* 2002; 40(10):1173-1177.
74. Sairam K, Priyambada S, Aryya NC, Goel RK. Gastroduodenal ulcer protective activity of *Asparagus racemosus*: an experimental, biochemical and histological study. *J Ethnopharmacol* 2003; 86(1):1-10.
75. Bhatnagar M, Sisodia SS, Bhatnagar R. Antiulcer and antioxidant activity of *Asparagus racemosus* Willd and *Withania somnifera* Dunal in rats. *Ann N Y Acad Sci* 2005; 1056:261-278.
76. World Health Organization Fact sheet N°330 August 2009 Available from [http://www.who.int/water\\_sanitation\\_health/diseases/diarrhoea/en/](http://www.who.int/water_sanitation_health/diseases/diarrhoea/en/).
77. Venkatesan N, Thiyagarajan V, Narayanan S, Arul A, Raja S, Vijaya Kumar SG et al. Anti-diarrhoeal potential of *Asparagus racemosus* wild root extracts in laboratory animals. *J Pharm Pharm Sci* 8.1 (2005): 39-46.
78. Bopana N, Saxena S. *Asparagus racemosus*--ethnopharmacological evaluation and conservation needs. *J Ethnopharmacol* 110.1 (2007): 1-15
79. Dalvi SS, Nadkarni PM, Gupta KC. Effect of *Asparagus racemosus* (Shatavari) on gastric emptying time in normal healthy volunteers. *J Postgrad Med* 36.2 (1990): 91-94.
80. Chopra RN, Chopra IC, Handa KL, Kapur LD. *Indigenous drugs of India*. Calcutta: Academic Publishers, 1994. p. 496.
81. Gaitonde BB, Jetmalani MH. Antioxytotic action of saponin isolated from *Asparagus racemosus* Willd (Shatavari) on uterine muscle. *Arch Int Pharmacodyn Ther* 179.1 (1969): 121-129.
82. Jagannath N, Chikkannasetty SS, Govindadas D, Devasankaraiah G. Study of antiurolithiatic activity of *Asparagus racemosus* on albino rats. *Indian J Pharmacol* 44 (2012): 576-9.
83. Christina AJ, Ashok K, Packialakshmi M, Tobin GC, Preethi J, Muruges N. Antilithiatic effect of *Asparagus racemosus* Willd on ethylene glycol-induced lithiasis in male albino Wistar rats. *Methods Find Exp Clin Pharmacol* 27.9 (2005): 633-638.

84. Mandal SC, Kumar CKA, Mohana LS, Sinha S, Murugesan T, Saha BP et al. Antitussive effect of *Asparagus racemosus* root against sulfur dioxide-induced cough in mice. *Fitoterapia* 71.6 (2000): 686-689.
85. Roy RN, Bhagwager S, Chavan SR, Dutta NK. Preliminary pharmacological studies on extracts of Root of *Asparagus racemosus* (Satavari), Willd, N.O. Liliaceae. *J Res Ind Med* 6 (1971): 132-8.
86. Kamat JP, Bolor KK, Devasagayam TP, Venkatachalam SR. Antioxidant properties of *Asparagus racemosus* against damage induced by gamma-radiation in rat liver mitochondria. *J Ethnopharmacol* 71.3 (2000): 425-435.
87. Lin MT, Beal MF Mitochondrial dysfunction and oxidative stress in neurodegenerative diseases. *Nature* 443.7113 (2006): 787-95.
88. Parihar MS, Hemnani T. Experimental excitotoxicity provokes oxidative damage in mice brain and attenuation by extract of *Asparagus racemosus*. *J Neural Transm* 111.1 (2004): 1-12.
89. Diwanay S, Chitre D, Patwardhan B. Immunoprotection by botanical drugs in cancer chemotherapy. *J Ethnopharmacol* 90.1 (2004): 49-55. Ibid.
90. Visavadiya NP, Narasimhacharya A. *Asparagus* root regulates cholesterol metabolism and improves antioxidant status in hypercholesteremic rats. *Indian J Pharmacol* 37.6 (2005): 376-80.
91. Bopana N, Saxena S. *Asparagus racemosus*-- ethnopharmacological evaluation and conservation needs. *J Ethnopharmacol* 110.1 (2007): 1-15
92. Oakenfull, D.G., 1986. Aggregation of bile acids and saponins in aqueous solution, *Australian Journal of Chemistry*, 39, 1671-1683.
93. Oakenfull, D.G., Sidhu, G.S. Could saponins be a useful treatment for hypercholesterolemia? *European Journal of Clinical Nutrition* 44 (1990): 79-88.
94. Muruganadan S, Garg H, Lal J, Chandra S, Kumar D. Studies on the immunostimulant and antihepatotoxic activities of *Asparagus racemosus* root extract. *J Med Aromat Plant Sci* 22 (2000): 49-52.
95. Hannan J M A, Marenah L, Ali L, Rokeya B, Flatt P R, Abdel Wahab Y H. Insulin secretory actions of extracts of *Asparagus racemosus* root in perfused pancreas, isolated islets and clonal pancreatic beta cells. *Journal of Endocrinology* 192.1 (2007): 159-68.
96. Kar A, Choudhary B K, Bandyopadhyay N G. Preliminary studies on the inorganic constituents of some indigenous hypoglycemic herbs on oral glucose tolerance test. *J Ethnopharmacol* 64 (1999): 179-84.
97. Braverman IM, Fonferko E Studies in cutaneous aging: I, the elastic fiber network. *The Journal of Investigative Dermatology* 78 (1982): 434-443.
98. Olikarnin A, Kallionen M A biochemical and immunohistochemical study of collagen in sunexposed and protected skin. *Photodermatology* 6 (1989): 24-31.
99. Smith JG, Davidson EA, Tindall JP, Sams WM Alterations in human dermal connective tissue with age and chronic sun damage. *The Journal of Investigative Dermatology* 39 (1962): 347-350.
100. Kambayashi H, Yamashita M, Odake Y, Takada K, Funasaka Y, Ichihashi M Epidermal changes caused by chronic low-dose UV irradiation induce wrinkle formation in hairless mouse. *Journal of Dermatological Science* 27.1 (2001): 19-25.
101. Yasui H, Sakurai H Age-dependant generation of reactive oxygen species in the skin of live hairless rats exposed to UVA light. *Exp. Dermatol* 12 (2003): 655-661.
102. Salano F, Briganti S, Picardo M, Ghanem G Hypopigmenting agents: An updated review on biological, chemical and clinical aspects. *Pigment Cell Res* 19 (2006): 550-71.
103. Narayanaswamy N, Duraisamy A, Balakrishnan K. P. Screening of some Medicinal Plants for their Antityrosinase and Antioxidant activities. *International Journal of PharmTech Research* 3.2 (2011): 1107-1112.
104. Garima Saxena et. al. Phytoestrogens Of *Asparagus Racemosus* Willd. *Journal of Herbal Medicine and Toxicology* 4.1 (2010): 15-20.
105. Goel RK, Prabha T, Kumar MM, Dorababu M, Prakash, Singh G. Teratogenicity of *Asparagus racemosus* Willd. root, a herbal medicine. *Indian J Exp Biol* 44.7 (2006): 570-573.
106. Muralidhar TGS, Chauhan B, Kulkarni R. Lack of Teratogenicity after Administration of D-400, an Oral Hypoglycemic Ayurvedic Formulation, during Gestation and Lactation. *J Biol Chem Res* 12.3-4 (1993): 151-156.
107. Dalvi SS, Nadkarni PM, Gupta KC. Effect of *Asparagus racemosus* (Shatavari) on gastric emptying time in normal healthy volunteers. *J Postgrad Med* 36.2 (1990): 91-94.
108. Gautam M, Diwanay S, Gairola S, Shinde Y, Patki P, Patwardhan B. Immunoadjuvant potential of *Asparagus racemosus* aqueous extract in experimental system. *J Ethnopharmacol* 91.2-3 (2004): 251-255.
109. Tabar AI, Alvarez MJ, Celay E, et al. Allergy to asparagus. *An Sist Sanit Navar* 26.2 (2003): 17-23
110. Bopana N, Saxena S. *Asparagus racemosus*-- ethnopharmacological evaluation and conservation needs. *J Ethnopharmacol* 110.1 (2007): 1-15
111. Bhatnagar M, Sisodia SS, Bhatnagar R. Antiulcer and antioxidant activity of *Asparagus racemosus* Willd and *Withania somnifera* Dunal in rats. *Ann N Y Acad Sci* 2005; 1056:261-278.