Review Article

Withania somnifera (Ashwagandha): A wonder herb with multiple medicinal properties

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https://doi.org/10.31024/ajpp.2018.4.2.5

Received: 18 February 2018 Revised: 5 March 2018 Accepted: 20 March 2018

Abstract

A flurry of new research from around the world on Ashwagandha (*Withania somnifera*) is proving the medicinal effects of this ancient Ayurvedic herbal remedy are more than just anecdotal. The past few years have been banner years for Ashwagandha research. Ashwagandha helps in improving immune system. It is a potent adaptogen and aphrodisiac herb used in impotency, cancer, frequent miscarriage, uterine weakness, infertility, asthma, anemia, cancer, arthritis (osteoarthritis, gout, rheumatoid arthritis), anxiety, stress, depression, ADHD (Attention deficit hyperactivity disorder), cerebellar ataxia, diabetes, high cholesterol, infertility, Parkinson's disease, fibromyalgia etc. Plants contains a myriad of constituents, including withanolides named withanolide A, withanolide B, withaferin A, and withanone, along with 12-deoxy withastramonolide, withanoside V, withanoside IV. Other complex molecules include trihydroxy-oxowitha-trienolide compounds. These compounds have been found to act synergistically to enable changes in gene expression within the cell – producing a variety of medicinal effects in addition to antioxidant effects. While some research is striving to isolate and extract that one constituent to be synthetically produced in a lab to make a patented drug, the research above and others over the past year testify that this Ayurvedic power house herb is best used in its whole or whole extract form.

***Keywords*:** Ashwagandha (*Withania somnifera),* withanolides, medicinal effects, immune system

Introduction

Ashwagandha (*Withania somnifera* Dunal.) belongs to the family solanaceae having chromosome number 2n = 48. *Withania* also known as Indian ginseng is an important medicinal plant, which is being cultivated for centuries in India. It is one of the most precious shrub and hold important places in Indian traditional systems of medicine, Ayurveda and Unani. Root and herb of ashwagandha are used as tonic, hypnotonic, sedative and diuretic (Jain and Defillip, 1991), has anticancer (Leyon and Kuttan, 2004), anti-stress, anti-inflammatory, anti-tumor anti-oxidative properties and used to treat various diseases associated with nerve tissue damage, heart disease, atherosclerosis, cancer, Aids and aging because of its strong anti-oxidative property. It is an ingredient in many formulations prescribed for a variety of musculoskeletal conditions (e.g., arthritis, rheumatism), and as a general tonic to increase energy, improve overall health and longevity, and prevent disease in athletes (Bhosale and More, 2014).

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Distribution of plant

Ashwagandha, is erect, evergreen, branched shrub, attains a height of 30-60 cm. It grows well in dry and arid soil (Patra et al., 2004) with preference to acid soil (Obidoska and Sadowska, 2003) in subtropicals and semiarid regions. In India it grows in Uttar Pradesh, Maharastra, Madhya Pradesh, Haryana, Rajasthan and few regions of Himanchal Pradesh.

Roots

Roots contain alkaloids, amino acids, steroids, volatile oil, starch, reducing sugars, glycosides, hentriacontane, dulcitol, withaniol. The total alkaloidal content of the Indian roots has been reported to vary between 0.13 and 0.31 percent, though much higher yields (up to 4.3%) have been recorded elsewhere (Anonymous, 2007). Basic alkaloids include cuscohygrine, anahygrine, tropine, pseudotropine, anaferine, isopelletierine, withananine, withananinine, pseudo-withanine, somnine, somniferine, somniferinine. Other alkaloids include withanine, withasomnine, and

visamine .The free amino acids identified in the root include aspartic acid, glycine, tyrosine, alanine, proline, tryptophan, glutamic acid, and cystine (Khare, 2007).

Leaves

The leaves of the plant (Indian chemotype) are reported to contain 12 withanolides, 5 unidentified alkaloids (yield, 0.09%), many free amino acids, chlorogenic acid, glycosides, glucose, condensed tannins, and flavonoids (Khare, 2007). Withaferin A, a steroidal lactone is the most important withanolide isolated from the extract of the leaves and dried roots of *Withania somnifera.*

Fruits

The green berries contain amino acids, a proteolytic enzyme, condensed tannins, and flavonoids. They contain a high proportion of free amino acids which include proline, valine, tyrosine, alanine, glycine, hydroxyproline, aspartic acid, glutamic acid, cystine and cysteine. The presence of a proteolytic enzyme, chamase, in the berries may be responsible for the high content of the amino acid.

Other Parts

The tender shoots are rich in crude protein, calcium and phosphorous, and are not fibrous. They are reported to contain scopoletin. The stem of the plant contains condensed tannins and flavonoids. The bark contains a number of free amino acids (Anonymous, 1982).

Figure 1. *Withania somnifera* plant

Varieties

Chetak (Naguri withania variety)

Variety CIMAP Chetak is a semi vigorous, medium green small leaves size and whitish green stem, was found to be highly promising for high dry root yield (11.77 ql/ha v/s check 5.45 ql/ha) with high total Withanolide content (0.40 v/s 0.20% in check). The fresh and dry leaf yield was also high (1.722 and 0.453 ql/ha v/s 0.872 and 0.147 ql/ha in check) with high withaferine content 1.223 v/s 0.788 % in the check.

Pratap

Variety CIMAP Pratap is a highly vigorous, dark green medium size leaves and dark green stem, highly promising for high dry root yield (34.95 ql/ha v/s Poshita 21.99 ql/ha) with high total Withanolide content (0.31 v/s 0.25% in Poshita). The fresh and dry leaf yield was also high (5.39 and 0.87 ql/ha v/s 2.83 and 0.50 ql/ha in Poshita) with high witheferin content in dry leaves 0.720 v/s 0.528 % in the check variety Poshita.

Poshita

Poshita is medium tall, semi broad, medium dark colour leaf with red coloured berries. The estimated dry root yield was 14q/ha v/s check which is 8q/ha. Total withanolides (kg/h) is 0.25. This variety is very popular in South India specially Anantnag.

Nmitli 118

New chemotypes identified under a NMITLI project effort was made to collect the Ashwagandha germplasm, which resulted into collection of 150 independent accessions from various geographical locations, with many of them having contrasting chemotypes. Efforts are underway to explore the pharmacological activities of selected chemotypes and individual molecule to identify the best chemotype for adaptogenic activity. Other Varieties are as Jawahar, WS 20 and tall Ashwagandha.

Cultivation of *Withania somnifera*

It is cultivated over an area of 10,780 ha with a production of 8429 tonnes in India. While the annual demand increased from 7028 tonnes (2001-02) to 9127 tonnes (2004-05) necessitating the increase in its cultivation and higher production (http://nmpb.nic.in). It is also well known in the traditional system of medicines of several countries for its sedative, hypnotic and antiseptic properties and occasionally the leaves and seeds are also used for medicinal purpose, root is economic part of the plant. The roots are used for curing rheumatism, dyspepsia, skin diseases, bronchitis, ulcers, sexual debility and snakebite. *W. somnifera* grows well in sandy loam or light red soil, having pH 7.5-8.0 with good drainage. It can be cultivated between 600-1200 m altitudes. The semi-tropical areas receiving 500-750 mm rainfall are suitable for cultivation of this rained crop. The crop requires dry season during its growing period. Temperature between 200C to 350C is most suitable for cultivation. Late winter rains are conducive for the proper development of the plant roots. The crop can be sown either by broad casting or in lines. Live to line method is preferred as it increases root production and also helps in performing intercultural practices properly. The seeds are usually sown about 1-3 cm deep in June- July in nursery. A light shower after shower after sowing ensures good germination. About 500-750 gm seeds are sufficient for 1 ha field. Seeds can be treated, with Thiram or Indofil or Dithane medicinal plants

-45 (@ 3 gm/kg seed), before sowing to protect seedlings from seed borne diseases .The seedling after 25-35 days after sowing can be transplanted in the field marinating 60 x 60 cm. Spacing between the plants & the rows. It may be noted that since 'Ashwagandha' is a rainy season Kharif crop, the time of sowing is decided by date of arrival of monsoon in that area. The seeds sown by broadcasting or in the line in furrows should be thinned out by hand at 25-30 days after sowing to maintain a plant population of about 30-60 plants per square meter (about 3.5 to 6 lakh plants/hectare). The plant density to be used may depend on the nature and fertility of the soil. On the marginal land the population is kept high. The medicinal plants have to be grown without chemical fertilizers and use of pesticides. Organic manures like, Farm Yard Manure (FYM), Vermi-Compost and Green Manure etc may be used as per requirement of the species (Raja et al., 2013). Light shower after transplantation ensures establishment of seedlings. There is no need of irrigation if rainfall is at regular intervals. Excessive rainfall/water is harmful to the crop. Life saving irrigations may be applied, if required. The plants start flowering and bearing fruits from December onwards. The crop is ready for harvest in January-March at 150 to 180 days after sowing. The maturity of crop is judged by drying out of leaves and yellow red berries. The entire plant is uprooted for roots which are separated from aerial parts by cutting the stem 1-2 cm above the crown. The roots are then either cut transversely into small pieces (7 to 10 cm) or dried as it is in the sun. About 650-800 kg roots can be obtained from 1 ha on drying it comes to 350-435 kg (Shrivastava et al., 2013). Berries are hand plucked separately. They are dried and crushed to take out the seeds. The dried roots, entire or transversely cut into smaller pieces, have to be further cleaned, trimmed and graded. The roots are beaten with a club which removes adhering soil and breaks off the thin, brittle lateral rootlets. Lateral branches, root crown and stem remains on roots are carefully trimmed with the help of knife. On an average yield from one hectare land under commercial cultivation is approx 3-5 quintals of dried roots and 50-75 kg seeds.

Micropropagation of *Withania somnifera*

Plant tissue culture has emerged as a potential tool and forms the backbone of plant biotechnology. Tissue culture techniques are widely applied for the improvement of field crops, forests, horticulture and plantation crops for increased agricultural and forestry production. This technique has been commercialized globally and contributed significantly towards the enhanced production of high quality planting material. Micropropagation is a complex multistep process and it is in effect the miniature version of conventional propagation which is carried out under aseptic conditions. The ease, by which plants can be micropropagated, varies from species to species. Mostly seeds, seedlings and juvenile plant parts are used as starting materials since they are easier to propagate. Tissue culture technique can play an important role in clonal propagation and qualitative improvement of this medicinally important plant. Direct regeneration of Ashwagandha plants from shoot buds and apical buds explants to regenerate *W. somnifera* plants have been explored.

The first step in any successful tissue culture programme is the selection of suitable explant followed by complete disinfecting. Disinfecting the surface generally involves sterilization with one or more disinfectants followed by washing. *Withania somnifera* nodal segments were collected and washed with teepol detergent for 15 minutes at slow speed on a magnetic stirrer and later washed thoroughly under running water for 2 hours. Surface sterilization was carried out with 0.1 % $HgCl_2$ for 10 minutes followed by washing thrice with double distilled water to remove the traces of $HgCl_2$. Sterilized explants were transferred aseptically to sterilized glass plate under laminar flow hood. The deduced method for multiplication of shoot induction was tried in five different chemotypes of *Withania somnifera*. These culture plates were finally kept in the culture growth room with temperature conditions 25± 1 °C, with a photoperiod of 16 hrs daylight and 8 hrs night break under the cool white fluorescent lightIn *Withania,* several procedures were available for inducing *in vitro* response using leaf explants (Baburaj et al., 1995). However, Furmanowa (2001) produced *in vitro Withania somnifera* plantlets from the shoot-tip of aseptically germinated seedlings. We used MS medium supplemented with different combinations of growth regulators for growth of *Withania* chemotypes. The highest percentage of plant regeneration was found in BAP supplemented medium. Ray and Jha (2001) grew shoot tips on MS media supplemented with BA (1.0 mg/l). Shoot induction was found to be 10.0 micro shoots per explant. The shoot bud regeneration frequency gradually increased up to (0.6 mg/l) of

BAP, with further increase in hormone concentration there was a sharp reduction in the number of shoots. Another protocol was developed for large scale propagation of *Withania somnifera* using seed as explants. The best callus production was observed in Murashige and Skoog (MS) medium supplemented with 1.0 µM Kn, 4.5 µM BAP, and 1.5 µM NAA within a 14 day dark period. Shoot initiation was observed in calli produced from shoot tips and nodal segments. The highest shoot multiplication was observed in calli from nodal segments cultured in the presence of 9.0 µM BAP and 1.0 µM IAA.

Propagation of *Withania somnifera* is primarily via seeds.

However, conventional propagation of this plant by seeds is not reliable and is inadequate to meet commercial demands because of the low viability of the stored seeds and low seed germination rates (Sabir et al. 2008). Therefore, a study was done to develop a high frequency direct regeneration system for *Withania somnifera* using leaf and explants for direct shoot regeneration. Direct regeneration of shoot buds was observed in MS basal medium supplemented with various concentrations of either benzyladenine (BA) or thidiazouron (TDZ) depending on the explant. Nodal explants formed multiple shoots both from pre-existing and *de novo* buds on Murashige and Skoog's medium (MS) containing 0.1–5.0 mg/l BA and a ring of *de novo* shoot buds on MS medium containing 0.2 and 0.3 mg/l TDZ. Internodal explants generates shoot buds on MS with 1.0 and 5.0 mg/l BA while the hypocotyl explants gave rise to multiple shoots only on MS with 0.5 mg/l BA. Callus cultures were initiated from nodal segments on Murashige and Skoog medium supplemented with 2, 4-D, BAP and Kinetin.

Pharmacological and Chemical view of *Withania*

W. somnifera and *W. coagualans* have shown diverse biological activities viz., cytotoxic, anti-inflammatory, anti-stress, antioxidant, anti-aging, diuretic, hypothyroid, immunomodulatory, anti-alzheimer's disease, antihyperglycemic, anti-hypercholesterolemic, antimicrobial, anti-feedent, cardiovascular, cell-differentiation-inducing activity, immunosuppressive and radio sensitizing activity, etc. (Kaur et al., 2013). Detailed bioassay guided phytochemical investigations have revealed that almost all these biological activities are due to the withanolides. Chemically, withanolides are steroidal lactones. The term withanolides is the composition of the "withan" from the genus Withania, and "olide" a chemical term for the lactone moiety. Withaferin A was the first withanolide isolated by Lavie (Lavie et al., 1965) from *W. somnifera*. Since then, more than 400 withanolides have been isolated from 58 solanaceous species belonging to 22 genera (Khodaei et al., 2012).

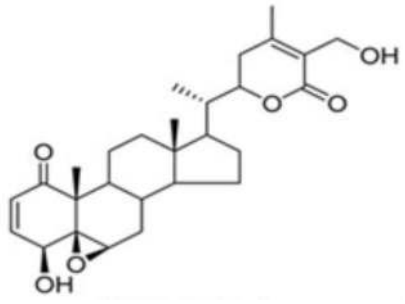

Figure 2. Structure of Withaferin A

Beside these two species (*W. somnifera* and *W. coagualans*), four other species viz., *W. adpressa*, *W. aristata*, *W. frutescens* and *W. obtusifolia* have also been investigated for the study of their phytochemical and biological aspects. But still these species are not well explored. For example, there are only two reports one on each of the antifungal (Askarne et al., 2012) and cytotoxic (Abdeljebbar et al., 2009*)* activity of *W. adpressa*. However, this antifungal activity is reported for the leaf of this plant but other parts have to be investigated. Further, no chemical constituents have been identified which are responsible for this antifungal activity. Similarly, three cytotoxic withanolides, 14α, 15α, 17β, 20β-tetrahydroxy-1-oxo-(*22R*)-witha-2,5,24 trienolide , withanolide F and withanolide J are isolated from the dichloromethane (CH_2Cl_2) fraction of the methanolic extract of the *W. adpressa* leaf. But no work has been carried out on the phytochemical investigation of the other parts of this plant as well as on other fractions of the methanolic extract of the leaves. Hence, the other parts viz., stem, root, fruits and flower and other fractions viz., *n*-hexane, ethylacetate, *n*-butanol of the methanolic extract of the leaf, require chemical investigation of the compounds responsible for the cytotoxicity and other biological activities.

Certainly, it will be great efforts in the area of drug discovery from the plants, which will nurther improve the economical significance of *W. adpressa* as well as of the genus *Withania*. Similarly, several withanolides have been isolated from the dichloromethane extract *W. aristata* leaves too. These withanolides have shown significant antimicrobial (Araujo et al., 2008), diuretic (Benjumea et al., 2009) and anti-proliferative cytotoxic (Llanos et al., 2012) activities. Similar to *W. adpressa*, other parts and different extracts of *W. aristata* leaves also require chemical and biological investigations for other biological activities and the novel withanolides responsible for these bioactivities.

Withania frutescens (L.) Pauquy is another species of this genus. The leaf extract of this plant showed significant protective and curative action against CCl_4-induced hepatotoxicity (Montilla et al., 1990), but so for no hepatoprotective chemical constituent has been isolated from this extract. Another reports demonstrated the isolation of some cytotoxic withanolides from the dichloromethane extract of *W. frutescens* leaves (Bouzidi et al., 2013). However, other plant parts require further chemical and biological investigations for the above and new biological activities as well.

Occurrence of withanolides has also been reported in *Withania obtusifolia* Dun by Modawi et al. (1986). But surprisingly no chemical and biological investigations have been carried out so for on this plant. Hence, it will be worth

exploring this plant for the discovery of other withanolides and their biological activities.

Withania somnifera is a very well phytochemically explored plant and a number of withanolides have been isolated from the different part of this plant. The soil-less aeroponically grown *W. somnifera* leaves and twigs afforded some unusual withanolides viz., 3α-(uracil-1-yl)-2,3dihydrowithaferin A**,** 3b-(adenin-9-yl)-2,3-dihydrowithaferin A and 2,3dihydrowithaferin A-3β-*O*-sulfate (Xu et al., 2011). The purpose of this study was to maximize the production and the structural diversity of the plant metabolites and studying the effect of *W. somnifera* grown under soil-less aeroponic conditions and its ability to produce withaferin A and other withanolides. The sulphated withanolides have also been reported from the normal *Withania somnifera* (Misra et al., 2005). Further, 2,3-dihydrowithaferin A-3β-*O*sulfate was also isolated from *W. frutescens* with undefined stereochemistry at C-3 position. These three novel withanolides possess significant cytotoxicity (0.54, 0.61 and 5.25 µM respectively) against human Ewing's sarcoma cell line CHP-100 (Wijeratne et al., 2014). Hence, It's provides a new idea to phytochemists in search of the new withanolides from *W. somnifera*.

Structure-activity relationship (SAR)

Withanolides isolated from *W. somnifera* are potent Cyclooxygenase-2 (COX-2) inhibitor (Jayprakasham and Nair, 2003) and it has been observed that the presences of double bond in α,β-unsaturated δ-lactone moiety is essential for the COX-2 inhibitory activity. Further, it has been observed that epoxide ring at 5,6- position is important for cholinesterase inhibition (Chaudhary et al., 2004, 2005). Ring A enone and epoxide ring at 5,6- position are also essential for the cytotoxicity of the withanolides (Llanos et al., 2012, Joshi et al., 2014, Wijeratne et al., 2014). Conversion of the epoxide ring into thioepoxide or cleavage of the epoxide bonds to produce hydroxyl and thiol group resulted 10 to 25 fold reduction in the cytotoxicity of withaferin A and other withanolides against different tested cancer cell lines (Joshi et al., 2014). Further, acetylation of 4 and 27 OH groups also resulted in significant improvement in cytotoxicity whereas introduction of the β-OH at C-12 position reduces the cytotoxicity of the withanolides (Llanos et al., 2010; Wijeratne et al., 2014). Acylation of 4-hydroxy group with 4-bromobenzoyl group in (4S, 20S, 22R)-4, 27-Dihydroxy-1-oxo-witha-2, 5, 16, 24-tetraenolide isolated from *W. aristata* enhanced the cytotoxicity up to 3-7 fold (Llanos et al., 2010). Hence, the above concept can be applied in the semi-synthesis of the other withanolide derivatives with improved biological activities. Protection of the 27-OH group with tertiarybutyldimethylsilyl (TBDMS) group also enhanced cytotoxicity by 3-10 folds against various tested cancer lines. Hence, the above observation suggested that increasing the lipophilicity of withanolides leads to the increase in their cytotoxicity. The functional groups within the circle are responsible for that particular activity.

Diseases affect *W. somnifera*

Several diseases affect *W. somnifera*, both under wild and cultivated conditions. But the crop is mainly attacked by fungal pathogens under field conditions, although deterioration of these crops due to other diseases has also been reported. Leaf spot is the most prevalent disease of *W. somnifera* caused by a fungus *Alternaria alternata* (Pati et al., 2008). The plant has also been reported to be affected by many other foliar diseases. It has been observed that *Alternaria alternata* causes severe leaf spot disease, while *Myrothecium roridum* and *Fusarium oxysporum* caused minor diseases and losses (Shivanna et al., 2013). Another disease of *W. somnifera* is wet rot. The causal organism was identified as *Choanephora* sp., a fungus which produces white aerial mycelia that later turned pale yellow (Saroj et al., 2012). In root rot and wilt disease the plants in the nurseries show symptoms of yellowing, drooping and decay at seedling stage leading to 30-50% mortality. The causal organism has been reported as *Fusarium solani* (Gupta et al., 2004)**.** The typical symptoms of another disease i.e. Witches broom disease consist of little leaf, shortening of internodes, excessive branching giving witches-broom appearance and premature drying and death of infected twigs and leaves. Phytoplasma was found to be associated with the disease on the basis of symptomatology**.**

Symptoms of the disease

Fungal plant pathogens are among the most important factors that cause serious losses to agricultural products every year. Monitoring of health and detection of diseases in plants and trees is critical for sustainable agriculture. Four fungal diseases have been reported on *W. somnifera* plant since 2007, *Pithomyces chartarum* causing leaf blight (Verma et al., 2007), *Alternaria dianthicola* causing leaf spot (Maiti et al., 2007), *Choanephora cucurbitarum* causing stem wet rot (Saroj et al., 2012) and *Pseudocercospora fuligena* causing black leaf spot (Saroj et al., 2014). Interestingly all above reported diseases affect foliar part of the plant and resulting in decrease of productivity of the crop.

Control Measures

The application of pesticides for effective pest's prevention and control of various diseases are most popular and beneficial method applied in agriculture. At present application of synthetic fungicides such as Blitox 50, Bavistin etc. are used for the treatment/ management of plant foliar diseases. However, the consistent use of fungicides could be a risk to the environment, particularly if residues

endure in the soil or percolate off-site and enter waterways (e.g. due to spray drift, run-off) (Komarek et al., 2010). Regular use of synthetic fungicides, may also lead to the development of resistant phytopathogens (Ishii, 2006) in future. Since last many decades, synthetic fungicides are used to protect plants from fungal diseases and now their fatal/ hazardous effect to ecosystem has been realized. After application, pesticide enters into ground water, lakes and marine water by various environmental processes. Moreover, some of the recent studies revealed that the aquatic organisms are being adversely affected by increased use of pesticides.

Biological and plant products were thoroughly investigated for their antifungal activity. Bio-control of plant diseases including fungal pathogens has been considered a viable alternative method to chemical control. In plant pathology, the term biocontrol applies to the use of microbial antagonists to suppress diseases. But it is also having some limitation for commercial use. Mainly bio-control showed variable performances under different environmental conditions in the field. Strategy to overcome this problem it is important to develop new formulations and application method of biocontrol microorganisms with advanced level of stability and survival.

Keeping in view the current scenario, it is essential to adopt safety concerns over the synthetic antimicrobial chemicals in plant protection. We have focused to explore the potential applications of fungal bio-control agent as an alternate to chemical control measures. fungal bio-control agent have a broad spectrum of anti-fungal properties (Kalemba and Kunicka, 2003, Sokovi´c and van Grien sven, 2006, Carmo et al., 2008) and they are eco-friendly (biodegradable, do not leave toxic residues or by-products to contaminate the environment) (Abdel-Kader et al., 2011) and have been used for the management of several diseases and results were highly encouraging (Sharif et al., 2010). *In vitro* antifungal assay showed many potent compounds. Here, I would like to mention that we should plan our research in such a way that we could be able to prepare sustainable fungicides for the management of Ashwagandha diseases.

In order to reduce crop loss, various management strategies such as chemical control, development of resistant varieties are employed invariably. Frequent breakdown of host resistance and various environmental and cost factors associated with the application of pesticides have necessitated the search for ecofriendly alternatives. Such approaches must enhance and sustain agricultural productivity and at the same time should be safe from environment and health perspectives. The use of environmentally safe measures has emerged as a sustainable concept for disease control; therefore there is further need for wider acceptance and promotion for eco-friendly approach.

Conclusion

Attention in traditional medicines and, in particular herbal medicines, has increased substantially in both developed and developing countries over the past two decades. Global and national markets for medicinal herbs have been increasing significantly. On the parameter of, the safety and quality herbal medicines have become important concerns for health authorities and the public. The safety and quality of raw medicinal plant materials and finished products depend on factors that may be classified as intrinsic (genetic) or extrinsic (environment, collection methods, cultivation, harvest, post-harvest processing, transport and storage practices) (Essono et al., 2007). Inadvertent contamination by microbial or chemical agents during any of the production stages can also lead to deterioration in safety and quality. *Withania somnifera* (Ashwagandha) is extensively utilized in preparation of medicines in Ayurvadic system. *W. somnifera* is native to India and commercially cultivated in different parts of the country. It promotes strength and vigor as an aphrodisiac and rejuvenator, in treatment of rheumatism, inflammation of joints and certain paralytic conditions (Basu and Kirtikar, 1991). Withania is the pharmacologically very important genus of the flowering plants and well known for its diverse biological activities. Withanolides are the major bioactive constituents in all the species of this genus. These withanolides possesses significant cytotoxicity against various cancer cell lines and it has been investigated that increasing the lipophilicity of these molecules enhances the cytotoxicity and vice-versa.

Acknowledgement

Authors are thankful to the Center of Excellence Programme of UP state Government Letter No.: 1205/70-4-2013-46 (43) 2010 TC-11 for financial support. Author Sonal Dixit is thankful to DSKPDF Cell, Pune, India, and University Grant Commission, New Delhi, India, for the award of the D.S. Kothari Postdoctoral Fellowship (F4-2/2006 (BSR)/BL/15-16/0156).

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