Review Article

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Withania Somnifera Linn as Herbal Source of Diverse Pharmacological Potential - A Comprehensive Review

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Abstract

Ashwagandha, also known as Indian winter cherry, belonging to the *Withania Somnifera* Linn. (Solanaceae) family, (commonly available as Churna). Africa, the Mediterranean, and India are all home to this species. It is 30-50cm high and mainly found in the drier parts of India. Since it raises haemoglobin (red blood count) and hair melanin. *Withania Somnifera* is known as "Rasayana," which means "strong rejuvenator" in Ayurvedic jargon. In ethnomedicine, it is a well-known health food and herbal tonic that is used to treat cardiovascular diseases. It can be used as a single herb or as part of polyherbal or herbo-mineral formulations for humans. It is traditionally used to treat various diseases such as inflammation, asthma, dyspepsia, hypertension, rheumatism, tumor, anxiety, hemopoietic, antimicrobial, depression, immunomodulation, antiulcer, hepatoprotective activities, Alzheimer's, Parkinson's disease, rejuvenating properties and syphilis. It has wide variety of chemical constituents such as withanoloides, flavonoid, saponins, glycosides, alkaloids, tannins, steroids have been studied. Despite the fact that previous review articles on this plant have been written, this review article is provided to bring together all of the most recent knowledge on its phytochemical and pharmacological activities.

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INTRODUCTION

Ashwagandha or Indian Ginseng is another name for WithaniaSomnifera Linn.(Solanaceae). For over 100 of years, it is demonstrated as a vital herb for homeopathy and in the medicinal system (Gupta *et al.*, 2004). The shoots are mainly, i.e.stem, veins, calyxare surrounded by with small star-shaped like hairs. WithaniaSomnifera leaves are looked like simple, ovalate, and petiolate like structure and up to10cm long. The flowers of this plant are small greenish, axillary, solitary and bisexual. There are

twenty-three species of WithaniaSomnifera exhibited, Islands of the Canary, the Mediterranean, Southwest Asia, and Northern Africa, that are mostly found in the parts of tropical and subtropical areas that are drier. In all those species, only two species that is WS and Indian Rennet, are reasonably and medicinally used and cultured in a plurality of areas. In this study, the basic focus is to an evaluation of various pharmacological activities of this plant under various experimental conditions.

Therapeutic uses

Rheumatoid arthritis, Emasculation, anti-microbial, anti-cancer, cardioprotective, Alzheimer's, Parkinson's, anti-asthamatic, skindisorder, anti-inflammatory, paramnesia, Psychological disorder, eczema etc. (Kaur *et al.*, 2001)

MORPHOLOGY

Ashwagandha is a tomentose, straight or vertical, evergreen and having branched bushes that grows up to a height of 30-150 cm. Ovate, simple, glabours and10cm lengthy leaves. Blossoms or florets are small, green, blonded and contra laterally made and umbel-like structure with a few flowers (short contra lateral structure). It has fruits name globose berries with a diameter of 6mm and, when mature phase, converted to an orange colour and closed in a permanent calyx that is stretched and diaphanous.

Macroscopic Properties

When dry, the thick, fleshy roots are circular in shape and taper off gradually, smooth,10-17.5inches high and 6-12millimeter wide, un branching. Fiber like secondary roots sprouts from the primary roots. When broken, the roots outer surface is brownish-white and ceamy white. It possessed short, inconsistent separation, a pleasant aroma, and a bitter, vinegary flavour.

Microscopic Properties

The epidermis of the young root is a single-layered and lobule cortex of 4-5 layers of cells, with fluoroscent stripes highlighting the endodermis. In the cortex's layer, the cork cambium forms. And after secondary development has occurred, the endodermis still exists.

PHYTOCHEMICAL STUDIES

According to a review of the literature, the following chemical constituents can be found in various sections of the plant, as shown in Figure 1.

Root

Amino acids, fructose, glycosides, withanoloid, an

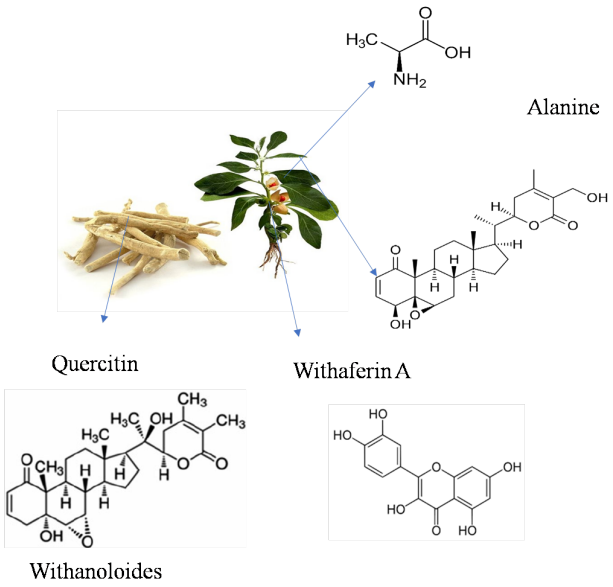

Figure 1: This diagram shows that Withania Somnifera exerts various chemical constituents like Alanine, Quercitin, Withaferin A, Withanoloides

acid (M.P-294-296) have all been found in the roots. The overall alkaloidal content of Indian roots is calculated to be between 0.13 and 0.31 per cent, with much higher yields (till 4.3 per cent) being written off.

The roots have been estimated to contain a variety of biochemically heterogenous alkaloids. Anahygrine, isopelletierine, withananinine, somniferine, cuscohygrine, somniferinine, pseudotropine, are some of the most common alkaloids. Withanine, visamine and withasominine are some of the other alkaloids. Withanine is classified in a hypnotic and sedative drug. Aspartic acid, alanine, glutamic acid, tyrosine, proline, glycine are appear or stated to have 5 unidentified alkaloids and 12 withanoloides, several free amino acids are glycosides, condensed tannins, chlorogenic acid are reported.

Leaf

The leaves of WithaniaSomnifera contain a group of C28 steroids with a 6-membered lactone ring in the 9-carbon atom in an aromatic ring.

Withaferin A, a steroidal lactone separated from the leaves of and dried roots of W. Somnifera, is the most important withanoloides. It's thermostable, inactivates slowly at ph 7.2, is insoluble in water, and comes in the form of a suspension.

For the extraction process, the leaves are collected with cold alcohol from the south Africa plants. Withaferin A is assigned to the remedial properties of the leaves and roots of WithaniaSomnifera.

Fruit

Proline, carnitine, glycine, aspartate, and serine are all amino acids; hydroxyproline, cysteine are among the amino acids that aren't bound present in the fruits of WithaniaSomnifera.

Shoots

They're high in calcium, crude protein and phosphorous, and their shoots aren't fibrous. They're also known to documented scopoletin.

Stem

Condensed tannins and flavanoids can be present in the plant's stem.

Bark

A variety of free amino acids present in the bark.

PHARMACOLOGICAL STUDIES

The medication is made up of Withaniasomnifera, which is listed as a sedative in the Indian pharmacopoeia, is dried roots. The existence of many alkaloids is thought to be responsible for the roots' pharmacological activity.The entire aqueous extracts seems to have the same property as the total alkaloids, but it is only around half as potent.

Anti-Inflammatory Activity

The anti-arthritic and anti-inflammatory properties of Withaferin A, a compound derived from WithaniaSomnifera, have been demonstrated. The biologically active steroids that contain Withaferin A are thought to be responsible for this activity. It functions in the same way as dose for dose, hydrocortisone sodium succinate. It was discovered that it inhibited the arthritic syndrome without causing any side effects. Hydrocortisone is a form of cortisone that is used to treat acne. It demonstrates that Withaferin A is more effective than hydrocortisone in rats with adjuvant-induced arthritis, a model that closely resembles human rheumatoid arthritis. The drug had a potent dose-response in oedema inhibiting activity when given intraperitoneally toa single dose of 12-25 mg/kg body weight had a fair duration of action in albino rats., as it., after 4 hours of administration, it may effectively inhibit inflammation. NFKB activation factor is block effectively by Withaferin A by preventing IjB kinase b activation caused by tumour necrosis factor (Kalra and Kaushik, 2017).

Anti-Microbial activity

Gram-positive clinical isolates of methicillin-resistant Staphylococcus aureus and Enterococcus spp. have provided possible results with WithaniaSomnifera showed antibacterial activity. Besides this, the Antimicrobial activity of WithaniaSomnifera against gram-negative bacteria such as E. coli, Salmonella Typhi, Proteus Miribilis, and Citrobacter freundii has been observed. (Arora *et al.*, 2004). Ashwagandha (WithaniaSomnifera) has an efficient in-vitro study that is anti-salmonella activity. With this, Ashwagandha (WithaniaSomnifera) extract enhances the rate of survival and decreased bacterial loads of several organs of mice with Salmonellosis. Collaboration of this, WithaniaSomnifera extract improves the anti-bacterial effect of Tibrium in case of Escherichia coli and Staphylococcus aureus.

The extracted part of root, stem, leaves, a flower of WithaniaSomnifera blocks six bacteria like to varying degrees, Bacillus subtilis, Staphylococcus aureus, Raoultellaplanticola, Pseudomonas aeruginosa, Enterobacteraerogens (Gram -ve), E. coli (Gram -ve), and two fungi, Aspergillus flavus and Candida albicans (Kalra and Kaushik, 2017).

Additionally, Glycoprotein extracted from WithaniaSomnifera shown a fungistatic activity in phytopathogenic and strand development in the aspergillus flavus fungus. Moreover, flavanoides from WithaniaSomnifera has been with a minimum inhibitory concentration of 0.038.5, and a fungicidal concentration of 0.039 is known to be the minimum., it is selective against Candida albicans. (Chopra *et al.*, 2004)

Anti-Cancer activity

Several models, both in vitro and in vivo, are justified that some phytoconstituents of WithaniaSomnifera is having anti-carcinogenic activities and chemo-preventive properties Sachdeva *et al.* (2013). The extent of neutrophils, leucocytes, lymphocytes, immune complexes and Ig that is induced by the azoxymethane is altered by the extract of WithaniaSomnifera, and it means the study shows that colon cancer is induced by the azoxymethane is treat by the WithaniaSomnifera (Singh and Kumar, 2011). In other studies, Withaferin A activates the PP2A by covalent binding to C377 of regulatory subunit PPP2RIA; due to this, Akt is inactivated, this therapy causes blocking of expansion of breast cancer cells. Similarly, the growth of patients derived mesothelioma is inhibited by Withaferin A. Like this, and Withaferin can also help with kidney cancer. Via down regulation of the Stat-3 pathway, A mediated dose-dependent apoptosis and PARP cleavage in cells. This study revealed that Withaferin is a form of withaferin that is Eukaryotic initiation factor-2a was phosphorylated as a result of A., and up regulation of glucose-regulated protein-78 are done by Withaferin-A.

Cardio-protective activity

Ashwagandha shows cardiovascular activity (Das *et al.*, 1964). Animal models of cardiotropic and cardioprotective properties are showed by WithaniaSomnifera (Ojha and Arya, 2009). In animal models, a combination of various herbs formulations with W. somnifera as a constituent shows cardioprotective effects. Khan *et al.* (2006) by activation of In an Nrf-2-dependent manner, nuclear Nrf-2 (factor-erythroid-2-related transcription factor) activates phase-II detoxification enzymes, preventing apoptosis. Moreover, it show shaematopoiesis. WithaniaSomnifera, a rat model of coronary artery occlusion, it was found that prophylactic therapy significantly improved myocardial oxidant/antioxidant steadiness, pro-apoptotic/anti-apoptotic impact, and decreased TUNEL positivity, as well as myocardial histopathologic deterioration. (Singh *et al.*, 2008, 2001)

Anti-Diabetic activity

When applied to humans, some polyherbal formulations from Medicine in Indian Structures (Dianix, Trasina) showed good for diabetic patients. In patients, WithaniaSomnifera aqueous extraction stabilized glucose in the blood that was compared to the oral hypoglycemic drug daonil, when administered orally for 30 days. Correspondingly, Insulin tolerance in non-insulin-dependent diabetes mellitus is measured using the insulin sensitivity index, and treatment with WithaniaSomnifera ameliorated the increase in the homeostasis model in rats. According to this study, Leaves and roots of W. somnifera refine glucose absorption leaf extract in skeletal myotubes and adipocytes in a dose-dependent manner exhibited better definite compared to the root extract. Extracts from both the roots and the leaves of Withaniasomnifera tissue glycogen levels, glucose-6-phophatase, urinary sugar, blood glucose in rats with Diabetes mellitus caused by alloxan. With this, Depletion was also discovered that strengthening nonenzymatic and enzymatic antioxidant defences was beneficial. (Udayakumar *et al.*, 2010). The blocking of Inflammatory response in islets damaged by cytokines in culture and after transplantation is done by Withaferin-A and showed the potential of the anti-glycating activity.

Anti-Stress activity

Ashwagandha has potential stress resistance in animals. In mice, Chronic anti-stress activity is induced by aqueous extracts of W. somnifera roots, which cause T cell population depletion and up-regulation of Th-1 cytokines. Serum cortisol content was decreased with no any significant side effects in a clinical trial on the protection orIn human participants, the efficacy of a high-concentration full-spectrum extract of W. somnifera roots. Moreover, Chronic electroshock stress instigates the levels of cerebral monoamines (glutamate, and almotriptan malate, noradrenaline) in EuMil, a polyherbal formulation. (Bhattacharya *et al.*, 2002). GABA, a brain inhibitory neurotransmitter, decreases brain waves and prevents neurocytes from overfiring; due to that, the restful impact is produced.

Neuroprotective properties

The neuroprotective effects of Ashwagandha have been identified in numerous studies (Murthy *et al.*, 2010). The two Glial cells and neuronal cells are protected from scopolamine-induced toxic changes by extraction of leaves and its chemical constituent with anyone. Withaniasomnifera remarkably lessened scopolamine triggers the inactivation of neuronal cell markers, including Nuclear factor,PSD-95, MAP-2, NF-H, DNA harm and oxidative stress markers, as well as GAP-43 and the glial cell marker glial fibrillary acidic protein (GFAP). By controlling the activity of GFAP, heat shock protein 70 (HSP70), mortalin, and the neural cell adhesion molecule, in glial cells, W. somnifera extract lessened the lead-induced toxicity (NCAM) (Kumar *et al.*, 2014). By injecting Superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) activity increased in a dose-dependent manner, glycowithanolides retrieved from Withaniasomnifera showed substantial antioxidant activity in the cortex and striatum of the rat brain (Bhattacharya *et al.*, 2002). The extract of W. somnifera protected treated mice from by minimizing oxidative stress. Streptozotocin-induced oxidative damage may be minimized. (Jain *et al.*, 2001) found that Root powder extract of W. somnifera significantly reduced after immobilization stress, the number of degenerating cells in the CA2 and CA3 sub-areas of the rat's hippocampus. In human neuroblastoma cell lines, Neurite outgrowth extensions are aided by W. somnifera root extract or derivatives. Withanolide-A mainly extends axons, while withanoloides-IV and VI mainly extend dendrites, In the rat (Kataria *et al.*, 2012), IMR-32 and C6 cells were shielded as a result of GABA toxicity by an extract of a leaf from Withania. Pre-treatment with W. somnifera fresh leaves extract block cell death caused by glutamate and reversible GABA and give rise to, HSP70 is up regulated in response to stress and consequently, it rehabilize plasticity of the brain by, angiogenesis, and brain plasticity markers, neuronal adherence of cell, and in polysialyted form. The extract of Ashwagandha is also decreased excitotoxic damage caused by kainic acid by reducing oxidative stress. (Parihar and Hemnani, 2003)

Anti-Parkinson activity

There is precedent in the evidence for Withaniasomnifera playing a significant role in Parkinson's disease. In a rat model of Parkinson's disease using 6-hydroxydopamine (6-OHDA), Ashwagandha is a plant that has been shown for lessened Dementia symptoms as well as morphology. This study showed that brain regions neurotrans with metabolites were restored more due to their strong Antioxidant properties, shown aside the findings. Ashwagandha has the potential to reverse functional impairments, including sensor motor activity, muscle control, and drug-induced rotational behaviour by increasing striatal catecholamine content. This study also showed that dopamine D2 receptor populations in the thallamus are upregulated after Parkinsonism; it acts as a compensatory mechanism is triggered, catching any accessible dopamine. Furthermore, the glycine carbonic anhydrase label revealed that W. somnifera increased the number of remaining dopamine pathways (Ahmad *et al.*, 2005). Intoxicated Parkinson's disease mice antioxidant status was restored with MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine)., decreased oxidative stress, and in consequence, normalized neurotrophic factor content in the mid brain by the root extract of W. somnifera. The model's functional behaviour increased as a result of these biochemical improvements. The standardized Rotenone-induced oxidative dysfunction and mitochondrial respiratory chain enzymes were decreased by a W. somnifera extract., which successively reduced cholinergic activity and repleted the brain. Parkinson's disease was studied in a Drosophila melanogaster model that is caused by rotenone, and these modifications were responsible for decreased sensor motor disturbances and effectiveness. Furthermore, W. somnifera root powder reduced atrazine toxicity in the brain stem and limbic system of mice's brains by serving as an antioxidant and anti-inflammatory, as well as repairing neuronal issues and problems. As a result of these changes, the striatum's synaptic functions and levels of dopamine were regained. The ethanolic extracts of Ashwagandha retained nerve fibers in a mouse model of Dementia condition caused by maneb-paraquat, resupplied dopaminergic levels of the basal ganglia, decreased sensor motor activity by dropping tenderness and proteolysis and antioxidant metabolism in different ways. W. somnifera, in general, hindered inducible Nitric Oxide Syntheses expression, an antioxidant enzyme marker. Ashwagandha down-regulated astrocyte activation and Glial fibriallary Acidic Protein expression, thus deactivating pro-apoptotic Bax and activating anti-apoptotic Bcl-2 protein expression.

Anti-Alzheimer activity

W. somnifera appears to play a significant role in drug production for Schizophrenia, according to the literature. In healthy human subjects, standardized leaf extracts of W. somnifera strengthened cognitive and psychosocial ability. By up-regulating W. somnifera root extract, behavioural deficiencies and neurological signals, as well as Ab release, were altered in Schizophrenia systems. (Sachdeva *et al.*, 2013). The active gradient binds with anamides-A and -C. of (Ab) Kaur *et al.* (2004) in a special way, according to parameter estimation. According to and propose that with anamides can prevent the formation of fibrils, thus protecting cells from Ab toxicity. Even so, docking design researches have proven that withanolide-A inhibits human acetyl acetylcholine receptor, which may be useful in the treatment of Schizophrenia. Singh and Kumar (2011) found that Withanoside-IV and its active metabolite, withanoside-IV, induced Ab. Praveen and Murthy (2010) induced hippocampal neurogenesis in a mouse by strengthening brain changes and blocking axon, dendrite, and synaptic loss. Subchronic exposure to propoxur causes hinderance of AChE activity and neurological problems in rats. W. somnifera elicits a defensive response and wants to abolish these effects. Ashwagandha ameliorates oxidative damage caused by doxorubicin, resulting in a beneficial effect on the cognitive disorder. W. somnifera reinforced cellular uptakein the Ab-treated SK-N-MC cell line, and levels of the peroxisome proliferator-activated receptor-c (PPAR-c) (Chandrasekaran *et al.*, 2013). It also caused cholinesterases activity to be inhibited. The health benefits of ashwagandha aqueous extraction against hydroxyl radicals and Ab (Dh) is dependent on the concentration- cytotoxic activity in PC12 cells that have been segregated.

Anti-Ischemic and Anti-Hypoxic activity

Ashwagandha has been shown to have a possible effect on oxidative stress, glioma area reduction, and neurological function stabilization in rats after a middle cerebral artery occlusion. Once Withania-Somnifera is inserted into mice, it causes a persistent occlusion of the middle cerebral artery, resulting in function repair and a reduction in infract structure. The explanation for this decrease is that in the mouse cortex, retrieval of Hemoxygenase-1pro-apoptotic protein expression and up regulation of PRAP-1 is lessened. It prevents the nuclear translocation of an apoptotic inducing agent, which blocks the apoptotic cascade. The treatment of Withaferin A from WithaniaSomnifera depleted glu-

tathione levels by activating the glutathione synthesis pathway, as well as theNFE2L2 associated factor two and Nitrogen monoxide pathways. ((Ingawale) and Namdeo, 2021)

CONCLUSIONS

WithaniaSomnifera Linn exhibited several clinical properties in medicine in the Indian system. In these studies that is done on animals, WithaniaSomnifera or its constituents shows many properties like, antarthritic, anti-inflammatory, antimicrobial, anti stress, anti-ischemic and ant hypoxic, Anti-Alzheimer, anti parkinsonian and neuroprotective types properties. The claim of uses of Withaniasomnifera is used to improve vigorously multi-purpose medicinal agent, and it appears to be promising. More clinical validation is needed before it can be used in primary care.

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Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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