

## Ashwagandha: Ancient Medicine for Modern Times

Abbas K Samadi\*

Neutriomix, San Diego, CA, USA

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- $\kappa$ 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.

### References

1. Bhattacharya SK, Bhattacharya A, Chakrabarti A (2000) Adaptogenic activity of Siotone, a polyherbal formulation of Ayurvedic rasayanas. *Indian J Exp Biol* 38: 119-128.
2. Elsakka M, Pavelescu M, Grigorescu E (1989) *Withania somnifera*, a plant with a great therapeutical future. *Rev Med Chir Soc Med Nat Iasi* 93: 349-350.
3. Kulkarni SK, Dhir A (2008) *Withania somnifera*: an Indian ginseng. *Prog Neuropsychopharmacol Biol Psychiatry* 32: 1093-1105.
4. Agarwal R, Diwanay S, Patki P, Patwardhan B (1999) Studies on immunomodulatory activity of *Withania somnifera* (Ashwagandha) extracts in experimental immune inflammation. *J Ethnopharmacol* 67: 27-35.
5. Mishra LC, Singh BB, Dagenais S (2000) Scientific basis for the therapeutic use of *Withania somnifera* (ashwagandha): a review. *Altern Med Rev* 5: 334-346.

6. Scartezzini P, Speroni E (2000) Review on some plants of Indian traditional medicine with antioxidant activity. *J Ethnopharmacol* 71: 23-43.
7. Vanden Berghe W, Sabbe L, Kaileh M, Haegeman G, Heynincx K (2012) Molecular insight in the multifunctional activities of Withaferin A. *Biochem Pharmacol* 84: 1282-1291.
8. Tohda C, Kuboyama T, Komatsu K (2000) Dendrite extension by methanol extract of Ashwagandha (roots of *Withania somnifera*) in SK-N-SH cells. *Neuroreport* 11: 1981-1985.
9. Davis L, Kuttan G (2002) Effect of *Withania somnifera* on cell mediated immune responses in mice. *J Exp Clin Cancer Res* 21: 585-590.
10. Kuboyama T, Tohda C, Komatsu K (2005) Neuritic regeneration and synaptic reconstruction induced by withanolide A. *Br J Pharmacol* 144: 961-971.
11. Chaurasiya ND, Uniyal GC, Lal P, Misra L, Sangwan NS, et al. (2008) Analysis of withanolides in root and leaf of *Withania somnifera* by HPLC with photodiode array and evaporative light scattering detection. *Phytochem Anal* 19: 148-154.
12. Misra L, Mishra P, Pandey A, Sangwan RS, Sangwan NS, et al. (2008) Withanolides from *Withania somnifera* roots. *Phytochemistry* 69: 1000-1004.
13. Lahat G, Zhu QS, Huang KL, Wang S, Bolshakov S, et al. (2010) Vimentin is a novel anti-cancer therapeutic target; insights from in vitro and in vivo mice xenograft studies. *PLoS One* 5: e10105.
14. Bargagna-Mohan P, Deokule SP, Thompson K, Wizeman J, Srinivasan C, et al. (2013) Withaferin A effectively targets soluble vimentin in the glaucoma filtration surgical model of fibrosis. *PLoS One* 8: e63881.
15. Grin B, Mahammad S, Wedig T, Cleland MM, Tsai L, et al. (2012) Withaferin A alters intermediate filament organization, cell shape and behavior. *PLoS One* 7: e39065.
16. Huber MA, Kraut N, Beug H (2005) Molecular requirements for epithelial-mesenchymal transition during tumor progression. *Curr Opin Cell Biol* 17: 548-558.
17. Sun B, Zhang S, Zhang D, Li Y, Zhao X, et al. (2008) Identification of metastasis-related proteins and their clinical relevance to triple-negative human breast cancer. *Clin Cancer Res* 14: 7050-7059.
18. Bargagna-Mohan P, Hamza A, Kim YE, Khuan Abby Ho Y, Mor-Vaknin N, et al. (2007) The tumor inhibitor and antiangiogenic agent withaferin A targets the intermediate filament protein vimentin. *Chem Biol* 14: 623-634.
19. Mohan R, Hammers HJ, Bargagna-Mohan P, Zhan XH, Herbstritt CJ, et al. (2004) Withaferin A is a potent inhibitor of angiogenesis. *Angiogenesis* 7: 115-122.
20. Thaiparambil JT, Bender L, Ganesh T, Kline E, Patel P, et al. (2011) Withaferin A inhibits breast cancer invasion and metastasis at sub-cytotoxic doses by inducing vimentin disassembly and serine 56 phosphorylation. *Int J Cancer* 129: 2744-2755.
21. Kaileh M, Vanden Berghe W, Boone E, Essawi T, Haegeman G (2007) Screening of indigenous Palestinian medicinal plants for potential anti-inflammatory and cytotoxic activity. *J Ethnopharmacol* 113: 510-516.

\*Corresponding author: Abbas K Samadi, Neutriomix, San Diego, CA, USA; E-mail: [asamadik@gmail.com](mailto:asamadik@gmail.com)

Received July 01, 2013; Accepted July 01, 2013; Published July 03, 2013

Citation: Samadi AK (2013) Ashwagandha: Ancient Medicine for Modern Times. *J Anc Dis Prev Rem* 1: e108. doi: [10.4172/2329-8731.1000e108](http://dx.doi.org/10.4172/2329-8731.1000e108)

Copyright: © 2013 Samadi AK. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

22. Ndlovu MN, Van Lint C, Van Wesemael K., Callebert P, Chalbos D, et al. (2009) Hyperactivated NF- $\kappa$ B and AP-1 transcription factors promote highly accessible chromatin and constitutive transcription across the interleukin-6 gene promoter in metastatic breast cancer cells. *Molecular and cellular biology* 29: 5488-5504.
23. Ichikawa H, Takada Y, Shishodia S, Jayaprakasam B, Nair MG, et al. (2006) Withanolides potentiate apoptosis, inhibit invasion, and abolish osteoclastogenesis through suppression of nuclear factor-kappaB (NF-kappaB) activation and NF-kappaB-regulated gene expression. *Mol Cancer Ther* 5: 1434-1445.
24. Aalinkeel R, Hu Z, Nair BB, Sykes DE, Reynolds JL, et al. (2010) Genomic Analysis Highlights the Role of the JAK-STAT Signaling in the Anti-proliferative Effects of Dietary Flavonoid-'Ashwagandha' in Prostate Cancer Cells. *Evid Based Complement Alternat Med* 7: 177-187.
25. Grogan PT, Sleder KD, Samadi AK, Zhang H, Timmermann BN, et al. (2013) Cytotoxicity of withaferin A in glioblastomas involves induction of an oxidative stress-mediated heat shock response while altering Akt/mTOR and MAPK signaling pathways. *Invest New Drugs* 31: 545-557.
26. Mayola E, Gallerne C, Esposti DD, Martel C, Pervaiz S, et al. (2011) Withaferin A induces apoptosis in human melanoma cells through generation of reactive oxygen species and down-regulation of Bcl-2. *Apoptosis* 16: 1014-1027.
27. Fong MY, Jin S, Rane M, Singh RK, Gupta R, et al. (2012) Withaferin A synergizes the therapeutic effect of doxorubicin through ROS-mediated autophagy in ovarian cancer. *PLoS One* 7: e42265.
28. Ozorowski G, Ryan CM, Whitelegge JP, Luecke H (2012) Withaferin A binds covalently to the N-terminal domain of annexin A2. *Biol Chem* 393: 1151-1163.
29. Yang H, Wang Y, Cheryan VT, Wu W, Cui CQ, et al. (2012) Withaferin A inhibits the proteasome activity in mesothelioma in vitro and in vivo. *PLoS One* 7: e41214.
30. Grover A, Shandilya A, Agrawal V, Pratik P, Bhasme D, et al. (2011) Hsp90/Cdc37 chaperone/co-chaperone complex, a novel junction anticancer target elucidated by the mode of action of herbal drug Withaferin A. *BMC Bioinformatics* 12 Suppl 1: S30.
31. Samadi A, Loo P, Mukerji R, O'Donnell G, Tong X, et al. (2009) A novel HSP90 modulator with selective activity against thyroid cancers in vitro. *Surgery* 146: 1196-1207.
32. Yu Y, Hamza A, Zhang T, Gu M, Zou P, et al. (2010) Withaferin A targets heat shock protein 90 in pancreatic cancer cells. *Biochem Pharmacol* 79: 542-551.
33. Choi MJ, Park EJ, Min KJ, Park JW, Kwon TK (2011) Endoplasmic reticulum stress mediates withaferin A-induced apoptosis in human renal carcinoma cells. *Toxicol In Vitro* 25: 692-698.
34. Samadi AK, Mukerji R, Shah A, Timmermann BN, Cohen MS (2010) A novel RET inhibitor with potent efficacy against medullary thyroid cancer in vivo. *Surgery* 148: 1228-1236.
35. Srinivasan S, Ranga RS, Burikhanov R, Han SS, Chendil D (2007) Par-4-dependent apoptosis by the dietary compound withaferin A in prostate cancer cells. *Cancer Res* 67: 246-253.

Citation: Samadi AK (2013) Ashwagandha: Ancient Medicine for Modern Times. J Anc Dis Prev Rem 1: e108. doi: 10.4172/2329-8731.1000e108

### Submit your next manuscript and get advantages of OMICS Group submissions

#### Unique features:

- User friendly/feasible website-translation of your paper to 50 world's leading languages
- Audio Version of published paper
- Digital articles to share and explore

#### Special features:

- 250 Open Access Journals
- 20,000 editorial team
- 21 days rapid review process
- Quality and quick editorial, review and publication processing
- Indexing at PubMed (partial), Scopus, DOAJ, EBSCO, Index Copernicus and Google Scholar etc
- Sharing Option: Social Networking Enabled
- Authors, Reviewers and Editors rewarded with online Scientific Credits
- Better discount for your subsequent articles

Submit your manuscript at: <http://www.editorialmanager.com/acrgroup/>