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PHYTOCHEMISTRY AND PHARMACOLOGY IN WITHANIA SOMNIFERA (L.) DUNAL –A REVIEW

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ABSTRACT
Withania somnifera(Linn.) Dunal (Ashwagandha) is a plant used in medicine from the time of Ayurveda, the ancient system of Indian medicine. The dried roots of the plant are used in the remedy of fearful and sexual problems. This overview article is introduced to collect all the up to date statistics on its phytochemical and pharmacological activities, studies point out ashwagandha possesses antioxidant, reminiscence enhancing, antiparkinsonian, antistress, hematopoietic, antivenom, anti-inflammatory, antitumor properties. Various different outcomes like immunomodulation, hypolipidemic, antibacterial, cardivascular protection, sexual behavior, tolerance and dependence have also been studied. These consequences are very encouraging and indicate this herb have to be studied more drastically to confirm these results and expose other manageable therapeutic effects. Clinical trials the usage of ashwagandha for a range of prerequisites need to additionally be conducted.

KEYWORD: Withania somnifera, Asgand, Anti-inflammatory activity, Immunomodulatory activity, Unani medicine.

INTRODUCTION
Withania somnifera (WS), additionally recognised as ashwagandha, Indian ginseng, and wintry weather cherry, it has been an essential herb in the Ayurvedic and indigenous clinical systems for over 3000 years.[1] It is in use for a very lengthy time for all age businesses and each sexes and even at some stage in being pregnant barring any facet consequences.[2] In Sanskrit, 'Ashwa'means horse and 'gandha' capability smell. Therefore 'Ashwagandha' means "smell of a horse" and consequently indicate that the herb imparts the vigor andelectricity of a stallion[3] Withania somnifera is one amongst the foremost medicinal herb in Ayurveda cloth medica and the Acharya Charaka integrated the plant in Balya and Brimhana-gana.[4] From its historic use to its modern perspective, it has been tested to be superb and protected for wide vary of disorder condition. Designated as the "Sattvic Kapha Rasayana" in Ayurveda, Ashwagandha has been distinctly used as astringent, anti-carbuncle, anti-stress, tonic, narcotic, diuretic and in opposition to worms, piles, goitre, leucoderma, worried breakdown, insomnia and constipation. It is the roots of the plant that have been significantly used in Unani and Ayurvedic structures of medicine. Roots are said to incorporate 0.13–0.31% alkaloids, risky oils, starch, amino acids, glycosides, lowering sugars, and steroids.[5] Besides, the root, leaves are beneficial to remedy fever and swellings, plant life have been used as astringent, diuretics, fruits are used to deal with pores and skin ulcers, tumors, carbuncles and seeds are wonderful in growing sperm count as nicely as in testicular increase.[6] This evaluation encompasses the various pharmacological activities of W. somnifera (WS) that have been reported in the last two a long time with notes on its traditional use, phytochemistry, clinical and toxicological aspects.[7]

TAXONOMICAL CLASSIFICATION
Kingdom : Plantae, Plants;
Subkingdom : Tracheobionta, Vascular plants;
Super division : Spermatophyta, Seeds plants;
Division : Angiosperma
Class : Dicotyledons
Order: Tubiflorae
Family : Solanaceae
Genus : Withania
Species: somnifera Dunal

Botanical description: WS is a small, woody shrub in the Solanaceae family that grows about two feet in height. It can be determined growing in Africa, the Mediterranean, and India. An erect, evergreen, tomentose shrub, 30-150 cm high, found throughout the drier components of India in waste places

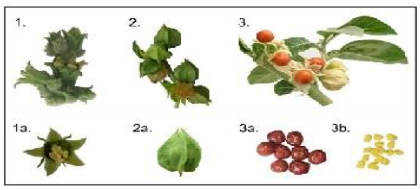
and on bunds. Roots are stout fleshy, whitish brown; leaves simple ovate, glabrous, these in the floral region smaller and opposite; flowers inconspicuous, greenish or lubrid-yellow, in axillary, umbellate cymes; berries small, globose, orange-red when mature, enclosed in the chronic calyx; seeds yellow, reniform. The roots are the main portions of the plant used therapeutically. The brilliant red fruit is harvested in the late fall and seeds are dried for planting in the following spring.

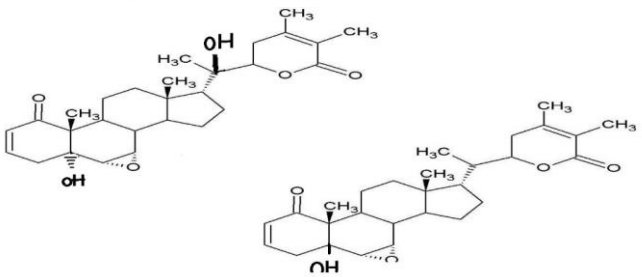
Parts used: Whole plant, roots, leaves, stem, green berries, fruits, seeds, bark are used.

Synonyms
Sanskrit: Ashwagandha, Turangi-gandha
English: Winter Cherry
Hindi: Punir, asgandh
Bengali: Ashvagandha
Gujrati; Ghodakun, Ghoda, Asoda, Asan
Telgu: Pulivendram, Panneru-gadda, panneru
Tamil: Amukkura, amkulang, amukkuram-kilangu, aswagandhi
Karnataka: Viremaddlinagadde, Pannaeru, aswagandhi, Kiremallinagida
Goa: Fatarfoda
Punjabi: Asgand, isgand
Bombay: Asgund, asvagandha
Rajasthani: Chirpotan

PHYTOCHEMISTRY OF WITHANIA SOMINIFERA

The phytochemicals profile of Withania somnifera always fascinating to researches because of is wide range of therapeutic application. The roots enrich with amino acid, alkaloids, dulcitol, glycosides hentriacontane, starch, steroid, reducing sugar, volatile oil, and withaniol.[7] Chemical constituents of WS are always of an interest for the researchers. The biologically active chemical constituents are alkaloids (ashwagandhine, cuscohygrine, anahygrine, tropine etc), steroidal compounds, including ergostane type steroidallactones, withaferin A, withanolides A-y, withasomniferin-A, withasomidienone, withasomniferols A-C, withanone etc. Other constituents include saponinscontaining an additional acyl group (sitoindoside VII and VIII), and withanolides with a glucose at carbon 27 (sitoindoside IX and X) (3, 4). Apart from these contents plant also contain chemical constituents like withaniol, acylsteryl glucosides, starch, reducing sugar, hantreacotane, ducitol, a variet amino acids including aspartic acid, proline, tyrosine, alanine, glycine, glutamic acid, cystine, tryptophan, and high amount of iron. The leaves of theplants comprise 12 editions of withanolides and 5 unidentified alkaloids. Withaferin A is the primary withanolide and in addition to that presence of free amino acids, condensed tannins, chlorogenic acid, flavonoids, glucose, and glycosides additionally current in leaves. As nicely the green berries comprise flavonoids, condensed tannis and proteolytic enzymes. Furthermore, the shoots specifically tender shoots are adequate supply of crude protein, calcium, flavonoids, phosphorous, condensed tannins and scopoletin (a coumarone).





A
Mol.formula =$C_{28}H_{35}O_6$
Mol.weight =470.59

B
Mol.formula=$C_{28}H_{35}O_5$
Mol.weight =454.61

PHARMACOLOGICAL STUDIES

Table No 1: Pharmacological Activity.

Antitumour Activity	Anti-inflammatory Activity
Antifungal Activity	Anti-ageing Effect
Antioxidant Activity	Hepatoprotective Activity
Anticonvulsant Activity	Antiviral Activity
Neuropharmacological Activity	Anti-stress/Adaptogenic Activity
Musculotropic Activity	Antibacterial Activity
Macrophage-Activating Effect	Anti-hyperglycaemic Effect

The drug consists of the dried roots of Withania somnifera which is authentic as a sedative in the pharmacopoeia of India. The pharmacological pastime of the roots is attributed to the presence of several alkaloids. The complete extract (70% alcoholic) of the roots possesses the equal houses as the complete alkaloids, however is almost half as robust. Centuries of Ayurvedic clinical journey the usage of Withania somnifera have published it to have pharmacological value as an adaptogen, antibiotic,aboritifacient, aphrosidiac, astringent, antiinflammatory, deobstruent, diuretic, narcotic, sedative, and tonic. Ashwagandha has been located to: Provide powerful antioxidant safety. Stimulate the activation of immune system cells, such as lymphocytes and phagocytes.[8] Counteract the results of stress and commonly promote wellness.[9]

ANTI-INFLAMMATORY ACTIVITY

Withaferin A exhibits fairly potent anti-arthritic and anti-inflammatory activities. Anti-inflammatory activity has been attributed to biologically active steroids, of which Withaferin A is a major component. It is as effective as hydrocortisone sodium succinate dose for dose.[10] It was found to suppress effectively arthritic syndrome without any toxic effect. Unlike hydrocortisone-treated animals which lost weight, the animals treated with Withaferin A showed gain in weight in arthritic syndrome. It is interesting that Withaferin A seems to be more potent than hydrocortisone in adjuvant-induced arthritis in rats, a close experimental approximation to human rheumatoid arthritis. In its oedema inhibiting activity, the compound gave a good dose-response in the dose range of 12-25 mg/kg body weigrats intraperitoneally and a single dose had a good duration of action, as it could effectively suppress the inflammation after 4 hours of its administration.[11] Asgand (Withania somnifera) has been shown to possess anti-inflammatory property in many animal models of inflammations like carrageenan-induced inflammation, cotton pellet granuloma and adjuvant-induced arthritis. Detailed studies were carried out to investigate the release of serum -1 globulin during inflammation by two models of inflammations viz. primary phase of adjuvant-induced arthritis and formaldehyde-induced arthritis. The experiments showed interesting results as most of the APR were influenced in a very short duration and also suppressed the degree of inflammation.[12]

ANTIOXITDANT ACTIVITY

An increase in these enzymes would representincreased antioxidant activity and a protective effect onneuronal tissue. Active glycowithanolides of WS were givenonce daily for 21 days, dose-related increased in all enzymes were observed; Iron overload induced marked increase in hepatic LPO and serum levels of the enzymes, which was attenuated by glycowithanolides (WSG) in a dose-related manner, and by silymarin.[13]

CARDIOVASCULAR PROTECTION

The alkaloids had a prolonged hypotensive, bradycardiac, and respiratory stimulant action in dogs. The study found that the hypotensive effect was mainly due to autonomic ganglion blocking action and that a depressant action on the higher cerebral centers also contributed to the hypotension. The alkaloids stimulated the vasomotor and respiratory centers in the brain stem of dogs. The cardio-inhibitory action in dogs appeared to be due to ganglion blocking and direct cardiodepressant actions. The alkaloids produced immediate predominant but short-lived cardiodepressant effects and a weak but prolonged cardiotonic effect in isolated normal and hypodynamic frog hearts. In another study, Left ventricular dysfunction was seen as a decrease in heart rate, left ventricular rate of peak positive and negative pressure change and elevated left ventricular end-diastolic pressure in the control group was recorded. WS showed strong cardioprotective effect in the experimental model of isoprenaline-induced myonecrosis in rats.[14]

ANTIDIABETIC

Many historical polyherbal formulations such as Dianix and Trasina ofIndian medicine confirmed potent antidiabetic endeavor in humans.[15,16] Patients administered with root powder of WS (3 g/day to each human issue for 30 days) were located to have a stabilized blood glucose concentration that ought to be compared to the impact of an oral hypoglycemic drug Daonil with no adverse effects.[17] Aqueous extracts of WS (200, four hundred mg/kg for 5 days) were determined to be effective in decreasing blood glucose, HbA1c, and insulin levels. Based on these reports, WS root and leaf extracts show up to be beneficial in improving glucose uptake in adipocytes and skeletal myotubes. However, the leaf extract was once found to exhibit a more stated effect than that of the root. Root and leaf extracts (200 and 400 mg/kg b.wt./day for eight weeks) significantly normalized the glucose levels in urine, blood, tissue glycogen, and glucose-6-phosphatase tiers in alloxan-induced diabetic rats. In addition to that, attenuated improvements of the enzymatic and nonenzymatic antioxidant defenses were also documented.[18] Phenolics and flavonoids existing in the extracts had been supposed to be accountable for the anti-diabetic activity. In addition, withaferin-A from WS may want to block the inflammatory responses brought about due to cytokine-induced injury to the islets of Langerhans in vitro after transplantation and it exhibited potential anti-glycating activity.[19,20]

ANXIOLYTIC AND ANTIDEPRESSANT

movements of the bioactive WSG,isolated from WS roots, in rats have been assessed. WSG was once administered orally as soon as every day for 5 days and the outcomes have been compared by means of these elicited with the aid of the benzodiazepine lorazepam for anxiolytic activity, and by way of the tricyclic antidepressant,imipramine. WSG brought about an anxiolytic impact used to be comparable to lorazepam, in the accelerated plus-maze, social interaction and feeding latency in an unfamiliar environment, tests. WSG additionally decreased rat Genius tiers of tribulin, an endocoid marker of medical anxiety, when the tiers have been increased following administration of the anxiogenic agent.[21,22]

TOLERANCE AND DEPENDENCE

Drug addiction, is one of the world's foremost fitness problem, with massive direct fitness costs. Chronic cure with benzodiazepine, ethanol or opioids precipitated tolerance and withdrawal signs. Benzodiazepine, ethanol and opioids induced tolerance and withdrawal additionally have blocked by using a polyherbal preparation, BR-16A (Mentat), which has WS as a one of its ingredient.[23,24,25]

ANTI-STRESS

Researchers the use of Withania somnifera located the animals given the herb an hour earlier than the foot shock skilled a appreciably decreased stage of stress. This lookup confirms the concept that Ashwagandha has a significant anti-stress adaptogenic impact.[26] Research carried out at the Department of Pharmacology, University of Texas Health Science Center indicated that extracts of Ashwagandha produce GABA-like activity, which may additionally account for the herb's anti-anxiety consequences.[27] GABA (Gamma Amino-butyric acid) is an inhibitory neurotransmitter in the brain. Its function is to limit neuron undertaking and inhibit nerve cells from over firing. This motion produces a calming effect.Excessive neuronal endeavor can lead to restlessness and insomnia, however GABA inhibits the wide variety of nerve cells that fireplace in the brain, and helps to result in sleep, uplift mood, and decrease anxiety. Ashwagandha has historically been used to stabilize temper in sufferers with behavioral disturbances. Research has published that the herb produces an anti -depressant and anti-anxiety impact in rodents similar to the anti-depressant drug imipramine and the anti-anxiety drug lorazepam (Ativan).[28]

ANTI-ISCHEMIC STROKE ACTIVITY

Stroke is a kind of acute cerebrovascular sickness that is the world's second best motive of mortality and a major supply of long-term impairment or everlasting in capacity[29,30]. Ischemic stroke is one of the most frequent motives of bodily harm in humans, accounting for roughly 87% of all strokes international.[31] Plasminogen activator is the solely clinically administered drug in ischemic stroke that serves solely a handful of patients. Several neuroprotective pills have been proved to be advantageous in animal fashions however failed miserably all through clinical trials, which led us to the present-day situation the place no neuroprotective pills are accessible for scientific use in ischemic stroke. Several research in animal fashions have highlighted the truth that pretreatment has proved to be a good deal fantastic than post-onset treatment, which has introduced about the notion of prophylactic neuroprotection.[32] Besides, reoccurrence is very ordinary in sufferers who have already skilled one incidence of stroke and a prophylactic approach for such sufferers is of utmost importance. One of the earliest reports of WS was once used as a continual remedy in an ischemic mannequin of stroke in rats to decide its prophylactic price in stroke sufferers who are at excessive chance.[33]

ANTI-ALZHEIMER'S DISEASE (AD) ACTIVITY

Alzheimer's ailment (AD) stands as one of the most well-known neurodegenerative illnesses that is acknowledged to have an effect on about 36 million people for the duration of the world.[34] The pathophysiology of AD is complex and characterised by using innovative loss of memory and cognizance of objects or persons, incapability of challenge performance, psychological signs like depression, intellectual upset, anxiety,and language deficits typically due to cholinergic neuronal degradation,dystrophic neuritis, gliosis, poisonous β-amyloid (Aβ) plaques,

strange neurofibrillary tangles and deficiency of critical neurochemicals necessary for regular neuronal transmission.[35] Oxidative stress due to overproduction of ROS during the early section of neuronal loss of life has been identified as a sign to set off apoptosis.[36] The function of aqueous extract of the root of WS in opposition to H2O2 and Aβ caused toxicity in vitro was once investigated by using Kumar et al.[37]

NEUROPROTECTIVE ACTIVITY

Neuroprotective things to do of WS have been nicely documented by usingmany studies. Reports received from preclinical researches and scientific trials have substantiated the neuroprotective function of WS.[38] Withanone discovered in the leaf extract can guard in opposition to scopolamine-induced toxicity in each glial and neuronal cells in experimental animals. Several neuronal mobile markers [Microtubule-associated protein two (MAP-2)], Neurofilament (NF)-H, Growth Associated Protein 43 (GAP-43) and postsynaptic density protein ninety five (PSD-95)], markers of glial cells [glial fibrillary acidic protein (GFAP)] and oxidative stress markers of DNA is located to be drastically decreased by means of WS extracts.[39] WS leaf extract may want to rescue retinoic acid differentiated IMR-32 and C6 cells from glutamatetoxicity. Pre-treatment with WS inhibited mobile phone loss of life through glutamate induction which similarly prompted reversal of glutamate evoked a stress response by means of upregulating HSP70 and restoring neuronal plasticity in neural CAMs, and its polysialylated structure.[40] The root extracts of the plant have been located to play a pivotal function against anxiety, depression, senile dementia, cognitive disorder, and many different neurodegenerative problems (such as Alzheimer's ailment and Parkinson's disease). Among the more than a few ingredients existing in the extract, glycowithanolides are principally accountable for neuroprotective activity owing to their greatest lipid peroxidation and inhibition properties. Later, in addition research have validated the attainable of withanolides and sitoindosides (VII-X) to improve the things to do of catalase and glutathione peroxidase.[41]

ANTICONVULSANT ACTIVITY

Administration of Asgand root extract was found to reduce jerks and clonus in 70% and 10% animals respectively with dose of 100mg/kg and reduction in the severity of pentylene tetrazole (PTZ)-induced convulsions was evident from EEG wave pattern. Asgand root extract showed reduction in severity of motor seizures induced by electrical stimulation in right basilateral amygdaloid nuclear complex through bipolar electrodes. The protective effect of Asgand extract in convulsions has been reported to involve GABAergic mediation.[42]

HYPOLIPIDEMIC EFFECT

In another study, hypoglycemic, diuretic and hypocholesterolemic effects of roots of WS were assessed on human subjects. Six mild NIDDM subjects and six mild hypercholesterolemic subjects were treated with the powder of roots of WS for 30 days. Suitable parameters were studied in the blood and urine samples of the subjects along with dietary pattern before and at the end of treatment period. Decrease in blood glucose was comparable to that of an oral hypoglycemic drug. Significant increase in urine sodium, urine volume, significant decrease in serum cholesterol, triglycerides, LDL (low density lipoproteins) and VLDL (very low density lipoproteins) cholesterol were observed indicating that root of WS is a potential source of hypoglycemic, diuretic and hypocholesterolemic agents.[43]

SEXUAL BEHAVIOR

Methanolic root extract of WS were orally administered at dose 3000 mg/kg/day of 7 days in rats. Their sexual behaviour was evaluated 7 days prior to treatment, day three and 7 of treatment, and day 7, 14 and 30 post-treatment by pairing each male with a receptive female. The WS root extract brought on a marked impairment in libido, sexual performance, sexual vigour, and penile erectile dysfunction. These effects were partly reversible on cessation of treatment. This antimasculine impact was not due to modifications in testosterone levels but attributed to hyperprolactinemic, GABAergic, serotonergic or sedative things to do of the extract. WS roots may be detrimental to male sexual competence.[44]

ANTIBACTERIAL PROPERTIES

Drug resistance in micro-organisms is a major and growing threat, although now widely recognized. In recent years, a significant increase in infections caused by drug-resistant strains has become a major problem. It is known that the reckless and often unwarranted use of antibiotics has resulted in the development of drug-resistant strains, and in some situations, these drugs have become completely ineffective. Ashwagandha, therefore, appears to be a valuable addition to pharmacotherapy in the treatment of bacterial infections. Many of the drugs currently used to treat bacterial infections, despite their efficacy, have many dangerous side effects related to their toxicity. Ashwagandha is a safe, non-toxic plant with almost no side effects. In the studies that have been conducted, it has been proven to effectively inhibit the growth of methicillin-resistant Staphylococcus aureus and Enterococcus spp,[45] Withania somnifera root extract has also been shown to effectively inhibit the growth of the Gram-negative bacteria Escherichia coli, Proteus mirabilis, Pseudomonas aeruginosa, Salmonella typhi, Citrobacter freundi, and Klebsiella pneumonia.[46,47]

CONCLUSIONS

Withania somnifera (Ashwagandha) is a plant used in remedy from the time of Ayurveda, the historical device

of Indian medicine. The plant has also been broadly studied for their a variety of pharmacological things to do like antioxidant, anxiolytic, adaptogen, reminiscence enhancing, antiparkinsonian, antiinflammatory, antitumor properties. Various different effects like immunomodulation, hypolipidemic, antibacterial, cardiovascular protection, sexual behaviour, have additionallybeen studied. Although the effects from this evaluation are pretty promising for the use of WS as a multi-purpose medicinalagent, quite a few obstacles presently exist in the cutting-edge literature. While WS has been used efficiently in Ayurvedic medicine for centuries, greater scientific trials ought to be performed to aid its therapeutic use.

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