ASHWAGANDHA (WITHANIA SOMNIFERA DUNAL): WONDER MEDICINAL PLANT

K.C. Verma

Department of Biochemistry, College of Basic Sciences and Humanities, Govind Ballabh Pant University of Agriculture and Technology, Pantnagar-263 145, India

ABSTRACT

Withania somnifera is a pantropic native medicinal plant growing all over western and central India. Ashwagandha is characterized by the presence of steroidal lactones (withanolides), alkaloids and flavonoids. Root contains maximum amount of alkaloids – nicotine, sominine, somniferin, somniferinine, withanine, withanonine, pseudo-withanine, tropin, withanolides etc. These compounds show relaxant and antispasmodic effects against several plasmogens on intestine, uterine, bronchial, tracheal, and blood vascular muscles. Roots of the plant show hypotensive, bradycardic, antitumor, respiratory stimulant activities and radiosensitizing effects in animals.

Key words: Ashwagandha, Withania somnifera, Withanolides.

Medicinal herbs constitute an effective source of traditional (Ayurvedic, Unani, Homeopathy) and modern medicine. Plant is a biosynthetic laboratory for various chemical compounds used for welfare of human being in different ways. The practice of use of medicinal herbs for treating diseases is well known from ancient times. There are a number of synthetic medicines which have been derived from medicinal herbs: Digoxin, Aspirin, Ephedrine, Quinine, Vincristine, Vinblastine, Artemisinin, Hypericin, Silymarin are some medicines derived from plants. Ashwagandha is well known for its medicinal properties since 1000 B.C. in ayurvedic texts including Charka samhita, Sushrut samhita, and Bhara prakasha, mentioned it to be a general tonic as well as a cure for morbidity arising from diseases such as pain, arthritis and inflammation (Dash and Junius, 1983). Withania somnifera significantly reduced hepatic lipid peroxidation and increases the activity of superoxide dismutase and catalase. It is also used to stimulate thyroidal activity and also promotes hepatic antioxidant activity.

It is a wide spread species disseminating from the South Mediterranean area to the Canary islands and to South East Africa, Congo, Madagascar, Palestine to North India, Covering Israel, Jordan, Egypt, Sudan, Iran, Afghanistan, Baluchistan and Pakistan. (El-Sisi et al., 1967; Gifri, 1992 and Parasa, 1960). Withania somnifera is one of the best known Ayurvedic herbs and holds a premium place in the Ayurvedic tradition similar to Ginseng in Chinese therapies. For that reason, Withania somnifera has been often referred to as the “Indian Ginseng”.

Over 39 active ingredients have been identified, extracted and isolated by different chromatographic techniques. These compounds can be classified in four different groups:


3. Saponins: Contains additional acyl group viz. sitostosides VII and VIII (Bhattacharya et al., 1987).


**Withanolides**: The distinctive earthy odour and flavour of ashwagandha is due to the presence of steroidal lactones collectively known as ‘Withanolides’ (Bhatnagar et al., 1976; Khotpal et al., 1993, Schwarting, 1963 and Kazutoshi et al., 1999). Withanolides possess antioxidant, antibacterial, antifungal, anti-tumour, anti-arthritic, anti-inflammatory and immunosuppressive activities (Singh and Kumar, 1998). It is a component of different formulations of Ayurvedic medicines, available commercially (Tripathi et al., 1996). In the pharmacopoeia of India the root and leaves have been regarded as a useful internal medicine in rheumatism and dyspepsia and to be fully diuretic (Warming, 1868). Five new withanolides namely Withanosominilide, Withasomniferanolide, Somnifernolide, Somnifera Withanolide and Somnithanolide have been isolated from stem bark of *W. somnifera* (Ali et al., 1997).

**Withanolides in cancer therapy**: A Special type of withanolide (Tubocapsanolide A: TA) inhibited Hsp90-Hsp70-based chaperone machinery in MDA-MB-231 cells. It is known that heat shock proteins (Hsp90 and Hsp70) play a key role as molecular chaperons maintaining the native conformation of proteins (Buchner, 1999; Hartl and Hayer 2002). In mammalian cells, Hsp90 forms a multichaperone complex with Hsp70 and other cofactors, which is responsible for folding and stabilizing a specific set of client proteins, such as Raf, Akt, v-Src, Her2, Cdk4, mutant p53, focal adhesion kinase, vascular endothelial growth factor receptor, and telomerase (Wegele et al., 2004). Inhibition of Hsp90 leads to misfolding and aggregation of client proteins, which results in ubiquitination and proteasome-mediated degradation (Mimnaugh, 1996 and Whitesell et al., 2000). Since Hsp90-dependent proteins are essential for regulating cell growth, apoptosis, angiogenesis, and metastasis. Hsp90 represents a promising therapeutic target for the treatment of cancer (Jolly and Morimoto, 2000; Bagatell and Whitesell, 2004). TA acts as inhibitor of Hsp90-Hsp70-based chaperone machinery, in following ways:

1) TA selectively decreased the protein levels of Hsp90 client proteins (Cdk4, cyclin D1, Raf-1, Akt, and mutant p53) without affecting the non-Hsp90 client proteins.
2) In the presence of proteasome inhibitors, either Akt or Cdk4 accumulated in Triton-insoluble fraction of TA-treated cells, suggesting that TA triggers proteasome-dependent degradation of misfolded/aggregated proteins.

3) Nonreducing SDS-PAGE revealed that TA caused disulfide-linked high molecular weight conformers of Hsp70 or Hsp90 both in Triton-soluble and insoluble fractions, indicating an oxidative insult of these proteins (Reed, 2001). TA directly inhibited chaperone activity in a Hsp90-Hsp70-rich rabbit reticular lysate system. Thus, TA is an inhibitor of Hsp90-Hsp70 chaperone machinery.

**Withanolides in healthier progeny:** Steroids of *Withania somnifera* are used to enhance liver glycogen stores. Reduction in metabolic rate also leads to under-utilization of glycogen stores in the liver, leading to its accumulation. The reduced adrenocortical activity may be attributed to steroids in the roots, which may act like exogenous adrenocortical steroids, lowering the ACTH secretion and consequently, endogenous steroid production. Thus, decoction of *Withania somnifera* promoted growth especially during the active growth period and helped produce healthier progeny (Mishra et al. 2000).

**Withaferin-A:** The active principle of ashwagandha viz. Withaferin-A and Sitoindocides VII increased cortical muscarinic acetylcholine receptor capacity, partially explaining the cognition enhancing and memory improving effects (Schliebs et al., 1997). Gupta et al., 1996 isolated and quantified Withaferin A (Fig 2) from different plant parts of *Withania somnifera*. Withaferin inhibit tumor growth and increase in survival rate in Swiss mice inoculated with Ehrlich ascites carcinoma (Devi et al., 1995 and Sharad et al., 1996). Withaferin A, isolated from the alcoholic extract of dried root, shows antitumor and radiosensitizing activity in Chinese hamster cells (Devi, 1995). Withaferin-A possess antibacterial activity against acid fast bacilli and gram positive microorganism.

**Sitoindocides VII:** Sitoindoxides VII-X (Fig 3) and Withaferin A also have showed anti-oxidant activity using the major free-radical scavenging enzymes such as catalase, superoxide dismutase and glutathione peroxidase (Bhattacharya et al., 1997). Sitoindosides IX with Glycowithanolides caused significant mobilization and activation of peritoneal macrophages, phagocytosis, and increase activity of the lysosomal enzymes. Both compounds produced significant antistress activity and augmented learning acquisition and memory retention in animals (Ghosal et al., 1989).
Sitoindocides in memory improvement: Sitoindosides and withaferin slightly enhanced acetylcholinesterase (AChE) activity in the lateral septum and globus pallidus, and decreased AChE activity in the vertical diagonal band. These changes were accompanied by enhanced [M.sub.1] - muscarinic-cholinergic receptor-binding in lateral and medial septum as well as in frontal cortices, whereas the [M.sub.2] - muscarinic receptor-binding sites were increased in a number of cortical regions including cingulate, frontal, piriform, parietal, and retrosperine cortex. These compounds preferentially affect events in cortical and basal forebrain cholinergic-signal-transduction cascade. The drug-induced increase in cortical muscarinic acetylcholine-receptor capacity might partly explain the cognition-enhancing and memory-improving effects of WS extracts in animals and in humans (Schliebs et al. 1997).

Roxburg (1874) referred to the medicinal use of this plant and stated that Telinya physicians treated the roots of ashwagandha as alexipharmic. The administration of an extract of *Withania somnifera* was found to significantly reduce leucopenia induced by clophomside treated experimental animals, thus it is useful in cancer therapy (Davis and Kuttan, 1998). Ashwagandha rasayana (An Ayurvedic polyherbal formulation) significantly reduced the lung tumor nodule formation upto 55.6 % in animals.

Ashwagandha was regarded as a tonic in Hindu medicine and was employed in consumption, emaciation and debility caused by old age. It was used in many tonic preparations as prescribed by Chakradutta and others and was a major constituent of the aphrodisiac medicines. (Kumar et al., 1980). Methanolic extracts of the aerial parts of *Withania somnifera* has antiinflammatory activities comparable to that of hydrocortisone sodium succinate (Al-Hindawi et al., 1992). In Garhwal Himalaya region, root powder of *Withania somnifera* is used in pulmonary tuberculosis and in the treatment of glandular swelling of bubonic plague (Maithani, 1973). Root powder significantly reduces...
in paw swelling and responsible for degenerative changes (Begum and Sadique, 1988). Root extracts of *W. somnifera* showed antifungal activity against *Fusarium solani* (Ramteke et al., 2003).

The review indicates that *Withania somnifera* may be useful in many ailments, including arthritis and other musculoskeletal disorders, stress-induced nervous exhaustion, and hypertension as a multi-purpose medicinal agent. Thus, it can be concluded that the major chemical constituents of ashwagandha responsible for its primary medicinal properties emanate, are based upon the action of certain steroidal lactones known as withanolide. Currently several limitations exist in the uses of active components of ashwagandha. While it has been used successfully in many Ayurvedic formulations for centuries, even more clinical trials should be conducted to support its therapeutic use (Schwarting, et al., 1963).

As for its use in fighting cancer, confirmatory studies in several other animal tumor systems must be conducted for more definitive findings. It is also important to recognize that either it is effective only in isolation, or it can be more potentiating effect when given in combination with other herbs or drugs.

**REFERENCES**


Schliebs, R. et al. (1997) Neurochem Int. 30(2):181-190
Schwarting, A. E. et al. (1963) Lloydia, 26:258
Warming, M. (1868) Medicinaly important plants of India. Pharmocoepia of India. pp. 247-251