Botanical, chemical and pharmacological review of *Withania somnifera* (Indian ginseng): an ayurvedic medicinal plant

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Abstract

Withania somnifera (L.) Dunal is a well known and important medicinal plant widely used in several indigenous systems of medicine for the treatment of various ailments, viz. asthma, bronchitis, inflammatory diseases, ulcer and stomach problems. Steroidal lactones have been reported as the major phytoconstituents of this species. Different pharmacological experiments in a number of *in vitro* and *in vivo* models have convincingly demonstrated the ability of *W. somnifera* to exhibit anti-inflammatory, anti-oxidative, antimicrobial, anti-anxiety, aphrodisiac, immunomodulation, anti-diabettic, anti-ulcer, anticancer, central nervous system depressant and hepatoprotective activities, lending support to the rationale behind several of its traditional uses. The species is also used to treat some neurological disorders like Parkinson's and Alzheimer's. The molecules such as withaferinA, withanolide A and withanolide D isolated from this plant are potential bioactive molecules. Due to the remarkable biological activity of *W. somnifera* and its constituents, it will be appropriate to develop them as a medicine and make them more potent by chemical modifications and biotransformation. This review has covered botany, chemistry and pharmacology of the plant besides its traditional and folkloric uses.

Key words: *W. somnifera*; Steroidal lactones; Withanolides; Ayurveda; Pharmacology.

1. Introduction

Plants play a dominant role in the discovery of new therapeutics and have been used in traditional medicine for thousands of years (Muthu *et al.,* 2006). They have always been a rich source of large variety of lead compounds. Pharmacological screening of natural products has led to the discovery of a number of drugs. The knowledge of medicinal plants has been accumulated in the course of many centuries based on different medicinal systems such as Ayurveda, Unani and Siddha.

Among the worldwide list of twenty six species, the genus *Withania* is represented in India by *W. somnifera* and *W. coagulans* (Chadha, 1976). Recently we have reported a third species *W. ashwagandha* from Indian germplasm using multidisplinary approaches (Mir *et al.,* 2010; Kumar *et al.,* 2011). Within the family Solanaceae, *Withania* belongs to subfamily Solanoideae, tribe Physaleae and sub-tribe Withaninae of which it is the type genus (Olmstead *et al.,* 2008). The generic name *Withania* commemorates the celebrated English 'Paleobotanist, 'Henry Thomas Maire Witham' with an orthographic variation of the final 'm' into an 'n' to which the commemorative termination –ia has been added. The specific epithet *somnifera* is a compound of two Latin words 'somnus' meaning sleep and 'fero' (ferere) meaning 'to bear'. Thus the specific epithet alludes to sleep inducing properties of the plant (Fig.1 & 2) .

W. somnifera is an erect, branched, grayish, stellate-tomentose under-shrub, 30-150 cm high with long tuberous roots. Leaves are simple, petiolate with the leaf blade varying in shape from elliptic-ovate to broadly ovate, entire along margins, acute to obtuse at apex, cuneate or oblique at base, clothed with a persistent grayish tomentum on sides, 4-10 cm long and 2-7 cm broad. Leaves on vegetative shoots are alternate and large and those on floral branches are opposite, arranged somewhat laterally in pairs of one large and one small leaf, bearing in their axil a cymose cluster of 5-25 inconspicuous pale green bisexual flowers. It produces flowers indeterminately round the year with a peak of flowering between March and July.

The species exhibits stigma-anther proximity caused by elongation of filaments to cover the bilobed stigmatic surface with dehiscing anthers (Kaul *et al.,* 2005). High pollen load on the stigma and stiff pollen competition within a flower strongly favours self-pollination (Mir *et al.,* 2012). The species has been reported to show ploidy level variations viz., diploids (2n = 24), tetraploid (2n = 48) and hexaploid (2n = 72) cytotypes besides polysomatomy (2n= 12, 2n= 18, 2n= 24, 2n= 36, 2n= 48 and 2n= 72) with a predominance of 2n= 48 type (Iqbal & Dutta, 2007).

In view of its varied therapeutic potential, it has also been the subject of numerous pharmacological investigations. There-

fore, the present review summarizes the reports that help to establish ashwagandha's potential to make this multi-potential plant more acceptable to the world community.

Fig.1. *World distribution of Withania somnifera*

Ethnobotany

In Ayurveda, *W. somnifera* is widely claimed to have aphrodisiac, sedative, rejuvenative and life prolonging properties. It is also used as a general energy-enhancing tonic known as Medharasayana (promotes learning and memory) and in geriatric problems (Nadkarni, 1976). The plant has traditionally been used to promote youthful vigor, endurance, strength, health, nurturing the time elements of the body and increasing the production of vital fluids, muscle fat, blood, lymph, semen and cells (Williamson, 2002). It also helps counteract chronic fatigue, weakness, dehydration, weakness of bones and loose teeth, thirst, impotence, premature ageing, emaciation, debility and muscles tension. The leaves of the plant are bitter in taste and used as an antihelmantic. The infusion is given in fever. Bruised leaves and fruits are locally applied to tumors and tubercular glands, carbuncles and ulcers (Nadkarni, 1976; Kapoor, 2001). The fruits of the plant have a milk-coagulating property attributed to the pulp and husk of the berry, which has been used in the preparation of vegetable rennet ferment for cheese (Atal & Sethi, 1963).

The fruits are reported to be sedative, emetic and stomachic, blood-purifier and febrifuge, as an alternative, diuretic and bitter tonic in dyspepsia as well as a growth promoter in infants. The roots are also used in constipation, senile debility, rheumatism, general debility, nervous exhaustion, loss of memory, loss of muscular energy and spermatorrhoea (Watt, 1972; Singh & Kumar, 1998). The detailed uses of different parts of this plant are listed in Table 1.

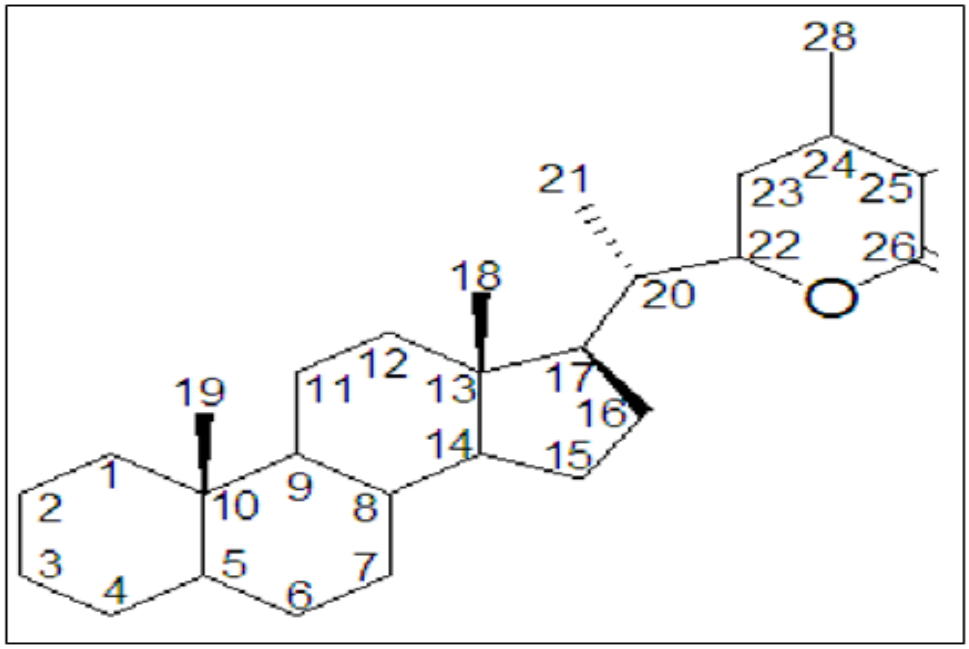
Besides its use as general tonic (Agarwal *et al.,* 1999; Dhuley, 2000), several recent reports have demonstrated immunomodulator and antitumor effects of ashwagandha as well (Sharad *et al.,* 1996; Budhiraja & Sudhir, 1987; Ziauddin *et al.,,* 1996; Agarwal *et al.,,* 1999; Devi, 1999; Mirjalili, 2009). Moreover, extracts of various parts of the plant have been reported to possess antioxidant, antiserotogenic, anticancer and anabolic properties and has beneficial effects in the treatment of arthritis, stress and geriatric problems (Asthana & Raina, 1989; Gandhi *et al.,* 1994; Davis and Kuttan, 2000; Singh *et al.,* 2001; Prakash *et al.,* 2001; Mishra *et al.,* 2000; Mirjalali *et al.,* 2009). The plant extracts are also used in folk, ayuvedic, Unini and Sidha systems of medicine and the biological activities associated with different extracts are summarized in Table 2. The plant was found to be active against a number of pathogenic bacteria (Kurup, 1956) and possess a strong antibacterial and antifungal activity against various pathogens including *Salmonella typhimurium* and in the treatment of murine aspergillosis (Dhuley, 1998; Ziauddin *et al.,* 1996; Owais *et al.,* 2005).

2. Chemistry

Phytochemical profile of *W. somnifera* has been extensively studied. Chemical characterization started with Power and Salway (1911) who isolated an amorphous alkaloid ($C_{12}H_{16}N_2$) from a South African strain of *W. somnifera*. Later, Ma-

jumdar and Guha (1933) investigated a plant from Bengal (India) and confirmed the presence of the alkaloid. Later on, they reported presence of nicotine and seven other alkaloids from the roots which they named (without structural information) as somniferine, somniferinine, somnine, withamine, pseudowithamine, withanmine and withanaminine (Majumdar, 1955). Several groups of chemical constituents such as steroidal lactones, alkaloids, flavonoids, tannins and saponins etc. have been identified, extracted, and isolated (Lavie *et al.,* 1975; Kirson *et al.,* 1977; Eastwood *et al.,* 1980; Kapoor, 2001; Atta-ur-Rahman *et al.,* 1991, 1993; Bandyopadhyay *et al.,* 2007).

Fig. 2. *Basic skeleton of Withania somnifera withanolides.*



Most of the therapeutic properties of *W. somnifera* are ascribed to bioactive steroidal lactones called withanolides- a group of naturally occurring C_{28} steroidal lactones built on an intact or rearranged ergostane framework, in which C-22 and C-26 are oxidized and make a six-membered lactone ring (Fig. 2). This class of compounds does not occur in all members of the Solanaceae family. However, the occurrence of withanolides is not restricted to Solanaceae. They have also been reported from marine organisms (soft corals) and from members of plant families Taccaceae and Leguminoseae (Maurya *et al.,* 2010). At present, more than 12 alkaloids, 40 withanolides and several sitoindosides (a withanolide containing a glucose molecule at carbon 27) have been isolated and reported from aerial parts, roots and berries of this plant. The concentration of major withanolides usually ranges from 0.001 to 1.5% dry weight (Atal *et al.,* 1975; Kapoor, 2001; Anonymous, 2004; Kumar *et al.,* 2007). The different active compounds isolated from various parts of *W. somnifera* are depicted in Table 3.

Withaferin A (4β, 27-dihydroxyl-1-oxo-5β, 6β-epoxywitha-2-24-dienolide) was the first member of this group of compounds to be isolated from a South-Asian strain (Fig. 3a) whose structure has been for the first time elucidated by Lavie *et al.,* (1965). The structural novelty and interesting biological activities elicited by this compound led to a thorough chemical investigation of the plant and numerous compounds with similar structural features were isolated (Glotter, 1991). Some important bioactive molecules isolated from this wonder medicinal plant that have a potential in the drug development programme are listed in Fig. 3. Examination of *W. somnifera* roots has resulted in the isolation of a new dimeric thiowithanolide, named as ashwagandhanolide as shown in Fig. 4 (Subaraju *et al.,* 2006; Mirjallili *et al.,* 2009).

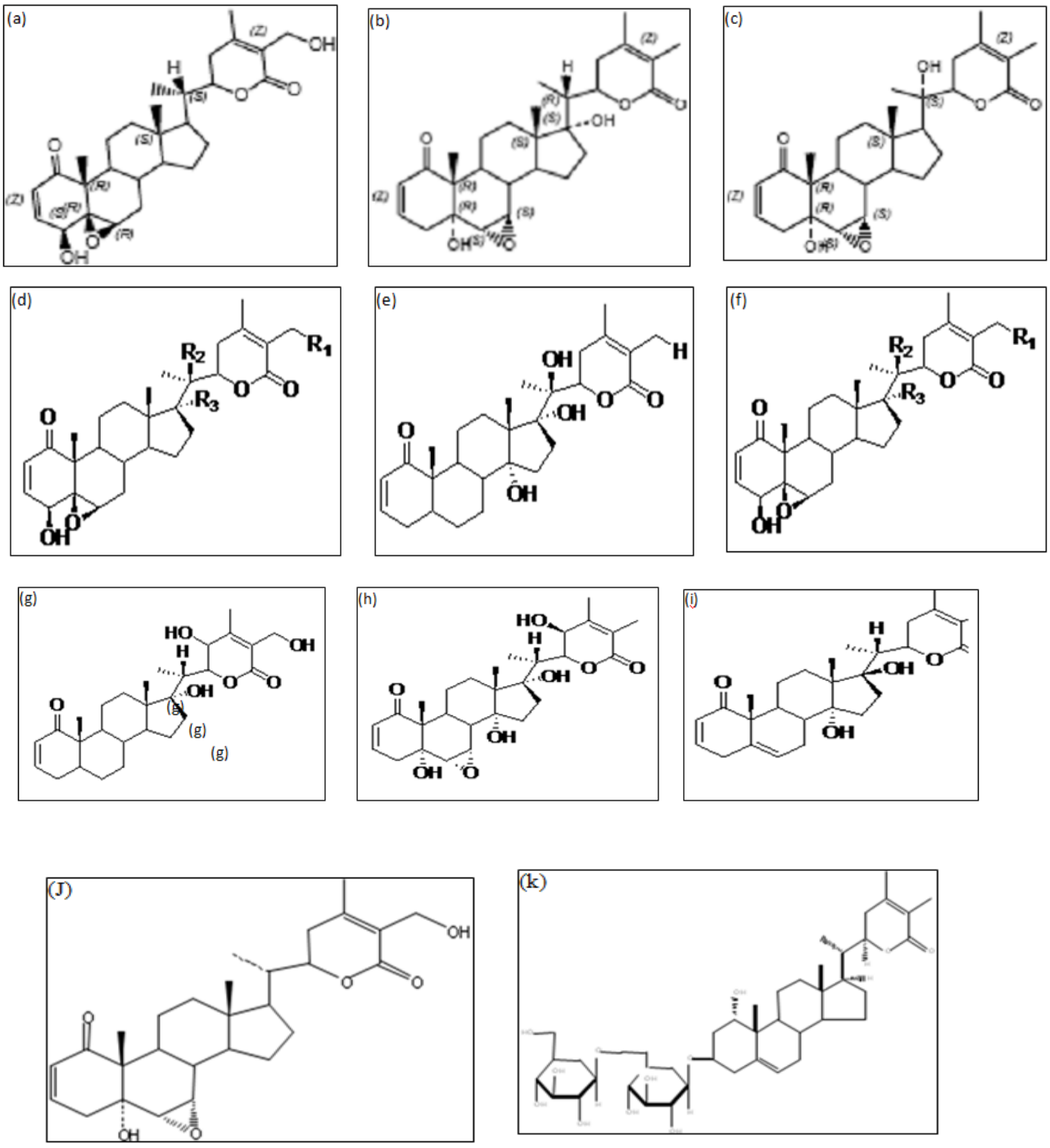
3. Pharmacological profile

3.1 Anticancer activity

Withaferin A and withanolide D are reported to be significant anti-tumor and radio-sensitizing withanolides (Devi *et al.,* 1992, 1993, 1996; Lyon and Kuttan, 2004). 1-oxo-5ß, 6β-epoxy-witha-2-enolide is another constituent of *W. somnifera* reported to reduce the skin carcinoma induced by UV radiations (Mathur *et al.,* 2004). Withaferin A acts as a mitotic poison

arresting the division of the cultured human larynx carcinoma cells at metaphase. It also produced a significant dose dependent retardation of the growth of Ehrlich ascites carcinoma, sarcoma 180, and sarcoma Black and E 0771 mammary adenocarcinoma (Davis and Kuttan, 1998).

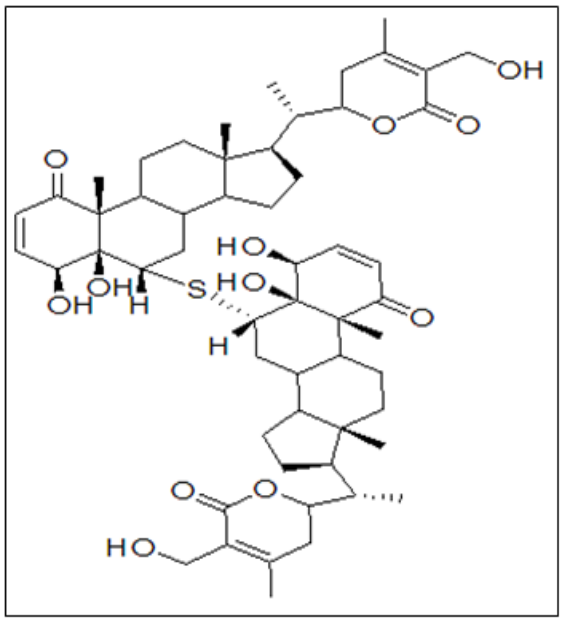
Fig.3. *Some bioactive molecules and their chemical structures isolated from Withania somnifera. (A) Withaferin A, (B) Withanone, (C) Withanolide A, (D) Withanolide D, (E) Withanolide E, (F) Withanolide G, (G) Withanolide Q, (H) Withanolide R, (I) Withanolide P, (J) 7-Hydroxy withanolide B and (K) Withanoside VI.*



Methanolic extract of *W. somnifera* has been used in stem cell proliferation (Kuttan, 1996). It also inhibited growth of breast, lung, central nervous system and colon cancer cell lines by decreasing their viability in doze dependent manner and therefore holds promise as a chemotherapeutic agent (Jayaprakasan *et al.,*2003). The withaferin A-mediated suppression of breast cancer cell viability correlated with apoptosis induction characterized by DNA condensation, cytoplasmic histone–associated DNA fragmentation, and cleavage of poly-(ADP-ribose)-polymerase (Silvia *et al.,* 2008). Chemo-preventive activity is attributed partly to the antioxidant/free radical scavenging activity of the ex-

tract (Prakash *et al.,* 2002).

Fig.4. *Ashwagandhanolide: a unique thio-dimer of withanolide isolated from the roots Withania somnifera.*



Cytoskeleton architecture alteration by covalently binding annexin II (Falsey *et al.,* 2006), anti-tumor capacity by inhibition of proteasomal chymotrypsin-like activity (Yang *et al.,* 2007) and apoptosis induction through the inhibition of protein kinase C or activation of caspase-3 (Sen *et al.,* 2007; Oh *et al.,* 2008) have also been explored. These studies are suggestive of anti-tumor activity as well as enhancement of the effects of radiation (Winter, 2006).

3.2 Anti-inflammatory properties

Ashwagandha acts as an anti-inflammatory agent through inhibition of complement, lymphocyte proliferation, and delayed-type hypersensitivity (Rasool & Varalakshmi, 2006). The extracts of *W. somnifera* have shown anti-inflammatory effects in a variety of rheumatological conditions (Anbalagan *et al.,* 1984; Al-Hindawi *et al.,* 1992). The extract was found to decrease the glycosaminoglycans content in the granuloma tissue by almost 100 percent and uncoupled the oxidative phosphorylation by significantly reducing the ADP/O ratio in mitochondria of granuloma tissue and increased the Mg2+ dependent-ATPase enzyme activity and subsequent reduction in succinate dehydrogenase activity in the mitochondria of the granuloma tissue (Begum *et al.,* 1988). The studies relate that cyclooxygenase inhibition may be involved in the mechanism of action of *W. somnifera*.

3.3 Antioxidant effects

The brain and nervous system are relatively more susceptible to free radical damage than other tissues because they are rich in lipids and iron, both known to promote the generation of reactive oxygen species (Halliwell & Gutteridge, 1989). Free radical damage of nervous tissue may be responsible for neural loss in cerebral ischemia and may be involved in aging and neurodegenerative diseases, e.g., epilepsy, schizophrenia, Parkinson's, Alzheimer's and other diseases (Jesberger & Richardson, 1991, Sehgal *et al.,* 2012). The active principles of *W. somnifera*, sitoindosides VII-X and withaferin A (glycowithanolides), are reported to increase levels of endogenous superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPX), and ascorbic acid, with a concomitant decrease in lipid peroxidation (Dhuley, 1998; Bhattacharya, 2001; Jayaprakasam *et al.,* 2004; Bhatnagar, 2005; Mirjalali *et al.,* 2009). A decrease in the activity of these enzymes is known to lead accumulation of oxidative free radicals and resulting in degenerative effects.

3.4 Anti-microbial activities

The antibacterial properties of this multipronged medicinal plant were for the first time reported by Kurup (1956) against *Salmonella aurens.* In past one decade, antimicrobial activity against a range of bacteria and fungi ascribed to withanolide were reported (Dhuley, 1998, Ziauddin *et al.,,* 1996; Dhuley, 1998; Mishra *et al.,* 2000; Owais *et al.,* 2005). However, the existing literature shows that this herb should be studied more extensively to explore its potential in the treatment of other infectious diseases as well.

3.5 Antistress and Aphrodisiac activity

Anti-stress activity associated with glycosides (sitoindosides VII and VIII) present in this plant was reported by Bhattacharya (1987; 2000 & 2003). The studies conducted by (Dhuley *et al.,* 2000; Singh *et al.,* 2001) lent support to the usefulness of ashwagandha as an antistress adaptogen.

Ashwagandha is also used as a tonic in the treatment of spermatopathia, impotence and seminal depletion (Nadkarni, 1954) and the men who used the herb enjoyed higher vigour performance (Boone, 1998). The higher concentrations of inorganic elements like Fe, Mg, K and Ni in the roots of this plant play a significant role in the diuretic and aphrodisiac activity of the drug (Lohar *et al.,* 1992). The decoction of the root boiled with milk and ghee is recommended for curing sterility in women (Singh & Kumar, 1998).

3.6 Anti-arthritic properties

Ashwagandha powder has been found useful in acute rheumatoid arthritis and reduces the discomfort associated with arthritis (Bector *et al.,* 1968). This property has been attributed to the active principle *withaferin A.*

Table 1. *Traditional uses of Withania somnifera (Ashwagandha).*

3.7 Cardiovascular Protection

Plant Part	System of medicine	Uses	Reference
Roots	Ayurveda	Rejuvenating drug, tonic, Alternative pungent, astringent, Aphrodisiac, Phthisis	Dutta (1877), Kumar et al., (1980), Sen Gupta (1984)
	Siddha	Aphrodisiac, fever, inflammation	SPC (1992)
	Unani	Asthma, bronchitis, leucoderma, Arthritis, emenagogue	Stewart (1869), Mathani (1973)
	Folklare	Abortificiant, cold, asthma, Tuberculosis, fever	Dutta (1877), Kumar et al., (1980), Singh and Kumar (1998)
Leaves	Ayurveda	Aphrodisiac, carbuncle, Ulcers, painful swelling	Dutta (1877), Kumar et al., (1980), Singh and Kumar (1998), Mhaskar et al., (2000)
	Siddha	Fever, chest pain, sores, swelling	SPC (1992)
	Unani	External pains, anti-inflammatory	UPC (1993)
	Folklare	Cure eyesores, boils, diuretic Narcotic, treatment of syphilis and hemorrhoids	Shah and Gopal (1985), Sharma et al., (1992)
Seeds	Ayurveda	Diuretic, narcotic and hypnotic	Dalzell and Gibson (1861)
	Siddha	Siddha	--
	Unani	Unani	--
	Folkalre	To coagulate milk, Applied on open wounds, Relieving the poison of a serpent rubbed on skin for ringworm in human beings and animals	Dalzell and Gibson (1861), Rao (1977), Sahu (1982), Shah and Gopal (1985), Dafni and Yaniv (1994)
Fruits		antihelmantic, ulcers and tubercular glands	Nadkarni (1976), Kapoor (2001)

Hypotensive effect due to autonomic ganglion blocking action as well as a depressant action on the higher cerebral centers are associated with the extracts of *W. somnifera* (Malhotra *et al.,* 1981). Recently *W. somnifera* was confirmed to be a cardio-protective agent that provides a scientific reason for rationale of the use of this medicinal plant in Ayurveda as Maha-rasayana (Gupta *et al.,* 2004; Mohanty *et al.,* 2004; Sehgal *et al.,* 2012).

3.8 Effect on nervous system

Ashwagandha is reported to have the sedative rather than stimulative action on the central nervous system, making it a superior medicine in exhaustion with nervous irritability. Ashwagandha alters the concentration of neurotransmitters that are known to play an important role in brain processes such as memory. The effects on nervous system are associated with Ashwagandholine (root extracts). It potentiates barbiturate-, ethanol- and urethane- induced hypnosis in mice and caused relaxant and antispasmodic effects against various agents that produce smooth muscle contractions in intestinal, uterine, tracheal and vascular muscles (Malhotra *et al.,* 1965). The bioactive compounds are reported to preferentially influence the events in the cortical and basal forebrain cholinergic-signal transduction cascade. The cognition and memory enhancing ef-

fects of *W. somnifera* extracts can be partly explained by the drug-induced enhancement of cortical muscarinic acetylcholine receptor capacity (Schliebs *et al.,* 1997). In general, Ashawagandha has been used traditionally as a tonic and nootropic agent (Sehgal *et al.,* 2012). It has also been associated with improvements in scopolamine-induced memory deficits in mice (Dhuley, 2001). *W. somnifera* extracts also show an antiparkinsonian effect on neuroleptic-induced catalepsy by inhibiting haloperidol or reserpine-induced catalepsy attributed to potent antioxidant, antiperoxidative and free radical quenching properties (Ahmad *et al.,* 2005; Kumar & Kulkarni, 2006; Sehgal *et al.,*2012).

Table 2. *Biological activity of root extracts of Withania somnifera (Ashwagandha).*

Root extracts	Biological activity
Alcoholic extract	Neurological, Radiosensitizer, Anticonvulsant, Antiinflammatory, Sedative, Antitumour, Antibacterial.
Methanolic extract	GABA mimetic activity GABA receptor mediates anti-convulsant activity, Protective effect as amygdaloid kidlling Antiiinflammatory (70% extract), Antistress.
Chloroform-Methanol extract	Prevention of Alzheimers disease (Sehgal, et al., 2012), Immunomodulatory, Antiinflammatory, Nematicidal, Hepatoprotective,
Water extract	Nephroprotective, Antistress, Antianxiety, Hypothyroidism.Anticonvulsnt, Antiinflammatory, Antiarthritic, Hepatoprotective,
Root powder	Antiulcerogenic, Antistress, Anticancer & Radiosensitizer, Psycophysiological, Pulmonary tuberculosis, Epilepsy, Nervinetonic, Easy abortion, General tonic in seminal disease, Glandular swellings in bubonic plague, Hypoglycemic diuretic.
Decoction	Anticonvulsant, Cold & Chills, Health restorative to old & pregnant.
Petroleum ether extract	Insecticidal

3.9 Immunity

W. somnifera show an immuno-potentiating and myeloprotective effects know roots by enhancing the levels of interferon (IFN)-γ, interleukin (IL)-2 and granulocyte macrophage colony stimulating factor in normal and cyclophosphamide-treated mice (Davis & Kuttan, 1999). As the plant is rich in iron, it contributes to red blood cell count. The effect of *W. somnifera* on the immune system is subtler than simply suppressing the immune/ inflammatory response. The active compound (withanolide A) in the roots of *W. somnifera* significantly increases the expression levels of T-helper 1 (Th1) cytokines, as well as CD4 and CD8 counts. It also enhances natural killer (NK) cell activity in a dose dependent manner with a faster recovery of CD4+ T cells in immune suppressed animals (Davis & Kuttan, 2002, Khan *et al.,* 2006, Bani *et al.,* 2006, Singh *et al.,* 2008). Apart from the above activated macrophage functioning indicated by enhanced secretion of nitrile, IL-2 and TNF-2, decreases moderately IL-4 with no effect on IL-10 suggesting that it only influenced Th1 profile of the cytokines. Root powder of this plant is also reported to stimulate the cell-mediated immunity, IgM and IgG and a prominent enhancement in proliferation and differentiation of lymphocytes as indicated by lymphocyte surface markers of T cells ($CD3^+$, $CD4^+$ and $CD8^+$) and B cells ($CD19^+$) (Singh *et al.,* 2008).

3.10 Immunomodulatory properties

Glycowithanolides and a mixture of sitoindosides IX and X isolated from *W. somnifera* were evaluated for their immunomodulatory and central nervous system effects (Ghosal *et al.,* 1989). Administrated orally (50-200 mg/kg orally) both compounds also produced significant antistress activity in albino mice and rats. They also augmented learning, acquisition and memory retention in both young and old rats. Root extract of *W. somnifera* was tested for immunomodulatory effects in three myelosuppression models in mice: cyclophosphamide, azathioprin or prednisolone (Ziauddin *et al.,,* 1996). Significant increase in hemoglobin concentration, red blood cell count, white blood cell count, platelet count and body weight were observed in *W. somnifera* -treated mice compared to controls. A significant increase in hemolytic antibody responses toward human erythro-

cytes (which indicated immunostimulatory activity) was also reported.

Table 3. *Chemical constituents of pharmaceutical importance identified in Withania somnifera.*

Plants Parts	Chemical Constituent	Reference
Roots	Sitoindosides VII (Acylsteryl-glucoside)	Bhattacharya et al., (1987)
	Sitoindosides VIII (Acylsteryl-glucoside)	Bhattacharya et al., (1987)
	Sitoindosides IX (Glycowithanolide)	Ghosal et al., (1988)
	Sitoindosides X (Glycowithanolide)	Ghosal et al., (1988)
	Withanine (Alkaloid)	Majumdar (1955)
	Withananine (Alkaloid)	Majumdar (1955)
	Ashwagandhanolide	Subaraju et al (2006), Mirjalili et al., 2009
Leaves	Withaferin (Steroidal lactone)	Anjaneyulu and Satyanarayana Rao (1997)
	Withaferin A (Steroidal lactone)	Kirson et al., (1970),Lavie et al., (1965) Lavie et al., (1966)
	Withanolie D (Steroidal lactone)	Kirson et al., (1970), Lavie et al., (1968)
	Withanolie E (Steroidal lactone)	Glotter et al., (1977)
	Withanone (Steroidal lactone)	Dhalla et al., (1961b), Kirson et al., (1971)
	Withanolide Z (Novel)	Pramanick et al (2008)
	Withanolide B	Pramanick et al (2008)
	7-hydroxywithanolide	Pramanick et al (2008)
	3α-methoxy-2, 3-dihydro-	Anjaneyulu and Satyanarayana Rao (1997)
	27-deoxywithaferin A (Steroidal lactone)	Kirson et al., (1970)
	4β, 17α-dihydroxy-1-1oxo-	Lavie et al., (1965)
	5β, 6β-epoxy-22R-witha-	Lavie et al., (1966)
	2, 24-dienolide (steroidal lactone)	Kirson et al., (1970), Lavie et al., (1968)
	4β-dihydroxy-5β, 6β-epoxy-	Glotter et al., (1977)
	1-oxo-22R-witha-2, 14-24-	Dhalla et al., (1961b),
	Trienolide (steroidal lactone)	Kirson et al., (1971)
	5, 20α (R)-dihydroxy-6α, 7α-epoxy-1-oxo- (5α) - Witha-2, 24-dienolide (steroidal lactone) 2, 3-dihydrowithaferin A-3beta-O-sulfate	Menben Von and Stapel (1973)
Seeds	Withanolide –WS 2 (aliphatic ester) Withanolide –WS 1 (aliphatic ketone)	Xu et al (2009), Kundu et al., (1976a, b), Khan et al (1993

3.11 Rejuvenating effect

W. somnifera was reported to possess growth-promoting effect when administered alone in powdered form or in combination with other drugs. The growth promoting activity is attributed to withanolides (Budhiraja & Sudhir, 1987). The study conducted in both children and old age people registered a significant improvement in hemoglobin, packed cell volume, mean corpuscular volume, serum iron, body weight, hand grip and total proteins. Serum cholesterol decreased and nail calcium was preserved in adults. Erythrocyte sedimentation rate decreased significantly and 71.4 percent of them reported increased vigour (Kuppurajan *et al.,*, 1996). In summary, these studies indicate *W. somnifera* may prove useful in younger as well as older populations as a general health tonic.

Hypoglycemic and diuretic effects of ashwagandha roots were also assessed in humans. A decrease in blood glucose comparable to that of an oral hypoglycemic drug was observed. Significant increases in urine sodium, urine volume, and decreases in serum cholesterol, triglycerides, and low-density lipoproteins were also recorded (Andallu & Radhika, 2000).

Table 4. *Biological and Pharmacological activities of Withanolides, glycowithanolides and alkaloids of Withania somnifera.*

Chemical constituent	Biological activity	
Glycowithanolides (Sitoindosides VII, VIII, IX & X)	Immunomodulatory, CNS effect, Antioxidant , Antistressor.	
Total alkaloids	Somniferine Visamine	CNS system, Respiration, Cardio-vascular system
		Hypnotic activity, Hypothermic & Nictinolytic
Withanolides	Withaferin A	Antibacterial and Antifungal Antibiotic and Antimitotic Antitumour & radiosensitizer Cytotoxic, Antiinflammatory Antiarthritic, Alzhiemers' Immunosuppressant
	Withanolide A	Sedative & Hypnotic Withanone
	Withanolide D	Antitumour
	Withanolide E	Antibacterial, Immunosuppressive, Insectantifeedant
	(3-β-hydroxy-2, 3-hydroxy Withanloide)	Antibacterial ,Antitumour, Antiinflammatory, Insect antifeedant
	5, 2O-α® dihydroxy-6α 7α-epoxy-1- OXO (5α-1 with a-2, 24-dienolide)	Immunolomodulatory
	4β, 20-didihydroxy-1-OXO-5β, 6β-epoxy with a-2, 24-dienolide	Antitumour

4. Conclusion

The use of herbal drugs is increasing worldwide as they have fewer or no side effects as compared with synthetic drugs. Ayurveda claims therapeutic potentials of various plants. A lot of work has been done on this multipurpose drug yielding plant till now. But all this information is fragmented therefore; the present review has been an attempt to compile this available information in a comprehensive manner. An extensive research has been done on this plant in past three decades but still there is an urgent need to carry out investigations on the biological activities, efficacies and modes of action of this traditional drug. In India, three species of the genus *Withania* are found, *W. somnifera, W. ashwagandha* and W*. coagulans.* Withanolides are the principal compounds found in all the three species, there are some withanolides specific to each of them. Withaferin A is a major compound found in *W. somnifera* and *W. ashwagandha*, whereas, coagulin L has been found in major amounts in *W. coagulans*. A unique thio-dimer of withanolide named Ashwagandhanolide has been found in *W. somnifera*. The plant has been used as an antioxidant, adaptogen, aphrodisiac, liver tonic, anti-inflammatory agent, anticancer, central nervous system depressant, hepatoprotective and astringent and more recently as an antibacterial, antihyperglycaemic, hypolipidaemic and antitumoral, as well as to treat ulcers, senile dementia, Parkinson's and Alzheimer's. It had the greater therapeutic value overall. The variety of activities reported for the extracts, fractions and withanolides isolated from this wonder medicinal plant provide promising evidence for future research. Withanolides could achieve an important place in the world of modern drugs. Isolation on a large scale, chemical transformations and synthesis of the active compounds will definitely enhance their pharmacological value. The pharmacophores of various pharmacologically active withanolides have not yet been identified. All these advantages prove the significance of *W. somnifera* in natural product research. Despite having immense medicinal properties a multipronged strategy is required for making Ashwagandha varieties more competitive. There is a need to augment the pharmacological properties by selecting and improving chemotypes producing prodigal amounts of the desired withanolide.

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