Chapter 12
Scientific Validation of the Usefulness of *Withania somnifera* Dunal in the Prevention and Treatment of Cancer

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12.1 Introduction

Cancer has demoralizing breakthrough event which happens in the life of the individuals which is the typical reason for death over the world. The prevalence of this bug is because of the changing lifestyle behavior of the humans. It has become a considerable burden on the communal health organization. The numerical analysis data showed that the cancer affects a third of the human population (Zaid et al. 2017). The studies on the cancer incidence in the body involve initiation, promotion, and progression, whereas reverting this process through therapeutic approaches by means of drugs is classically known as chemotherapy. The chemotherapeutic molecules currently employed in the treatment of cancer have the effects on normal characteristics like immune suppression, hair loss, vomiting, nausea, and impotence, and importantly the procedure is expensive which is not handy to the poor people and also interferes the metabolic events needful for the cell division. To overcome the above said issues and to maintain a better medical practice, the use of natural drugs is highly encouraged. The standardization and maintaining consistency of the synthetic drugs is a risky job, however the natural agents are safer with negligible or no side effects and easily available in the dietary procedure, and they had an ancient customary in disease regulations which are scientifically proven (Sak 2012; Amawi et al. 2017).

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Dietary food-based chemoprevention is gaining more importance recently because of the fact that it is reasonably an inexpensive approach and can improve the quality of life universally. Further, correct identification of chemopreventive agents from foods might be more beneficial in combating the problem of cancer. Traditional medicine is revalued by an extensive activity of research on different plant species and their therapeutic principles all over the world (Mohanty et al. 2017). More recently, medicinal plants as a source for discovering novel drug molecules has become a topic of global importance (Swamy and Sinniah 2016). The presence of various bioactive compounds and the mode of actions of these phytocompounds have further witnessed the significance of medicinal plants for therapeutical applications (Swamy and Sinniah 2015; Arumugam et al. 2016; Swamy et al. 2017). Certainly, some parts of these medicinal plants or phytocompounds have been used as nutraceuticals or dietary supplements to overcome various human health problems including cancer. In Ayurveda medicines, *Withania somnifera* (Ashwagandha) has been validated for rejuvenating potential, and the plant plays an essential role in improving the quality as well as prolonged life in human beings. Considering the above facts, this chapter highlights the importance of Ashwagandha as a perspective for treating and preventing cancer.

12.2 Botanical Aspects of *Withania somnifera*

Withania somnifera, colloquially known as Ashwagandha or Indian winter cherry or Indian ginseng, is a plant found in the tropical areas of Asia (Singh et al. 2010). Ashwagandha is a member of the Solanaceae plant family, and its name is supposed to be originated from Sanskrit meaning "horse's smell" principally because of the roots (Ashwa = horse; Gandha = smell). The plant prefers growing in variety of soil but favorable in sandy loom or literate soil with pH range of 7.5–8 (Verma and Kumar 2011). The plant is a perennial small woody shrub found growing in dry climate and belongs to family Solanaceae. The plants are found to be growing in summer vocational parts in the South Asian countries along the regions of Mediterranean belt and the zone of canaries. In India, the plants are found in the higher altitudes of Himalayas and as in other hotter parts. The plant grows up to a height of 30–170 cm in optimal conditions and is a stout shrub with central stem, star-shaped branching, and thin fine hairy structure. The plant bears yellow-colored flowers and red berries with long fleshy tap root system (Uddin et al. 2012; Verma and Kumar 2011).

12.3 Traditional Uses

Ashwagandha is arguably known as the most important medicinal herb in the Indian pharmacopeia and has been used in the various traditional customary of medicines like Ayurveda, Siddha, Unani, Tibetan, Sri Lankan, Arabic, and many folk systems

in the Asian subcontinent. In the Ayurvedic system of medicine, Ashwagandha is considered to be a *Rasayana herb* and to rejuvenate the body (Ovadje et al. 2015; Verma and Kumar 2011). The roots, which are the most important plant part, have been reported to possess myriad benefits in various literature. In practice, the fresh root system of the herb is used in cheese making for the coagulation as a substitute for rennet before drying; the constituents were added to the milk and boiled for coagulation. Due to all these benefits, Ashwagandha is known as *Queen of Ayurveda* and an important medicinal agent in the Indian pharmacopeia (Davis and Kuttan 2000; Mir et al. 2012).

12.4 Ethnomedicinal Effects

In ancient medical science practiced on *W. somnifera* and declared as Ramayana or rejuvenative, adaptogenic herb nourishes and tones the entire body with their aphrodisiac, sedative, and life-delaying properties. It is also used in geriatric problems and in Medhya Rasayana which promotes learning and memory as a general energy-reserving and enhancer tonic. The plant extracts from different sources are used in folk, Ayurvedic, Unani, and Siddha systems of medicine and the biological activities associated with different extract systems. The leaf part of the plant tastes like bitter and is used as an anthelmintic. The combination is given in cold and fever. Bruised leaves and fruits are typically used to treat tumors and tubercular glands by local application and also for carbuncles and ulcers. The fruit berries of the plant have a milk-coagulating activity which attributed to the pulp and husk of the fruit, used in the preparation of vegetable rennet during the fermentation for cheese production. The fruits are reported to be sedative, emetic and stomachic, blood purifier, and febrifuge (fever reduction), as an alternative, diuretic, and bitter tonic in dyspepsia as well as a growth promoter in infants. The root part extracts are also useful in constipation, depression, nervous exhaustion, loss of memory, loss of muscular energy, and spermatorrhoea (Singh et al. 2010; Mir et al. 2012).

12.5 Phytochemistry

Ashwagandha is one of the most well-investigated plants, and numerous studies have shown it to possess more than 35 chemical components. Pharmacognostic studies confirm that the plant contains alkaloids, steroidal lactones, steroids, salts, flavonoids, and nitrogen-containing compounds extracted from different parts of the plant. Each plant part bears an endless medical value in it as shown in the Table 12.1.

Table 12.1 Phytochemistry of *Withania somnifera*

Nature of compounds	Phytochemicals present in the herb	References
Alkaloids	Withanine, withaninine, somniferine, tropeltigloate, somniferinine, somninine, nicotine, visamine, withasomine	Kaur et al. (2013), SaiduluCh and GangadharRao (2014), and Chaurasia et al. (2013)
Salts	Cuscohygrine, anahygrine, tropine, pseudotropine, anaferine	
Steroidal lactones	Withaferin A, withanone, WS-1, withanolide E, withanolide F, withanolide G, withanolide H, withanolide I, withanolide J, withanolide K, withanolide L, withanolide M	
Nitrogen-containing compounds	Withanol, somnisol, somnitol	
Steroids	Cholesterol, β-sitosterol, stigmasterol, diosgenin, stigmastadien, sitoinosides VII, sitoinosides VIII, sitoinosides IX, sitoinosides X	
Flavonoids	Kaempferol, quercetin	
Other components	Resins, fat, coloring matters, a reducing sugar, phytosterol, ipuranol, and saturated and unsaturated organic acids	

12.6 Scientifically Validated Pharmacological Properties

Ashwagandha is arguably one of the highly employed plants in Ayurveda and in various folk systems of medicine. In the traditional system of medicine, this plant is claimed to have adaptogenic, immune stimulatory, and life-prolonging properties. The plant decoction (especially of roots) is a proven rejuvenator and is used to treat nervous exhaustion, memory-related conditions, insomnia, tiredness potency issues, skin problems, and coughing. Scientific studies carried out in accordance to the modern system of medicine have shown that the plant extracts do indeed possess anti-inflammatory (Mishra et al. 2000; Giri 2016), antioxidant (Chaudhuri et al. 2012), anti-stress (Kaur et al. 2001), antimicrobial (Mir et al. 2012), cardioprotective (Ojha and Arya 2009), antidepressant (Bhattacharya et al. 2000), immunomodulatory (Davis and Kuttan 2000), and antidiabetic (Jena et al. 2016) effects. In addition to the various extracts of the plant, studies have also shown that the major phytoconstituent of Ashwagandha, withaferin A, is extracted from the leaves and roots of plant (Verma and Kumar 2011). Chemically, withaferin A is a member of steroidal lactone containing cycloalkane rings and lactone rings and has been reported to possess myriad benefits including in cancer. Various pharmacological properties of this plant are given and summarized in tabular form (Table 12.2).

Table 12.2 Pharmacological activities of *Withania somnifera* phytocomponents

Phytocomponents	Pharmacological activity against various disorders	References
Withaferin A	Anti-inflammatory, antiarthritic, antidepressant, antibiotic	Singh et al. (2010) and Kaur et al. (2013)
Sitoinosides VII-X	Antioxidant, nootropic activity	
Withanoside IV	Alzheimer's disease	
Glyco-withanosides	Parkinson's disease	
Withanolide E	Antifeedant	
Withanolide 5	Immunomodulatory	
Withanolide D	Anticancer	
Sitoinosides IX, X	Immunomodulatory, CNS effects	

12.7 Effectiveness of Ashwagandha Against Cancer

The process of neoplasia is extended and involves myriad overlapping events. The process initiates with mutation that with time leads to cellular transformation and hyperproliferation and culminates in the acquisition of invasive and angiogenic properties that ultimately leads to metastatic lesions (Aggarwal et al. 2006). In Indian traditional system of medicine the Ayurveda, it is a well-known potential herb which fights against cancer and in addition to that helps in the maintenance of normal diet in the quality of life. Ashwagandha has been investigated for its anticancer effects, and studies have shown it to be effective (Tables 12.3 and 12.4). In the subsequent section, the anticancer effects of Ashwagandha will be addressed in detail against various cancer types.

12.7.1 Ashwagandha in Breast Cancer

The second foremost reason of the death in the world is because of breast cancer. On an average, out of ten, one woman will progress with this disease in their lifetime. Cause for the breast tumor is dependent on several issues like gender, diet, hereditary, lifestyle, and hormonal imbalance due to endocrine aspects. There are some other important factors that lead to breast cancer, like previous benign and mammographic density, but still it is not confirmed which factor is the most important in breast carcinogenesis (Abdulkareem 2013). Several studies involving Ashwagandha against the breast cancer show potent inhibitory activities in various cell lines (MCF-7 and MDA-MB-231). These studies have established that the cell cycle arrest at G2/M phase leading to the apoptosis as the chief mechanism of action (Maliyakkal et al. 2013). Similar experimental had been done against breast cancer cell lines with Ashwagandha extract which inhibited cell proliferation at both in vitro and in vivo with significant reduction in the cytokine and CCL2 expression; thereby it reduces the migration and invasiveness in MDA-MB-231 cells (Khazal and Hill 2015).

Table 12.3 Effect of *Withania somnifera* extracts on various type of cancers

Type of study	Type of cancer	Cell lines and IC50	Type of extract and dosage	Parameters studies	Inference	References
Cell culture studies	Breast	MCF-7	Ethanol extract	Cytotoxicity, apoptosis	Cell cycle arrest	Maliyakkal et al. (2013)
		22.33 µg/ml				
		MDA-MB-231				
		31.99 µg/ml				
		MCF-7	Aqueous extract			
		388.0 µg/ml				
		MDA-MB-231				
		471.40 µg/ml				
	Colorectal	HCT 116	Methanol extract	Cytotoxicity, antiproliferative effect	Caspase 3 activation	Alfaifi et al. (2016)
		2.19 µg/ml				
	Liver	HepG2	Methanol extract	Cytotoxicity, antiproliferative effect	Caspase 3 activation	Alfaifi et al. (2016)
		1.89 µg/ml				
	Laryngeal	Hep2	Chloroform and aqueous extract	Cytotoxic activity, anti- angiogenesis activity	Cell cycle regulation, anticancer activity. VEGF targets and inhibits neovascularization	Mathur et al. (2006)
		25 µg/ml	5–100 µg/ml			
	Human T leukemia	Human T-lymphoblastoid cells	Root powder in DMSO	Cytotoxicity, DNA damage, ROS production, Ca^{2+} and oxidative stress induction	Proapoptotic with intercellular Ca^{2+} accumulation, causes immunogenic cell death, genotoxicity	Turrini et al. (2016)
			0–1.6 mg/mL			
	Melanoma	A375:	Deionized water (aqueous) extract	Cytotoxicity, morphological analysis	DNA fragmentation, induction of nuclear blebbing and apoptotic body formation	Halder et al. (2015)
		350 µg/ml/24 h,	6.25–400 µg/ml			
		250 µg/ml/48 h and 200 µg/ml/72 h				
	Neuroblastoma	IMR-32, TGW, SH-SY5Y, Neuro-2a	Water (aqueous) extract	Cell proliferation, morphological analysis, gene expression studies, wound healing assay	Antiproliferative, anti-migratory, modulation of survival	Kataria et al. (2013)
			0.01–1.0% in media		Markers inducing cell death	
	Prostate	PC-3	Ethanol extract	Cytotoxicity, genomic analysis	Antiproliferative	Aalinkeel et al. (2010)
			0.5–1 µg/ml		Involves in the modulation of gene expression and signaling markers to stimulate apoptosis	

Animal studies	Transplantable tumor lymphoma	Dalton's lymphoma ascites (DLA)	Ethanol extract, 200 mg/kg	Hematological parameters	Antitumor	Christina et al. (2004)
	Transplantable tumor carcinoma	Ehrlich ascites carcinoma(EAC)	Petroleum ether and ethyl alcohol extract conjugated with gadolinium III oxide nanocomposite	Cytotoxicity, biochemical parameters	Radiosensitization, antitumor, ROS-mediated apoptosis, DNA fragmentation	Abdallah et al. (2016)
			227 mg/kg			
	Melanoma	B16F10	Methanol Extract	Biochemical parameters	Anti-metastatic	Leyon and Kuttan (2004)
			20 mg/dose/animal	Histopathology		
	DMBA induced Skin cancer	–	Methanol extract,	Antioxidant	Chemopreventive	Davis and Kuttan (2001)
			20 mg/dose/animal	Enzyme activation		
	Benzo(a) pyrene-induced forestomach papillomagenesis	–	Root powder mixed with food pellets	Enzyme activities, histopathological examination	Chemopreventive	Padmavathi et al. (2005)
			2.5% and 5%			
	Azoxymethane-induced colon	–	Ethanolic extract	Immune function test, histopathologic evaluation	Chemopreventive	Muralikrishnan et al. (2010)
	Carcinogenesis		400 mg/kg			

Table 12.4 Active component Withaferin A effects on various cancer cells and cancer models

Type of study	Type of cancer	Cell lines	Parameters studies	Inference	Reference
Cell culture studies	Endothelial cells	HUVECs	Cytotoxicity, vessel formation studies	Anti-angiogenic activity	Mohan et al. (2004) and Kumar et al. (2009)
	Prostate cancer	PC-3, LNCaP, PzHPV-7, CWR22Rv-1, DU-145,	Cytotoxicity, immunocytochemistry, ELISA, xenografts, transfection, and PCR	Proapoptotic through Par-4 and caspase activation	Srinivasan et al. (2007) and Das et al. (2016)
	Leukemia	U937, Caki, AMC-HN-4, HT-29	Cytotoxicity, gene expression studies	Apoptosis inducer through AKT dephosphorylation	Oh et al. (2008)
		SEM, REH, RS4	Cytotoxicity, Western blot analysis	Antileukemic activity, cell death	Shi et al. (2015)
	Colorectal cancer	HCT-116	Cell proliferation, migration, and docking studies, wound healing assays, xenografts	Suppressing AKT-induced tumor growth and stimulates cell death	Suman et al. (2016a) and Choi and Kim (2015)
	Uveal melanoma	OMM2.3, MEL290,	Cell proliferation and migration studies	Antiproliferative activity	Samadi et al. (2012)
	Fetal fibroblast cells	MRC-5			
	Breast cancer	MCF-7, MDA-MB-231,	Cytotoxicity, cell cycle analysis, transient transfection studies, ROS detection	Cell cycle arrest, stimulates apoptosis	Stan et al. (2008) and Zhang et al. (2011)
	Osteosarcoma	U2OS, MG-63	Cell proliferation, PCR	Induces antiproliferation with cell cycle arrest at G2/M phase	Ting-Zhuo and Wang (2015)
	Ovarian cancer	A2780, CAOV3	Cytotoxicity, ROS determination, Western blotting, xenografts, immunohistochemistry	Enhancement of ROS production, DNA damage, autophagy, antitumor activity	Fong et al. (2012)
	Oral cancer	HSC-3, HSC-4	Cytotoxicity, immunocytochemistry	Chemotherapeutic, apoptosis inducer	Yang et al. (2013)
	Thyroid cancer	DRO81–1	Xenograft, Western blot analysis	Antitumor activity	Samadi et al. (2010)

Animal studies	Prostate cancer in C57BL/6	–	Immunohistochemistry	Anticarcinogenic activity	Suman et al. (2016b)
	Transplantable carcinoma in Balb/c	Ehrlich ascites carcinoma	Irradiation by ^{60}CO gammatron	Radiosensitization, antitumor, anti-angiogenic activity	Sharada et al. (1996) and Kumar et al. (2009)
			Teletherapy, tumor toxicity		
	Melanoma in nude mice	92.1	Cell proliferation and migration studies	Antitumor, apoptosis inducer	Samadi et al. (2012)
	DMBA-induced oral cancer in hamsters	–	Biochemical parameters	Chemoprevention	Manoharan et al. (2009)

The major phytoconstituent of Ashwagandha, withaferin A, has revealed a promising antitumorigenic effectiveness in the carcinoma of breast cell lines MCF-10A and MDA-MB-231 owing to their anti-invasive and anti-metastatic activities by inhibiting epithelial-mesenchymal transition (EMT) stimulated by tumor necrosis factor-α (TNF-α) and transforming growth factor-β1 (TGF-β), and also it regresses the pro-metastatic intermediate filament protein which is part of EMT, vimentin program to promote metastasis. The activity of withaferin A was revealed by pathway enrichment investigation that specifically targets carcinogenesis resulting in the apoptosis; cell cycle and proliferation could be functionally evaluated through the flow cytometry and cell proliferation analysis. Withaferin A also plays a role in the invasion inhibition as determined by single-cell collagen invasion assay supported by lower gene expression of extracellular matrix-degrading proteases like uPA, PLAT, ADAM8, cell adhesion molecules such as integrins, laminins, pro-inflammatory mediators which involved in metastasis-promotion present within the tumor microenvironment and also involved in the colonization of the tumor such as TNFSF12, IL6, ANGPTL2, CSF1R and metastasis suppressor gene that had concomitant increased expression of BRMS1 were investigated (Szarc vel Szic et al. 2014; Lee et al. 2015; Yang et al. 2013).

12.7.2 Ashwagandha in Lung Cancer

Lung cancer is the leading cause of cancer death in the United States and around the world. Oncogenesis in the lung is due to the mutation caused by the carcinogens leading to the transition of epithelial cells that results in the metastasis through the activation of cellular signals by the cancer cells. The steroidal lactone, withaferin A, found in the Ashwagandha showed a promising effect in non-small cell lung cancer (NSCLC; A549 cell line) cells through the involvement of reactive oxygen species (ROS)-induced cellular toxicity (Liu et al. 2017). Experimental evidences of *Withania somnifera* have shown it to be a potent anticancer activity in lung carcinoma induced by chemical carcinogen benzo(a)pyrene in male Swiss albino mice studies. The molecular inhibitory mechanism along with paclitaxel involves chemotherapeutic activities like cellular damage mediated through free radicals, and the treatment showed the defending role of these molecules through reducing ROS-mediated cellular damages; thereby the extract of Ashwagandha in conjunction with paclitaxel affords the stabilization of membrane-bound enzyme levels and decreases the lipid peroxidation in animal studies (Senthilnathan et al. 2006).

12.7.3 Ashwagandha Targets in Gastric Cancer

Gastric cancer is one of the five most leading cancers that commonly causes death which is associated with less survival rate. The chronic gastric cancer that mainly occurs as part of syndromic disease in that 90% of the cancer is associated with the adenocarcinoma ultimately involves the long-standing mucosal inflammation consequences (Rugge et al. 2017). More than 50% of the world's population are chronically infected with gastric cancer due to the colonization of gram-negative bacteria *Helicobacter pylori* due to excess secretion of IL-1β, and it is the main risk factor for gastric cancer, and progression is linked with chronic inflammation and recruitment of immune cells (Kim et al. 2015). The phytochemical studies showed that the major withanolide, withaferin A (WA) component present in the Ashwagandha, exerted persuasive anticancer effect on *H. pylori*-linked gastric tumor. The molecular mechanism involves the regression in the secretion of IL- IL-1β in bone marrow-derived dendritic cells and the underlying cellular signals. WA showed the low release of IL-1β results due to NF-κB activation inhibition. Additionally it targets the NLRP3 inflammasome mediated by ATP and MSU activators. These analysis of WA against gastric cancer suggested that it can inhibit IL-1β production and secretion via dual cellular mechanisms (Kim et al. 2015).

12.7.4 Ashwagandha in Other Cancers and in Experimental Animals

Ashwagandha is also shown to possess anticancer properties against prostate cancer (Aalinkeel et al. 2010), colon and liver cancer (Alfaifi et al. 2016), leukemia (Turrini et al. 2016), skin cancer (Halder et al. 2015), and head and neck cancer (Mathur et al. 2006) of various human carcinomas. Mounting evidence from research aspects on cell culture and animal studies suggested that Ashwagandha has potent roles in cancer prevention (Palliyaguru et al. 2016). Ashwagandha showed a promising antitumor effect on transplantable tumor models DLA and EAC (Christina et al. 2004. Abdallah et al. 2016), metastatic skin cancer cell lines in mice (Leyon and Kuttan 2004), and chemopreventive potential of Ashwagandha has been analyzed against forestomach and colon cancer in murine model system (Padmavathi et al. 2005; Muralikrishnan et al. 2010) indicating that the anticancer effect observed in cell culture was replicating in the animal models.

12.8 Preclinical and Clinical Studies of Ashwagandha

Queen of Ayurveda (*Withania somnifera*) is a medicinal traditional plant of Solanaceae family in which it has potent phytoconstituents which play an essential role in various disorders which are clinically proven such as hypnosedative, immunomodulation, fertility enhancement, anti-inflammatory, antiarthritic, anticarcinogenic and angiogenesis inhibitor in the prevention of cancer, anticholinesterase activity, antioxidant, and antibacterial. Among the diverse phytocompounds of Ashwagandha, withaferin A is one of the best well-studied steroid lactone agents as much as pharmacological investigations are carried out. And for further evaluation in this vicinity, more research is essential and very much needed for future progression in the field of medicine. The detailed summary of the preclinical and clinical evidence has been shown in Table 12.5.

Table 12.5 Pre-clinical evaluation of *Withania somnifera* against multi-cancer models

Preclinical evaluation	Part of the plant extract/ phytocompound used	References
Chemo-protective activity	Herbal extract	Davis and Kuttan (2001), Padmavathi et al. (2005), Muralikrishnan et al. (2010), and Krutika et al. (2016)
Effective source for L-asparaginase	Root	
Azoxymethane-induced colon cancer and their immune dysfunction	Root extract/withaferin A	
Breast cancer with lung metastasis mouse model	Withaferin A	
Breast carcinoma and colon cancer inhibition	Withaferin A	
Benzo(A)pyrene-induced lung carcinoma in albino mice	Root extract	
Nontoxic normal lymphocytes for control proliferation	Pure herbal isolated nutraceutical; withanolide D	
Skin cancer mice model and UV-exposed rats as skin carcinogenesis model	Phytocomponents isolated from the root of Ashwagandha	
Skin carcinogenesis in Swiss albino mice by DMBA (7,12-dimethylbenz[a] anthracene)		
Cytotoxic efficacy on human cancer cells (MCF-7, A549)	Isolated from leaf	
Swiss albino mouse model of fibrosarcoma induced by 20-methylcholantrene	Phytochemical isolated from leaf of the herb	
In vitro and in vivo studies on various cancer types	Withaferin A and other steroid lactones of Ashwagandha	

12.9 Conclusion and Future Prospects

Ashwagandha is arguably one of the most researched medicinal plants, and studies have shown that various plant extracts as well as the principal phytochemical, withaferin A possess myriad benefits. Experiments have shown that these pharmacological effects are due to antioxidant, free radical scavenging, anti-inflammatory, antimutagenic, and induction of apoptosis in neoplastic cells. Mechanistic studies have shown that the apoptotic effects are mediated by induction of free radicals, accumulation of Ca^{2+}, cell cycle arrest, activation of caspase 3, DNA fragmentation, induction of nuclear blebbing, and apoptotic body. Moreover, Ashwagandha is also shown to decrease VEGF and to inhibit neovascularization indicating its usefulness as an anti-metastatic agent. In addition to the crude extract, withaferin A plays predominant modulatory activities and exhibits anti-inflammatory, pro-apoptotic, anti-invasive, and anti-angiogenic effects against various cancer conditions. Thus, it is considered as a potential drug candidate for treatment of different types of cancer. Mechanistically, withaferin A is shown to restrain TNF-induced IκB kinase and NF-κB activation and also stimulates apoptotic signals through triggering reactive oxygen species production. Withaferin A exerts multifunctional role in prevention of various cancer types through imparting signal transduction and their modulation. Thus, Ashwagandha is used in the Ayurvedic medicine for its rejuvenating power to enhance the immune system against stress, memory loss, neurodegenerative disorders, inflammation, arthritis, and high blood pressure and also used as immunomodulator in the improvement of fertility. Nowadays, this herb is extensively applied in the field of adjunctive therapy to treat the severe life-threatening disorders like cancer and other infectious diseases. Preclinical studies and clinical trials on animal models infer the importance of Ashwagandha use in the treatment of various medicinal practices to cure anxiety, cognitive and neurodegenerative disorders, and inflammation. Its chemopreventive effect on different conditions of an individual at their chemopreventive and radiotherapy level requires further more research in the near future (Fig. 12.1).

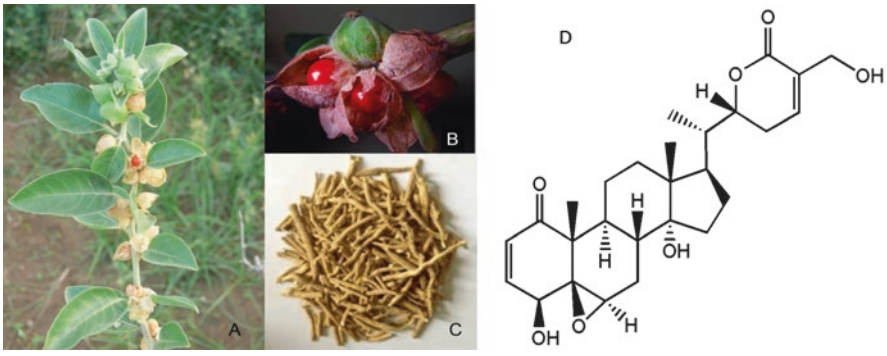

Fig. 12.1 Morphology of *Withania somnifera*; (**a**) plant, (**b**) berries, and (**c**) roots; (**d**) chemical structure of withaferin A

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