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## ASPARAGUS RACEMOSUS – A PHYTOESTROGEN

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### Abstract:

*Asparagus racemosus* Wild, F: *Aspargaceae* is an ayurvedic plant with medical importance of tropical and subtropical India. Its medical usage has been reported in Indian & British Pharmacopeias and in traditional system of medicine such as Ayurveda, Unani & Siddha. *Asparagus racemosus* is mainly known for its phytoestrogenic properties with an increasing awareness about the harmful effects with synthetic oestrogens, the interest in plant derived oestrogens has increased tremendously making *Asparagus racemosus* particularly important. Its beneficial uses in correcting menstrual irregularities are mentioned in ancient literature, till date they are prescribed by ayurvedic physicians to correct menstrual irregularities with products available in the markets. *Asparagus racemosus* has been shown to have many other properties like Antistress, Anti-diarrhoeal, Antidyspepsia, Adaptogenic action, Antiulcerogenic action, Antioxidant & Cardio protection. This article aims to evaluate the biological activities, pharmacological applications & Clinical studies of *Asparagus racemosus* to provide direction for further phytoestrogenic properties and unexplored areas in which *Asparagus* can be proved to have potential to cure diseases like osteoporosis.

**Key words:** *Asparagus*, *Asparagus racemosus*, Phytoestrogen and Menopause.

## **Introduction:**

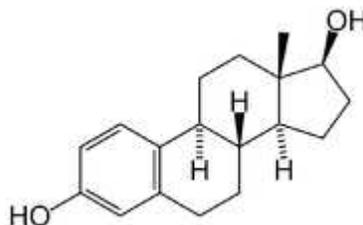
*Asparagus racemosus* is an important medicinal plant of tropical and subtropical India. Its medicinal usage has been reported in the Indian and British Pharmacopoeias and in indigenous systems of medicine. The genus *Asparagus* includes about 300 species around the world. The genus is considered to be medicinally important because of the presence of steroidal saponins and sapogenins in various parts of the plant. Out of the 22 species of *Asparagus* recorded in India; *Asparagus racemosus* is the one most commonly used in traditional medicine. Use of *Asparagus racemosus* was mentioned in the ancient literature of Ayurveda (Charaka samhita). It is used to rectify the gynecological problems like irregularities in menstrual cycle and sexual dysfunction. Even till today the formulations containing *Asparagus racemosus* are used to correct the menstrual irregularities by ayurvedic practitioner many formulations containing *Asparagus racemosus* are presently available in market for use. Therapeutic use of the *Asparagus* is due to the Phytoestrogenic components present in it.

*Asparagus racemosus* Willd. (family Asparagaceae; Liliaceae), is commonly called Satavari, Satawar or Satmuli in Hindi; Satavari in Sanskrit; Shatamuli in Bengali; Shatavari or Shatmuli in Marathi; Satawari in Gujarati; Toala-gaddalu or Pilli-gaddalu in Telegu; Shimaishadavari or Inli-chedi in Tamil; Chatavali in Malayalam; Majjigegadde or Aheruballi in Kannada; Kairuwa in Kumaon; Narbodh or atmooli in Madhya Pradesh; and Norkanto or Satawar in Rajasthan<sup>1</sup>.

The plant grows throughout the tropical and subtropical parts of India up to an altitude of 1500 m. The plant is a spinous under-shrub, with tuberous, short rootstock bearing numerous

succulent tuberous roots (30–100 cm long and 1–2 cm thick) that are silvery white or ash coloured externally and white internally. These roots are the part that finds use in various medicinal preparations. The stem is woody, climbing, whitish grey or brown coloured with small spines. The plant flowers during February–March leaving a mild fragrance in its surrounding and by the end of April, fruits can be seen with attractive red berries<sup>1</sup>.

Phytoestrogens are defined by the British Working Group on Phytoestrogens of the Committee of Toxicity of Chemicals in Food, Consumer Products and the Environment of the Food Standards Agency (FSA, 2003) as *any plant substance or metabolite that induces biological responses in vertebrates and can mimic or modulate the actions of endogenous oestrogens usually binding to oestrogen receptors*<sup>2</sup>. The majority of phytoestrogens belong to a large group of substituted phenolic compounds known as flavonoids. Three classes of flavonoid, the isoflavones, coumestans and prenylated flavonoids are phytoestrogens that possess the most potent oestrogenic activity<sup>2</sup>.



**Fig-1**

The phytoestrogen classes mentioned above have a similar structure to oestradiol and are able to bind the estrogen receptor (ER), preferably the ER $\alpha$ , although their binding affinity is lower than that of endogenous estradiol. All the structures of the phytoestrogens possess the

phenolic (bottom, left) and hydroxyl (top, right) moieties of the oestradiol structure and the distances between the two groups in each compound are similar<sup>2</sup>.

#### **Active constituents in *Asparagus racemosus*:**

The major active constituents of *Asparagus racemosus* are steroidal saponins (Shatavarins I–IV) that are present in the roots. Shatavarin IV is a glycoside of sarsasapogenin having two molecules of rhamnose and one molecule of glucose (Fig. 1). Other active compounds such as quercetin, rutin (2.5% dry basis) and hyperoside are found in the flowers and fruits; while diosgenin and quercetin-3 glucuronide are present in the leaves<sup>1</sup>.

The molecular structure of the major phytoestrogens, i.e., the isoflavones and coumestans, are given in comparison to 17 $\beta$ -estradiol, the most potent naturally occurring estrogen. The similarities in the structure of the phytoestrogens versus 17 $\beta$ -estradiol are sufficient to permit occupancy of the estrogen receptor (ER) by the phytoestrogens, but occupancy time or affinity for the receptor is significantly reduced compared to 17 $\beta$ -estradiol. The structure of ginstein and daidzein differ by only the absence of a hydroxyl group on the A ring. Coumestrol's ring structure is more similar than that of isoflavones to the true estrogens<sup>3</sup>.

Five steroidal saponins, shatavarins VI–X, together with five known saponins, shatavarin I (or asparoside B), shatavarin IV (or asparinin B), shatavarin V, immunoside and schidigerasaponin D5 (or asparanin A), have been isolated from the roots of *Asparagus racemosus* by RP-HPLC and characterized by spectroscopic (1D and 2D NMR experiments) and spectrometric (LCMS) methods<sup>33</sup>. The presence of sarsasapogenin in natural plants of *Asparagus racemosus* as well as in *invitro* cultures<sup>4</sup>. Synthesis of sarsasapogenin in the callus cultures of *Asparagus racemosus* was also reported<sup>5</sup>. 'Racemofuran' a new antioxidant compound was identified from *Asparagus*

*racemosus* and separated by DPPH ( $\alpha,\alpha$ -diphenyl-picrylhydrazyl) autography-directed separation<sup>6</sup>. Isolation and spectral data of a new isoflavone, 8-methoxy-5,6,4-trihydroxyisoflavone 7-*o*- $\beta$ -D-glucopyranoside, was reported from the roots of the plant<sup>7</sup>.

The isolation and characterization of a polycyclic alkaloid called 'Asparagine' from *Asparagus racemosus* that exhibited a unique cage-type structure and remarkable anti-oxytocic activity<sup>8</sup>. Later, a new 9, 1-dihydrophenanthrene derivative named 'Racemosol' was isolated from the ethanol extract of roots<sup>9</sup>. Its structure was elucidated by spectroscopic analysis as 9, 10-dihydro-1, 5-dimethoxy-8-methyl-2, 7-phenanthrenediol. Sarsasapogenin and kaempferol have been isolated from the woody portion of tuberous roots of *Asparagus racemosus*. These compounds were identified on the basis of chemical and spectroscopic evidence<sup>10</sup>. Survey on the seeds of 16 species of the genus *Asparagus* and found barely detectable levels of phytoecdysteroids in *Asparagus racemosus*<sup>11</sup>.

#### **Phytoestrogenic properties of *Asparagus racemosus*:**

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>12</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>13</sup>. Considering the threat associated with oestrogen replacement therapy<sup>14</sup>. Studied the relationship between hormone replacement therapy and the risk of endometrial cancer. They concluded that there is a substantial increase in risk associated with long periods of oestrogen use and this risk persisted even several years after discontinuation of oestrogen use.

The interest in plant-derived oestrogens or 'phytoestrogens' has increased due to the realization that hormone replacement therapy is neither as safe nor as effective as previously envisaged<sup>14</sup>. Phytoestrogens are defined as any plant compound structurally and/or functionally similar to ovarian and placental oestrogens and their active metabolites<sup>15</sup>. Phytoestrogens 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, pituitary, breast 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 phytoestrogens<sup>16</sup>. However, contradictory studies also exist regarding this evaluation. Studies found no association between phytoestrogens and breast cancer<sup>17</sup>. *Asparagus racemosus* is well known for its phytoestrogenic properties and use as a hormone modulator demonstrated the inhibitory action of *Asparagus racemosus* on DMBA-induced mammary carcinogenesis in rats<sup>18</sup>. The root powder obtained after extraction with chloroform and methanol (1:1) was added in different percentages to the animal feed. Rats fed on a 2% *Asparagus racemosus* diet showed a significant ( $p < 0.05$ ) decline in both tumour incidence and mean number of tumours per tumour bearing animal. They concluded that *Asparagus racemosus* root extract exerted a mammotropic and/or lactogenic influence on normal as well as on oestrogen primed animals thereby rendering the mammary epithelium refractory to the carcinogen.

The root extract of *Asparagus racemosus* has also been traditionally used in Ayurveda to increase milk secretion during lactation. The aqueous extract of *Asparagus racemosus* roots increased the weight of mammary glands in post-partum and oestrogen-primed rats and the uterine weight in the oestrogen-primed group<sup>19</sup>. This effect could be attributed to the action of released

corticoids or prolactin. Oral administration of the alcoholic extract of *Asparagus racemosus* rhizome (30 mg/100 g body weight, daily for 15 days) to adult pregnant female albino rats had an oestrogenic effect on the female mammary glands and genital organs<sup>20</sup>. An increase in milk secretion after administration of *Asparagus racemosus* in the form of Ricalex® tablets (Aphali Pharmaceuticals; 40 mg concentrated root extract per tablet) to women suffering from deficient milk secretion<sup>21</sup>. Randomized controlled trials to evaluate the effect of *Asparagus racemosus* as a lactagogue in lactational inadequacy among women who had delivered at term without complications. Each 100 g dose of the medicine contained 15 g *Asparagus racemosus* root extract. However, it is found that a 4-week treatment with *Asparagus racemosus* extract did not have any lactagogue effect<sup>22</sup>.

‘U-3107’ or EveCare® (containing 32 mg *Asparagus racemosus* extract per 5ml syrup) is a herbal preparation formulated by the Himalaya Drug Co., Bangalore, to treat various menstrual disorders and threatened abortion. Administration of ‘U-3107’ in normal rats increased wet and dry uterine weights and also resulted in a marked increase in oestrogen levels with no change in progesterone levels as compared to control. The primary changes in uterine tissues are controlled by oestrogen and progesterone. The oestrogenic effect in this case was observed only in the presence of functional ovaries indicating that the formulation per se does not possess any oestrogenic activity. The effect is only evident in cases where the ovaries are functional. The rats from both controlled and treated group showed normal oestrous cycle<sup>23</sup>.

The saponin-rich fraction obtained from *Asparagus racemosus* was found to inhibit oxytocin induced uterine contractions *in vivo*<sup>24</sup>. ‘U-3107’ did not possess any oxytocin-like activity which may prove to be useful in conditions associated with hypermotility of the uterus as in

dysmenorrhoea and threatened abortion<sup>23</sup>. 'EveCare' capsules proved to be effective in the treatment of dysfunctional uterine bleeding (DUB). Seventy women in the age group of 20–45 years with DUB were included in this study. They found that by the end of the treatment, 63 women had achieved a regularized menstrual cycle. This action can be attributed to the local healing of the endometrium stimulated by endometrial microvascular thrombosis caused by high doses of phytoestrogens<sup>25</sup>. In another study, a group of 40 patients suffering from dysmenorrhoea and pre-menstrual syndrome (PMS) were found to be symptom free after treatment with 'EveCare'<sup>26</sup>. A drug prepared from *Asparagus racemosus* (about 85 parts), patented has been shown to be effective in the treatment of PMS in human females who experience adverse symptoms<sup>27</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. Menosan® (containing 110 mg *Asparagus racemosus* extract per tablet) is another polyherbal formulation that was found to cause an increase in uterine weight and uterine glycogen without altering serum oestrogen and progesterone levels in immature rats as against ovariectomized rats used as control<sup>28</sup>. This study indicates that the phytoestrogen performs its function by binding directly to the oestrogen receptor without enhancing the endogenous oestrogen levels. Women undergoing menopause often experience a decline in the quality of life due to sleep deprivation, mood swings, lack of concentration, etc. 'Menosan' has also been studied for the treatment of post-menopausal symptoms<sup>29</sup>. In a trial comprising 27 women in the age group of 35–56 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'. The study had concluded that since *Asparagus racemosus* also has anti-bacterial activity in addition to it being a phytoestrogen; it is responsible for relief from symptoms like hot flashes and night sweats.

The flip side in the use of phytoestrogens is corroborated by a study conducted by which indicated certain teratogenic effects in rats after the administration of methanolic extract of *Asparagus racemosus* (ARM). In a prenatal study, they observed that ARM treatment caused swelling of legs, slow growth of foetal body and placental parts and an increase in the resorption of foetuses; while in the post-natal study, ARM treated groups exhibited a smaller litter of pups with increased mortality and delayed development<sup>30</sup>. However, this study was unable to identify any specific constituent as being responsible for this teratogenicity and therefore needs to be investigated further.

Taking into account the existing literature on the subject, we can safely construe that although hormone replacement therapy is less effective in treating various menopausal symptoms and may actually increase the risk of cancer; the use of phytoestrogens derived from *Asparagus racemosus* cannot be blindly advocated due to the incomplete understanding and insufficient evidence regarding their potential health effects. It is also important to keep in mind that phytoestrogenic foods are different from phytoestrogenic herbs. While foods rich in phytoestrogens containing low amounts of the active compound (like soy bean, rye, oats, barley, etc.) can be consumed on a regular basis, phytoestrogenic herbs are usually extremely potent and not advisable for long term use and therefore the dosage and duration are extremely important. Clearly, more research is needed to define the effect of phytoestrogens from *Asparagus racemosus*

and at the same time standardizing and characterising formulations and/or isolated phytoestrogens is imperative. In addition, developing an understanding of the effects of phytoestrogens from *Asparagus racemosus* as opposed to human oestrogens also holds great promise for further research<sup>32</sup>.

Satavari has also been studied for its influence on the male reproductive system<sup>31</sup>. They found that rats fed with *Asparagus racemosus* root powder (0.5 g/kg rat feed) for 21 consecutive days exhibited significantly high testes weights as compared to untreated controls. This however, is an isolated report and can be investigated further to broaden our understanding regarding the effect of Satavari on the male reproductive system as well.

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