

Ashwagandha: Ancient Medicine for Modern Times

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Ashwagandha (*Withania somnifera* Dunal) is a popular Indian medicinal plant and has been used for over 3000 years in Ayurvedic medicine to treat diverse range of diseases. Ashwagandha is a member of the class of herbs called *rasayana*, long prized for rejuvenating effects on health. It is believed that it assists body to respond appropriately to stressors, both acute and chronic [1]. The plant was first mentioned in English language text by Van Rheede in 1868, who described the use of its leaves in home ointments. Other parts of the Ashwagandha plant, including roots, shoots, seeds, and berries have also been used in daily tonics and various home remedy recipes to increase health and longevity [2]. The plant is a source of unique alkaloids and withanolides that have been shown to act as steroidal hormones and antioxidants with favorable impacts on human health [3]. Several recent studies have provided evidence for its anti-stress, antioxidant, analgesic, anti-inflammatory, anti-cancer, cardioprotective adaptogenic, anti-spasmodic, immunomodulatory and immunostimulant activity [4-10].

Withaferin A (WA) is the most abundant compound in *W. somnifera* extract [11,12]. Recent studies reported that WA elicits strong anti-cancer activity in several cancer models. WA by specific binding to vimentin cytoskeleton protein promotes apoptosis of cancer cells [13-15]. A classical epithelial mesenchymal transition (EMT) protein, vimentin overexpression in cancer correlates with metastatic disease, induction of epithelial to mesenchymal transition and reduced patient survival. Several reports show increased expression of vimentin in invasive human tumors but are nearly undetectable in non-invasive, stationary tumors [16,17]. WA has vimentin-dependent proteosomal inhibitory activity that leads to anti-angiogenic effects [18-20]. Furthermore, WA induces apoptotic cell death and anti-tumor activity by targeting NF- κ B [21-23], JAK-STAT [24], reactive oxygen species (ROS) activation [25,26], ROS-mediated autophagy [27], annexin [28], proteasome [29], Hsp90 [30-32], endoplasmic reticulum stress [33], RET protooncogene [34], Bcl-2 [26], and Par-4 tumor suppressor protein [35].

W. somnifera is one of the most important herbs used as a traditional remedy for several illnesses. Withanolides from *W. somnifera* inhibited the growth of human cancer cells. Therefore, it can be postulated that the consumption of *W. somnifera* leaves as a dietary supplement may prevent or decrease the growth of tumors in cancer patients as well as the formation of new tumors. Clinical trials using purified withanolides including WA as single therapy or in combination with standard cancer therapy is suggested.

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