

ASWAGANDHA (*WITHANIA SOMNIFERA*) – AYURVEDIC BEQUEST FOR THE PATIENTS OF CANCER: AN UPDATE ON CURRENT RESEARCH

Rao Paramkusha Madupu.^{1*}, Khemani Naresh²

Post Graduate Department of Dravyaguna Vignyan, T.T.D.'s S.V. Ayurveda College, Tirupati, India

Post Graduate Department of Dravyaguna Vignyan, National Institute of Ayurveda, Jaipur, India

Received: 03-11-2010; Revised: 28-11-2010; Accepted: 04-12-2010

ABSTRACT

Aswagandha (*Withania somnifera*) is a popularly known medicinal plant said in Ayurveda. It has been used to promote vigor and strength. The current ongoing researches are approving the plant can be useful in malignancies at various levels and with different mechanisms. An effort has been made in this paper to review such results focused at cancer therapy and management.

Aswagandha (*Withania somnifera*) is also known as Indian ginseng proves to be a beacon for blinded minds of cancer sufferers.

KEYWORDS: Aswagandha (*Withania somnifera*), Carcinogenesis, tumorigenesis, Radiosensitizing, Angiogenesis, Cancer Preventing, Anti Tumor Activity, Radio Sensitization Activity, withaferin, lipid peroxidation.

***Corresponding Author**

Dr. M. Paramkusha Rao

Reader & H.O.D.

P.G. Dept. of Dravyaguna

S.V. Ayurveda College

Tirupati, India

Email: paramkusha@gmail.com

INTRODUCTION

Scientific basis for the therapeutic use of Aswagandha (*Withania somnifera*)

Worldwide Scientific researchers are conducted frequently on Aswagandha (*Withania somnifera*) in recent years. Review of the literature through all publications and through a systematic search of major computerized databases pertaining to chemical properties, therapeutic benefits, and toxicity of relevant to Aswagandha (*Withania somnifera*), it is found that Aswagandha possesses several activities like:

1. Anti-inflammatory
2. Anti-tumor
3. Anti-stress
4. Anti-oxidant
5. Immuno-modulatory
6. Hemopoietic
7. Rejuvenating

It also appears to exert a positive influence on the endocrine, cardiopulmonary, and central nervous systems. The mechanisms of action for these properties are not fully understood. Toxicity studies reveal that Aswagandha appears to be a safe compound.

Several preliminary studies on Aswagandha (*Withania somnifera*) internationally have found various constituents of Aswagandha exhibit a variety of therapeutic effects with little or no associated toxicity.¹

Inhibitory effect on Fore-stomach and Skin Carcinogenesis

School of Life Sciences, Jawaharlal Nehru University, New Delhi, evaluated the cancer chemo-preventive efficacy of the Aswagandha (*Withania somnifera*) root. It is said studies showing mechanism-based cancer chemopreventive efficacy are limited. They studied the effect of dietary administration of *Withania* root on hepatic phase I, phase II and antioxidant enzymes by estimation of its level/activity, as well as in attenuating carcinogen-induced fore stomach and skin tumorigenesis in the Swiss albino mouse model. The findings showed that roots of Aswagandha (*Withania somnifera*) inhibit phase I, and activates phase II and antioxidant enzymes in the liver. Further, in a long-term tumorigenesis study, Aswagandha (*Withania somnifera*) inhibited benzo(a)pyrene-induced fore-stomach papilloma genesis, showing up to 60 and 92% inhibition in tumor incidence and multiplicity, respectively.

Similarly, Aswagandha (*Withania somnifera*) inhibited 7, 12-dimethylbenzanthracene-induced skin papilloma genesis, showing up to 45 and 71% inhibition in tumor incidence and multiplicity. In both studies, Aswagandha (*Withania somnifera*) showed no apparent toxic effects in mice as monitored by the body weight gain profile. Together, these findings suggest that Aswagandha (*Withania somnifera*) root has chemo preventive efficacy against fore-stomach and skin carcinogenesis and warrants the identification and isolation of active compounds responsible for its anticancer effects.²

Anti Tumor & Radiosensitizing Activity

Study on anti-tumor and radiosensitizing properties of *Withania somnifera* (Ashwagandha), have yielded encouraging results. The alcoholic extract of the dried roots of the plant as well as the active component Withaferin A isolated from the extract showed significant anti-tumor and radiosensitizing effects in experimental tumors in vivo, without any noticeable systemic toxicity. Withaferin A gave a sensitizer enhancement ratio of 1.5 for in vitro cell killing of V79 Chinese hamster cells at a non-toxic concentration of approximately 2 microM. The mechanism of action of this compound is not known. The studies so far indicate that *Withania somnifera* (Ashwagandha) could prove to be a good natural source of a potent and relatively safe radiosensitizer/chemotherapeutic agent.³

Angiogenesis inhibitor / Cancer Preventing Effect

In a hypothesized study, it is presumed that the Aswagandha (*Withania somnifera*) extracts might contain angiogenesis inhibitors. Researchers employed an endothelial cell-sprouting assay to monitor the purification of substances from Aswagandha (*Withania somnifera*) root extracts and isolated as the active principle the previously known natural product withaferin A.

It is shown that withaferin A inhibits human umbilical vein endothelial cell (HUVEC) sprouting in three-dimensional collagen-I matrix at doses which are relevant to NF-kappa B-inhibitory activity. Withaferin A inhibits cell proliferation in HUVECs (IC₅₀ =12 nM) at doses that are significantly lower than those required for tumor cell lines through a process associated with inhibition of cyclin D1 expression.

By these findings it is proposed that the inhibition of NF-kappa B by withaferin A in HUVECs occurs by interference with the ubiquitin-mediated proteasome pathway as suggested by the increased levels of poly-ubiquitinated proteins. Finally, withaferin A is shown to exert potent anti-angiogenic activity in vivo at doses that are 500-fold lower than those previously reported to exert anti-tumor activity in vivo. The findings identify a novel mode of action of withaferin A, which highlights the potential use of this natural product for cancer treatment or prevention.⁴

Anti Tumor Activity

In another study it is found that Withaferin-A and alkaloid present in *Withania somnifera* (ASVAGANDHA) was entrapped in niosomes. The release of the drug from the niosome was slower compared to plain withaferin A dispersed in phosphate buffered saline. The mean survival time (MST) of the animals treated with Withaferin A entrapped in the niosome was enhanced compared to the plain drug⁵

Cyclophosphamide toxicity reducer

The drugs used in chemotherapy like Cyclophosphamide and Cadmium are likely to cause carcinoma. sometimes the side effects produced by the chemotherapy and radiotherapy is more hazardous than the disease proper. Several researchers have aimed at reducing the side effects of radiation as well as chemotherapeutic agents with the help of Aswagandha (*Withania somnifera*).

Administration of *Withania somnifera* (ASWAGANDHA) extract was found to significantly reduce leucopenia induced by cyclophosphamide (CTX) treatment. The total WBC count on the 12th day of the CTX-treated group was 3720 cell/mm³ and that of CTX along with Aswagandha (*Withania somnifera*) was 6120 cell/mm³. Treatment of Aswagandha (*Withania somnifera*) along with CTX was found to significantly (P less than 0.001) increase the bone marrow cellularity compared to CTX alone treated group. Administration of Aswagandha (*Withania somnifera*) extract increased the number of alpha-esterase positive cells in the bone marrow of CTX treated animals compared to the CTX-alone treated group. The major activity of *Withania somnifera* (Aswagandha) has been reported to be the stimulation of stem cell proliferation. *Withania somnifera* (Aswagandha) has been suggested to reduce the cyclophosphamide induced toxicity and usefulness in cancer therapy.⁶

Radio Sensitization Activity

In a study the alcoholic extract of the dried roots of *Withania somnifera* (ASWAGANDHA), as well as the active component Withaferin-A isolated from the extract showed significant antitumor activity and gave a sensitizer enhancement ratio of 1.5 for in vitro cell killing of V79 Chinese hamster cells at a non toxic concentration of 2microM.

The mechanism of action of this compound is not known. The studies so far indicate that Aswagandha (*Withania somnifera*) could prove to be a good natural source of a potent and relatively safe radio sensitizer/chemotherapeutic agent.⁷

Radio Sensitizer Action

In another study the radiosensitizing effect of withaferin A, a withanolide from *Withania somnifera* (ASWAGANDHA) on the B16FI mouse melanoma was studied in vivo. Treatment of 100 mm³ tumors with 10 to 60 mg/kg withaferin A intraperitoneally produced a dose dependent increase in growth delay and volume doubling time. Injection of 30-50 mg/kg withaferin A, followed by 30 Gy local gamma irradiation, significantly enhanced the tumor response. No systemic or local adverse reactions were noted in these groups. The drug was most effective when injected intra-peritoneally 1h before irradiation. However, neither the individual agents nor their combination could produce any complete response (tumor cure). Melanoma is a relatively radioresistant tumor. The present results indicate that the radiation response of this tumor can be significantly enhanced by pre-treatment with withaferin A.⁸

Radio Protective Action & Cadmium Toxicity Reducer

The protective action of Aswagandha (*Withania somnifera*) on cadmium-induced toxicity in liver and kidney tissues of mice, has been studied. Aqueous extract of 40 mg/0.1 ml concentration was prepared from dried roots of Aswagandha (*Withania somnifera*). Mice were fed with Cd C12 + Aswagandha (*Withania somnifera*) extract and Aswagandha (*Withania somnifera*) extract alone (1.14g/kg body wt.), for 20 days. Results based on lipid peroxidation indicate that Aswagandha (*Withania somnifera*) is capable of reducing toxicity caused by cadmium. So far, no plant product has been reported to regulate cadmium-induced toxicity in animals. Thus Aswagandha (*Withania somnifera*) extract may prove useful in regulation of metal-induced clinical toxicity.⁹

Ochratoxin A's Toxicity Reducer

The effect of Asparagus racemosus (Satavari), Tinospora cordifolia, *Withania somnifera* (Asvaganadha) and Picrorhiza kurroa (Katuki) on the functions of macrophages obtained from mice treated with the carcinogen ochratoxin A (OTA) was investigated.

The chemotactic activity of murine macrophages was significantly decreased by 17 weeks of treatment with OTA compared with controls. Production of interleukin-1 (IL-1) and tumour necrosis factor (TNF) was also markedly reduced. Treatment with A. racemosus, T. cordifolia, Aswagandha (*Withania somnifera*) and P. kurroa significantly inhibited OTA-induced suppression of chemotactic activity and production of IL-1 and TNF-alpha by macrophages.

It was found that *Withania somnifera* (Asvaganadha) treated macrophage chemotoxicity and that A. racemosus induced excess production of TNF-alpha when compared with controls.¹¹

Effect on Stress Induced Carcinoma

In studies conducted on experimental stress induced carcinoma and gastric ulcer, Rasayana drugs showed promising results. Aswagandha (*Withania somnifera*), Jeebanti (Desmodium illyricum), Chyavanprash (A Popular Ayurveda formulation) were found to be effective both in clinical improvement and immunosurvivalance parameters in pulmonary tuberculosis.¹²

Reducer of Bad Effects of Radiation

In a study the immuno-potentiating capabilities of Aswagandha (*Withania somnifera*) to circumvent the immuno-suppression produced during radiation treatment in mice is conducted. Administration of a 75% methanolic extract of the plant was found to significantly increase the total WBC count in normal Balb/c mice and reduce the leucopenia induced by sub lethal dose of gamma radiation. Treatment with Aswagandha (*Withania somnifera*) was found to increase the bone marrow cellularity significantly, the percentage increase being 146.3. Treatment with Aswagandha (*Withania somnifera*) had normalised the ratio of normo-chromatic erythrocytes and polychromatic erythrocytes in mice after the radiation exposure. Major activity of Aswagandha (*Withania somnifera*) seemed to be in the stimulation of stem cell proliferation.¹³

Mixed with other herbs for Anti Cancer Effect

Several malignant cases (10 patients) of advanced stages of cancer management has been dealt with Ayurvedic herbal drugs. Malignant cases include, Squamous cell carcinoma, breast cancer, lung cancer, Hodgkin's lymphoma, vocal cord cancer, multiple myeloma, adenocarcinoma. Patients were administered with ayurvedic preparations made of plant materials such as Mesua ferrea (NAGAKESARA), Asparagus racemosus (Satavari), Adhatoda vasica (Vasa), Tinospora cordifolia (Guduchi), Hemidesmus indicus (Sariva), *Withania somnifera* (Aswagandha), Smilax glabra (Chopachini BH.), Piper cubeba (Kankola), Piper longum (Pippali), Glycyrrhiza glabra (Yasti), Tribulus terrestris (Gokshura), Pterocarpus santalinus (Rakta Chandana) and Terminalia bellerica (Vibhitaki). It was found that, herbal mixture to be an effective treatment in advanced malignancies though not a total cure.¹⁴

Effect on Prostate Cancer

In a recent study it is also identified that in combination, Aswagandha (*Withania somnifera*) and anti-

androgen synergistically induced Par-4 and apoptosis in androgen-responsive prostate cancer cells. When judiciously combined with anti-androgens, Aswagandha (*Withania somnifera*) inhibits survival of both androgen-responsive and androgen-refractory prostate cancer cells by a Par-4-dependent mechanism. As Par-4 up-regulation induces apoptosis in most tumor cells.¹⁵

CONCLUSION

After going through the current researches Aswagandha (*Withania somnifera*) can be comfortably used in the cancer patients very safely to achieve the following:

1. To prevent the cancer in suspected cases
2. To arrest the progress of carcinogenesis
3. To use as an adjuvant to reduce the dosage of chemotherapeutic agents
4. To use as an adjuvant to reduce the side effects in radiation and chemotherapies in cancer affected patients.
5. Aswagandha (*Withania somnifera*) can also be comfortably used along with other Rasayana group of drugs said in Ayurveda.

When it is known that no promising drug is available to cure cancer it is judicious use Ayurveda drugs as an alternate solution and solace. From this view point Aswagandha (*Withania somnifera*) is a must drug for the patients of all cancers. It is truly a gift from Ayurveda for the cancer patients.

REFERENCES

1. Mishra LC, Singh BB, Dagenais S. Scientific basis for the therapeutic use of *Withania somnifera* (Ashwagandha): a review., *Altern. Med. Rev.* 2000; 5(4):334-46
2. Bandhuvula Padmavathi *et al.* Roots of *Withania somnifera* inhibit forestomach and skin carcinogenesis in mice, *Evid. Based Complement Alternat. Med.* 2005; 2(1): 99–105
3. Devi PU. *Withania somnifera* Dunal (Ashwagandha): Potential plant source of a promising drug for cancer Chemotherapy and Radiosensitization., *Indian J Exp Biol.* 1996; 34(10):927-32
4. Mohan R, Hammers HJ, Bargagna-Mohan P, Zhan XH, Herbstritt CJ, Ruiz A, Zhang L, Hanson AD, Conner BP, Rougas J, Pribluda VS. Withaferin A is a potent inhibitor of angiogenesis, *Angiogenesis Discovery Research EntreMed.* 2004;7(2):115-22
5. Sheena IP, Singh UV, Kamath R, Uma Devi P, Udupa N. Niosomal withaferin a with better antitumor efficacy, *Indian Journal of Pharmaceutical Sciences* 1997; 60(1): p. 45-48
6. Davis L, Kuttan G. Amelioration of cyclophosphamide induced toxicity using *Withania somnifera*, *Amala Research Bulletin* 1996; 16: 109-112
7. Uma Devi P, Kamath R, Rao BS. Radiosensitization of a mouse melanoma by Withaferin a : in vivo studies, *Indian Journal of Experimental Biology* 2000; 38(5): 432-437
9. Panda S, Gupta P, Kar A. Protective role of Aswagandha in cadmium-induced hepatotoxicity and nephrotoxicity in male mouse., *Current Science* 1997: 546-547
11. Dhuley JN. Effect of some Indian herbs on macrophage functions in ochratoxin a treated mice, *Journal of Ethnopharmacology* 1997; 58(1): 15-20
12. Datta OK, Debnath PK. Immunomodulatory activity of some Ayurvedic rasayana drugs, *Proceedings of International Congress on "Ayurveda-2000"*, Chennai, TN, India, p. 217-218, January 28-30, 2000
13. Girija Kuttan. Use of *Withania somnifera* dunal as an adjuvant during radiation therapy, *Indian Journal of Experimental Biology* 1996; 34: 854-856
14. Kulkarni Anagha. A Ray of Hope for Cancer Patient, *Proceedings of International Seminar on Holistic Management of Cancer (Ayurveda Education Series no. 67)*, p. 5-11, 1998
15. Srinivasan S, Ranga RS, Burikhanov R, Han SS, Chendil D. Par-4-dependent apoptosis by the dietary compound Withaferin A in prostate cancer cells, *Cancer Res.* 2007; 67(1):246-53

Source of support: Nil, Conflict of interest: None Declared