



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

9 July 2013
EMA/HMPC/733313/2012
Committee on Herbal Medicinal Products (HMPC)

List of references supporting the assessment of *Withania somnifera* (L.) Dunal, radix

Final

The Agency acknowledges that copies of the underlying works used to produce this monograph were provided for research only with exclusion of any commercial purpose

Aalinkeel R, Hu Z, Nair BB, Sykes DE, Reynolds JL, Mahajan SD, et al. 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* 2010, 7:177-87

Alam N, Hossain M, Khalil MI, Moniruzzaman M, Sulaiman SA, Gan SH. High catechin concentrations detected in *Withania somnifera* (ashwagandha) by high performance liquid chromatography analysis. *BMC Complement Altern Med* 2011, 11:65

Andrade C, Aswath A, Chaturvedi SK, Srinivasa M, Raguram R. A double-blind, placebo-controlled evaluation of the anxiolytic efficacy of an ethanolic extract of *Withania somnifera*. *Indian J Psychiatry* 2000, 42(3):295-301

Anwer T, Sharma M, Pillai KK, Iqbal M. Effect of *Withania somnifera* on insulin sensitivity in non-insulin-dependent diabetes mellitus rats. *Basic Clin Pharmacol Toxicol* 2008, 102(6):498-503

Bhattacharya SK, Muruganandam AV. Adaptogenic activity of *Withania somnifera*: an experimental study using a rat model of chronic stress. *Pharmacol Biochem Behav* 2003, 75(3):547-55

Bhattacharya SK, Satyan KS, Ghosal S. Antioxidant activity of glycowithanolides from *Withania somnifera*. *Indian J Exp Biol* 1997, 35(3):236-9

Chatterjee S, Srivastava S, Khalid A, Singh N, Sangwan RS, Sidhu OP, et al. Comprehensive metabolic fingerprinting of *Withania somnifera* leaf and root extracts. *Phytochemistry* 2010, 71(10):1085-94

Chaurasiya ND, Uniyal GC, Lal P, Misra L, Sangwan NS, Tuli R, et al. Analysis of withanolides in root and leaf of *Withania somnifera* by HPLC with photodiode array and evaporative light scattering detection. *Phytochem Anal* 2008, 19(2):148-54

Chen LX, He H, Qiu F. Natural withanolides: an overview. *Nat Prod Rep* 2011, 28(4):705-40



- Chopra A, Lavin P, Patwardhan B, Chitre D. A 32-week randomized, placebo-controlled clinical evaluation of RA-11, an Ayurvedic drug, on osteoarthritis of the knees. *J Clin Rheumatol* 2004 Oct, 10(5):236-45
- Chopra A, Saluja M, Tillu G, Venugopalan A, Narsimulu G, Sarmukaddam S, et al. Evaluating higher doses of Shunthi - Guduchi formulations for safety in treatment of osteoarthritis knees: A Government of India NMITLI arthritis project. *J Ayurveda Integr Med* 2012 Jan, 3(1):38-44
- Choudhary MI, Yousuf S, Nawaz SA, Ahmed S, Attaur R. Cholinesterase inhibiting withanolides from *Withania somnifera*. *Chem Pharm Bull* 2004, 52(11):1358-61
- Cooley K, Szczurko O, Perri D, Mills EJ, Bernhardt B, Zhou Q, et al. Naturopathic care for anxiety: a randomized controlled trial ISRCTN78958974. *PLoS One* 2009, 4(8):e6628
- Ganzera M, Choudhary MI, Khan IA. Quantitative HPLC analysis of withanolides in *Withania somnifera*. *Fitoterapia* 2003, 74(1-2):68-76
- Gautam M, Diwanay SS, Gairola S, Shinde YS, Jadhav SS, Patwardhan BK. Immune response modulation to DPT vaccine by aqueous extract of *Withania somnifera* in experimental system. *Int Immunopharmacol* 2004, 4(6):841-9
- Ghosh M. Purification of a lectin-like antifungal protein from the medicinal herb, *Withania somnifera*. *Fitoterapia* 2009, 80(2):91-5
- Grover A, Shandilya A, Punetha A, Bisaria VS, Sundar D. Inhibition of the NEMO/IKKbeta association complex formation, a novel mechanism associated with the NF-kappaB activation suppression by *Withania somnifera*'s key metabolite withaferin A. *BMC Genomics* 2010, 11 Suppl 4:S25
- Gupta GL, Rana AC. Protective effect of *Withania somnifera* Dunal root extract against protracted social isolation induced behavior in rats. *Indian J Physiol Pharmacol* 2007 Oct-Dec, 51(4):345-53
- Gupta GL, Rana AC. Effect of *Withania somnifera* Dunal in ethanol-induced anxiolysis and withdrawal anxiety in rats. *Indian J Exp Biol* 2008, 46(6):470-5
- Harikrishnan R, Balasundaram C, Jawahar S, Heo MS. Immunomodulatory effect of *Withania somnifera* supplementation diet in the giant freshwater prawn *Macrobrachium rosenbergii* (de Man) against *Aeromonas hydrophila*. *Fish Shellfish Immunol* 2012, 32(1):94-100
- He QP, Ma L, Luo JY, He FY, Lou LG, Hu LH. Cytotoxic withanolides from *Physalis angulata* L. *Chem Biodivers* 2007, 4(3):443-9
- Hemalatha S, Wahi AK, Singh PN, Chansouria JP. Hypoglycemic activity of *Withania coagulans* Dunal in streptozotocin induced diabetic rats. *J Ethnopharmacol* 2004, 93(2-3):261-4
- Hosny Mansour H, Farouk Hafez H. Protective effect of *Withania somnifera* against radiation-induced hepatotoxicity in rats. *Ecotoxicol Environ Saf* 2012, 80:14-9
- Iuvone T, Esposito G, Capasso F, Izzo AA. Induction of nitric oxide synthase expression by *Withania somnifera* in macrophages. *Life Sci* 2003, 72(14):1617-25
- Jain S, Shukla SD, Sharma K, Bhatnagar M. Neuroprotective effects of *Withania somnifera* Dunn. in hippocampal sub-regions of female albino rat. *Phytother Res* 2001, 15(6):544-8
- Jatwa R, Kar A. Amelioration of metformin-induced hypothyroidism by *Withania somnifera* and *Bauhinia purpurea* extracts in Type 2 diabetic mice. *Phytother Res* 2009, 23(8):1140-5
- Jayaprakasam B, Padmanabhan K, Nair MG. Withanamides in *Withania somnifera* fruit protect PC-12 cells from beta-amyloid responsible for Alzheimer's disease. *Phytother Res* 2010, 24(6):859-63

- Jayaprakasam B, Zhang Y, Seeram NP, Nair MG. Growth inhibition of human tumor cell lines by withanolides from *Withania somnifera* leaves. *Life Sci* 2003, 74(1):125-32
- Kasture S, Vinci S, Ibba F, Puddu A, Marongiu M, Murali B, et al. *Withania somnifera* prevents morphine withdrawal-induced decrease in spine density in nucleus accumbens shell of rats: a confocal laser scanning microscopy study. *Neurotox Res* 2009, 16(4):343-55
- Kataria H, Shah N, Kaul SC, Wadhwa R, Kaur G. Water extract of ashwagandha leaves limits proliferation and migration, and induces differentiation in glioma cells. *Evid Based Complement Alternat Med* 2011, 267614
- Kataria H, Wadhwa R, Kaul SC, Kaur G. Water extract from the leaves of *Withania somnifera* protect RA differentiated C6 and IMR-32 cells against glutamate-induced excitotoxicity. *PLoS One* 2012, 7(5):e37080
- Katz M, Levine AA, Kol-Degani H, Kav-Venaki L. A compound herbal preparation (CHP) in the treatment of children with ADHD: a randomized controlled trial. *J Atten Disord* 2010, 14(3):281-91
- Kaur K, Rani G, Widodo N, Nagpal A, Taira K, Kaul SC, et al. Evaluation of the anti-proliferative and anti-oxidative activities of leaf extract from in vivo and in vitro raised ashwagandha. *Food Chem Toxicol* 2004, 42(12):2015-20
- Kaurav BP, Wanjari MM, Chandekar A, Chauhan NS, Upmanyu N. Influence of *Withania somnifera* on obsessive compulsive disorder in mice. *Asian Pac J Trop Med* 2012, 5(5):380-4
- Khan B, Ahmad SF, Bani S, Kaul A, Suri KA, Satti NK, et al. Augmentation and proliferation of T lymphocytes and Th-1 cytokines by *Withania somnifera* in stressed mice. *Int Immunopharmacol* 2006, 6(9):1394-403
- Khan S, Malik F, Suri KA, Singh J. Molecular insight into the immune up-regulatory properties of the leaf extract of ashwagandha and identification of Th1 immunostimulatory chemical entity. *Vaccine* 2009, 27(43):6080-7
- Konar A, Shah N, Singh R, Saxena N, Kaul SC, Wadhwa R, et al. Protective role of ashwagandha leaf extract and its component withanone on scopolamine-induced changes in the brain and brain-derived cells. *PLoS One* 2011, 6(11):e27265
- Krishnamurthy YL, Shashikala J. Inhibition of aflatoxin B production of *Aspergillus flavus*, isolated from soybean seeds by certain natural plant products. *Lett Appl Microbiol* 2006, 43(5):469-74
- Kuboyama T, Tohda C, Komatsu K. Neuritic regeneration and synaptic reconstruction induced by withanolide A. *Br J Pharmacol* 2005, 144(7):961-71
- Kuboyama T, Tohda C, Komatsu K. Withanoside IV and its active metabolite, sominone, attenuate Abeta(25-35)-induced neurodegeneration. *Eur J Neurosci* 2006, 23(6):1417-26
- Kulkarni SK, Akula KK, Dhir A. Effect of *Withania somnifera* Dunal root extract against pentylenetetrazol seizure threshold in mice: possible involvement of GABAergic system. *Indian J Exp Biol* 2008, 46(6):465-9
- Kulkarni SK, Dhir A. *Withania somnifera*: an Indian ginseng. *Prog Neuropsychopharmacol Biol Psychiatry* 2008, 32(5):1093-105
- Kulkarni SK, Ninan I. Inhibition of morphine tolerance and dependence by *Withania somnifera* in mice. *J Ethnopharmacol* 1997, 57(3):213-7

- Kumar A, Kalonia H. Effect of *Withania somnifera* on Sleep-Wake Cycle in Sleep-Disturbed Rats: Possible GABAergic Mechanism. *Indian J Pharm Sci* 2008, 70(6):806-10
- Kumar S, Harris RJ, Seal CJ, Okello EJ. An aqueous extract of *Withania somnifera* root inhibits amyloid beta fibril formation in vitro. *Phytother Res* 2012, 26(1):113-7
- Kumar S, Seal CJ, Howes MJ, Kite GC, Okello EJ. In vitro protective effects of *Withania somnifera* (L.) Dunal root extract against hydrogen peroxide and beta-amyloid(1-42)-induced cytotoxicity in differentiated PC12 cells. *Phytother Res* 2010, 24(10):1567-74
- Kuroyanagi M, Murata M, Nakane T, Shiota O, Sekita S, Fuchino H, et al. Leishmanicidal active withanolides from a pakistani medicinal plant, *Withania coagulans*. *Chem Pharm Bull* 2012, 60(7):892-7
- Kushwaha S, Roy S, Maity R, Mallick A, Soni VK, Singh PK, et al. Chemotypical variations in *Withania somnifera* lead to differentially modulated immune response in BALB/c mice. *Vaccine* 2012, 30(6):1083-93
- Kushwaha S, Soni VK, Singh PK, Bano N, Kumar A, Sangwan RS, et al. *Withania somnifera* chemotypes NMITLI 101R, NMITLI 118R, NMITLI 128R and withaferin A protect *Mastomys coucha* from *Brugia malayi* infection. *Parasite Immunol* 2012, 34(4):199-209
- Lee J, Hahm ER, Singh SV. Withaferin A inhibits activation of signal transducer and activator of transcription 3 in human breast cancer cells. *Carcinogenesis* 2010, 31(11):1991-8
- Lee W, Kim TH, Ku SK, Min KJ, Lee HS, Kwon TK, et al. Barrier protective effects of withaferin A in HMGB1-induced inflammatory responses in both cellular and animal models. *Toxicol Appl Pharmacol* 2012, 262(1):91-8
- Leyon PV, Kuttan G. Effect of *Withania somnifera* on B16F-10 melanoma induced metastasis in mice. *Phytother Res* 2004, 18(2):118-22
- Lizano S, Domont G, Perales J. Natural phospholipase A(2) myotoxin inhibitor proteins from snakes, mammals and plants. *Toxicon* 2003, 42(8):963-77
- Llanos GG, Araujo LM, Jimenez IA, Moujir LM, Bazzocchi IL. Withaferin A-related steroids from *Withania aristata* exhibit potent antiproliferative activity by inducing apoptosis in human tumor cells. *Eur J Med Chem* 2012, 54:499-511
- Llanos GG, Araujo LM, Jimenez IA, Moujir LM, Vazquez JT, Bazzocchi IL. Withanolides from *Withania aristata* and their cytotoxic activity. *Steroids* 2010, 75(12):974-81
- Machiah DK, Girish KS, Gowda TV. A glycoprotein from a folk medicinal plant, *Withania somnifera*, inhibits hyaluronidase activity of snake venoms. *Comp Biochem Physiol C Toxicol Pharmacol* 2006, 143(2):158-61
- Machiah DK, Gowda TV. Purification of a post-synaptic neurotoxic phospholipase A2 from *Naja naja* venom and its inhibition by a glycoprotein from *Withania somnifera*. *Biochimie* 2006, 88(6):701-10
- Madina BR, Sharma LK, Chaturvedi P, Sangwan RS, Tuli R. Purification and characterization of a novel glucosyltransferase specific to 27beta-hydroxy steroidal lactones from *Withania somnifera* and its role in stress responses. *Biochim Biophys Acta* 2007, 1774(9):1199-207
- Mahdi AA, Shukla KK, Ahmad MK, Rajender S, Shankhwar SN, Singh V, et al. *Withania somnifera* Improves Semen Quality in Stress-Related Male Fertility. *Evid Based Complement Alternat Med* 2011, Article ID 576962, 9 pages

Maitra R, Porter MA, Huang S, Gilmour BP. Inhibition of NFκB by the natural product Withaferin A in cellular models of Cystic Fibrosis inflammation. *J Inflamm* 2009, 6:15

Malik F, Kumar A, Bhushan S, Mondhe DM, Pal HC, Sharma R, et al. Immune modulation and apoptosis induction: Two sides of antitumoural activity of a standardised herbal formulation of *Withania somnifera*. *Eur J Cancer* 2009, 45(8):1494-509

Malik F, Singh J, Khajuria A, Suri KA, Satti NK, Singh S, et al. A standardized root extract of *Withania somnifera* and its major constituent withanolide-A elicit humoral and cell-mediated immune responses by up regulation of Th1-dominant polarization in BALB/c mice. *Life Sci* 2007, 80(16): 1525-38

Mamidi P, Thakar AB. Efficacy of ashwagandha (*Withania somnifera* Dunal. Linn.) in the management of psychogenic erectile dysfunction. *Ayu* 2011, 32(3):322-8

Mandal C, Dutta A, Mallick A, Chandra S, Misra L, Sangwan RS. Withaferin A induces apoptosis by activating p38 mitogen-activated protein kinase signaling cascade in leukemic cells of lymphoid and myeloid origin through mitochondrial death cascade. *Apoptosis* 2008, 13(12):1450-64

Martin-Herrera D, Abdala S, Benjumea D, Gutierrez-Luis J. Diuretic activity of some *Withania aristata* Ait. fractions. *J Ethnopharmacol* 2008, 117(3):496-9

Martin-Herrera D, Abdala S, Benjumea D, Perez-Paz P. Diuretic activity of *Withania aristata*: an endemic Canary Island species. *J Ethnopharmacol* 2007, 113(3):487-91

Mathur R, Gupta SK, Singh N, Mathur S, Kochupillai V, Velpandian T. Evaluation of the effect of *Withania somnifera* root extracts on cell cycle and angiogenesis. *J Ethnopharmacol* 2006, 105(3):336-41

Matsuda H, Murakami T, Kishi A, Yoshikawa M. Structures of withanosides I, II, III, IV, V, VI, and VII, new withanolide glycosides, from the roots of Indian *Withania somnifera* Dunal. and inhibitory activity for tachyphylaxis to clonidine in isolated guinea-pig ileum. *Bioorg Med Chem* 2001, 9(6):1499-507

Maurya R. Chemistry and pharmacology of *Withania coagulans*: an Ayurvedic remedy. *J Pharm Pharmacol* 2010, 62(2):153-60

Maurya R, Akanksha, Jayendra, Singh AB, Srivastava AK. Coagulanolide, a withanolide from *Withania coagulans* fruits and antihyperglycemic activity. *Bioorg Med Chem Lett* 2008, 18(24):6534-7

Minhas U, Minz R, Bhatnagar A. Prophylactic effect of *Withania somnifera* on inflammation in a non-autoimmune prone murine model of lupus. *Drug Discov Ther* 2011, 5(4):195-201

Mirjalili MH, Moyano E, Bonfill M, Cusido RM, Palazon J. Steroidal lactones from *Withania somnifera*, an ancient plant for novel medicine. *Molecules* 2009, 14(7):2373-93

Mirzajani F, Ghassempour A, Jalali-Heravi M, Mirjalili MH. Optimisation of a microwave-assisted method for extracting withaferin A from *Withania somnifera* Dunal using central composite design. *Phytochem Anal* 2010, 21(6):544-9

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

Misra DS, Maiti R, Ghosh D. Protection of swimming-induced oxidative stress in some vital organs by the treatment of composite extract of *Withania somnifera*, *Ocimum sanctum* and *Zingiber officinalis* in male rat. *Afr J Tradit Complement Altern Med* 2009, 6(4):534-43

Misra L, Lal P, Chaurasia ND, Sangwan RS, Sinha S, Tuli R. Selective reactivity of 2-mercaptoethanol with 5β,6β-epoxide in steroids from *Withania somnifera*. *Steroids* 2008, 73(3):245-51

- Misra L, Lal P, Sangwan RS, Sangwan NS, Uniyal GC, Tuli R. Unusually sulfated and oxygenated steroids from *Withania somnifera*. *Phytochemistry* 2005, 66(23):2702-7
- Misra L, Mishra P, Pandey A, Sangwan RS, Sangwan NS, Tuli R. Withanolides from *Withania somnifera* roots. *Phytochemistry* 2008, 69(4):1000-4
- Mohanty I, Arya DS, Dinda A, Talwar KK, Joshi S, Gupta SK. Mechanisms of cardioprotective effect of *Withania somnifera* in experimentally induced myocardial infarction. *Basic Clin Pharmacol Toxicol* 2004, 94(4):184-90
- Mohanty IR, Arya DS, Gupta SK. *Withania somnifera* provides cardioprotection and attenuates ischemia-reperfusion induced apoptosis. *Clin Nutr* 2008, 27(4):635-42
- Mondal S, Bhattacharya K, Mallick A, Sangwan R, Mandal C. Bak compensated for Bax in p53-null cells to release cytochrome c for the initiation of mitochondrial signaling during Withanolide D-induced apoptosis. *PLoS One* 2012, 7(3):e34277
- Mondal S, Mandal C, Sangwan R, Chandra S. Withanolide D induces apoptosis in leukemia by targeting the activation of neutral sphingomyelinase-ceramide cascade mediated by synergistic activation of c-Jun N-terminal kinase and p38 mitogen-activated protein kinase. *Mol Cancer* 2010, 9:239
- Monograph. *Withania somnifera*. *Altern Med Rev* 2004, 9(2):211-4
- Munagala R, Kausar H, Munjal C, Gupta RC. Withaferin A induces p53-dependent apoptosis by repression of HPV oncogenes and upregulation of tumor suppressor proteins in human cervical cancer cells. *Carcinogenesis* 2011, 32(11):1697-705
- Murthy HN, Dijkstra C, Anthony P, White DA, Davey MR, Power JB, et al. Establishment of *Withania somnifera* hairy root cultures for the production of withanolide A. *J Integr Plant Biol* 2008, 50(8):975-81
- Musharraf SG, Ali A, Ali RA, Yousuf S, Rahman AU, Choudhary MI. Analysis and development of structure-fragmentation relationships in withanolides using an electrospray ionization quadrupole time-of-flight tandem mass spectrometry hybrid instrument. *Rapid Commun Mass Spectrom* 2011, 25(1):104-14
- Nagareddy PR, Lakshmana M. *Withania somnifera* improves bone calcification in calcium-deficient ovariectomized rats. *J Pharm Pharmacol* 2006, 58(4):513-9
- Nagella P, Murthy HN. Establishment of cell suspension cultures of *Withania somnifera* for the production of withanolide A. *Bioresour Technol* 2010, 101(17):6735-9
- Naidu PS, Singh A, Kulkarni SK. Effect of *Withania somnifera* root extract on reserpine-induced orofacial dyskinesia and cognitive dysfunction. *Phytother Res* 2006, 20(2):140-6
- Oza VP, Trivedi SD, Parmar PP, Subramanian RB. *Withania somnifera* (ashwagandha): a novel source of L-asparaginase. *J Integr Plant Biol* 2009, 51(2):201-6
- Padmavathi B, Rath PC, Rao AR, Singh RP. Roots of *Withania somnifera* inhibit forestomach and skin carcinogenesis in mice. *Evid Based Complement Alternat Med* 2005, 2(1):99-105
- Panda S, Kar A. *Withania somnifera* and *Bauhinia purpurea* in the regulation of circulating thyroid hormone concentrations in female mice. *J Ethnopharmacol* 1999, 67(2):233-9
- Panjamurthy K, Manoharan S, Menon VP, Nirmal MR, Senthil N. Protective role of withaferin-A on 7,12-dimethylbenz(a)anthracene-induced genotoxicity in bone marrow of Syrian golden hamsters. *J Biochem Mol Toxicol* 2008, 22(4):251-8

- Parihar MS, Chaudhary M, Shetty R, Hemnani T. Susceptibility of hippocampus and cerebral cortex to oxidative damage in streptozotocin treated mice: prevention by extracts of *Withania somnifera* and *Aloe vera*. *J Clin Neurosci* 2004, 11(4):397-402
- Pawar P, Gilda S, Sharma S, Jagtap S, Paradkar A, Mahadik K, et al. Rectal gel application of *Withania somnifera* root extract expounds anti-inflammatory and muco-restorative activity in TNBS-induced inflammatory bowel disease. *BMC Complement Altern Med* 2011, 11: 34
- Prakash J, Gupta SK, Kochupillai V, Singh N, Gupta YK, Joshi S. Chemopreventive activity of *Withania somnifera* in experimentally induced fibrosarcoma tumours in Swiss albino mice. *Phytother Res* 2001, 15(3): 240-4
- Pramanik SS, Sur TK, Debnath PK, Bhattacharyya D. Effect of *Pueraria tuberosa* tuber extract on chronic foot shock stress in Wistar rats. *Nepal Med Coll J*. 2010, 12(4):234-8
- Prashanth D, Padmaja R, Samiulla DS. Effect of certain plant extracts on alpha-amylase activity. *Fitoterapia* 2001, 72(2):179-81
- Pretorius E, Oberholzer HM, Becker PJ. Comparing the cytotoxic potential of *Withania somnifera* water and methanol extracts. *Afr J Tradit Complement Altern Med* 2009, 6(3):275-80
- Raja Sankar S, Manivasagam T, Sankar V, Prakash S, Muthusamy R, Krishnamurti A, et al. *Withania somnifera* root extract improves catecholamines and physiological abnormalities seen in a Parkinson's disease model mouse. *J Ethnopharmacol* 2009, 125(3):369-73
- Rajasankar S, Manivasagam T, Surendran S. Ashwagandha leaf extract: a potential agent in treating oxidative damage and physiological abnormalities seen in a mouse model of Parkinson's disease. *Neurosci Lett* 2009, 454(1):11-5
- Rani G, Kaur K, Wadhwa R, Kaul SC, Nagpal A. Evaluation of the anti-genotoxicity of leaf extract of ashwagandha. *Food Chem Toxicol* 2005, 43(1):95-8
- Rasool M, Varalakshmi P. Suppressive effect of *Withania somnifera* root powder on experimental gouty arthritis: An in vivo and in vitro study. *Chem Biol Interact* 2006, 164(3):174-80
- Rasool M, Varalakshmi P. Immunomodulatory role of *Withania somnifera* root powder on experimental induced inflammation: An in vivo and in vitro study. *Vascul Pharmacol* 2006, 44(6):406-10
- Rasool M, Varalakshmi P. Protective effect of *Withania somnifera* root powder in relation to lipid peroxidation, antioxidant status, glycoproteins and bone collagen on adjuvant-induced arthritis in rats. *Fundam Clin Pharmacol*. 2007, 21(2):157-64
- Sandhu JS, Shah B, Shenoy S, Chauhan S, Lavekar GS, Padhi MM. Effects of *Withania somnifera* (ashwagandha) and *Terminalia arjuna* (arjuna) on physical performance and cardiorespiratory endurance in healthy young adults. *Int J Ayurveda Res* 2010, 1(3):144-9
- Sangwan RS, Chaurasiya ND, Lal P, Misra L, Uniyal GC, Tuli R, et al. Withanolide A biogenesis in in vitro shoot cultures of ashwagandha (*Withania somnifera* Dunal), a main medicinal plant in Ayurveda. *Chem Pharm Bull (Tokyo)* 2007, 55(9):1371-5
- Sangwan RS, Das Chaurasiya N, Lal P, Misra L, Tuli R, Sangwan NS. Withanolide A is inherently de novo biosynthesized in roots of the medicinal plant ashwagandha (*Withania somnifera*). *Physiol Plant* 2008, 133(2):278-87
- Sanyal B, Chatterjee S, Variyar PS, Sharma A. Application of EPR spectroscopy to identify irradiated Indian medicinal plant products. *J Food Sci* 2012, 77(6):C710-8

- Saxena B. Anti-hyperlipidemic activity of *Withania coagulans* in streptozotocin-induced diabetes: A potent anti-atherosclerotic agent. *Drug Discov Ther* 2010, 4(5):334-40
- Scartezzini P, Speroni E. Review on some plants of Indian traditional medicine with antioxidant activity. *J Ethnopharmacol* 2000, 71(1-2):23-43
- Schliebs R, Liebmann A, Bhattacharya SK, Kumar A, Ghosal S, Bigl V. Systemic administration of defined extracts from *Withania somnifera* (Indian Ginseng) and Shilajit differentially affects cholinergic but not glutamatergic and GABAergic markers in rat brain. *Neurochem Int* 1997, 30(2):181-90
- Sehgal N, Gupta A, Valli RK, Joshi SD, Mills JT, Hamel E, et al. *Withania somnifera* reverses Alzheimer's disease pathology by enhancing low-density lipoprotein receptor-related protein in liver. *Proc Natl Acad Sci U S A* 2012, 109(9):3510-5
- Singh N, Bhalla M, de Jager P, Gilca M. An overview on ashwagandha: a Rasayana (rejuvenator) of Ayurveda. *Afr J Tradit Complement Altern Med* 2011, 8(5 Suppl):208-13
- Sumantran VN, Kulkarni A, Boddul S, Chinchwade T, Koppikar SJ, Harsulkar A, et al. Chondroprotective potential of root extracts of *Withania somnifera* in osteoarthritis. *J Biosci* 2007, 32(2):299-307
- Vetvicka V, Vetvickova J. Immune enhancing effects of WB365, a novel combination of ashwagandha (*Withania somnifera*) and maitake (*Grifola frondosa*) extracts. *N Am J Med Sci* 2011, 3(7):320-4
- Winters M. Ancient medicine, modern use: *Withania somnifera* and its potential role in integrative oncology. *Altern Med Rev* 2006, 11(4):269-77
- Yadav CS, Kumar V, Suke SG, Ahmed RS, Mediratta PK, Banerjee BD. Propoxur-induced acetylcholine esterase inhibition and impairment of cognitive function: attenuation by *Withania somnifera*. *Indian J Biochem Biophys* 2010, 47(2):117-20
- Zhao J, Nakamura N, Hattori M, Kuboyama T, Tohda C, Komatsu K. Withanolide derivatives from the roots of *Withania somnifera* and their neurite outgrowth activities. *Chem Pharm Bull* 2002, 50(6):760-5