REVIEW ARTICLE

Asgand (*Withania somnifera* (L.) Dunal - A prophylactic and immune-modulator AYUSH-Unani botanical drug

Mohd Kashif Husain[1], Khan Zeeshan Amanullah[2], Fahmeeda Zeenat[3], Wasim Ahmad[4], Ghufran Ahmad[5], Munawwar Husain Kazmi[1]

[1]Survey of Medicinal Plants Unit, National Research Institute of Unani Medicine for Skin Disorders (NRIUMSD- Under CCRUM), Hyderabad, Telangana, India, [2]Department of Qabalat wa Amraze Niswan, Mohammadia Tibbia College, Malegaon, Maharashtra, India, [3]Department of Amraze Niswan wa Atfal, Faculty of Unani Medicine, AMU, Aligarh, Uttar Pradesh, India, [4]Department of Ilmul Advia, Mohammadia Tibbia College, Malegaon, Maharashtra, India, [5]Department of Ilmul Advia, Faculty of Unani Medicine, AMU, Aligarh, Uttar Pradesh, India

Abstract

Withania somnifera (L.) Dunal is a valuable plant of family Solanaceae, which is commonly known as *Asgand* in Unani system of medicine (*Tibb-e-Unani*). The plant is found throughout the drier parts of India and other parts of the world. The main drug component comprises of the roots that is used for its therapeutic actions either singly or as an ingredient in compound formulations. *Asgand* is well described in Unani classics as *Musakkin* (sedative), *Muqawwi* (tonic) *Muhallil-e-waram* (anti-inflammatory), *Muaddil* (alterative), and *Muqawwi-e-Bah* (aphrodisiac). In Unani system, it is prescribed for rheumatism, gynecological disorders, cough, hiccup dropsy, and as a sedative in cases of senile debility. Studies indicate that the pharmacological activities of the root and leaf are attributed to the presence of several alkaloids and steroidal lactones including withanine, somniferine, somnine, and somniferinine. Leaves contain a group of (nearly twelve) "Withanolides" including "Withaferin-A" with antibiotic and anti-tumor activity. *Asgand* possesses anti-inflammatory, antioxidant, anxiolytic, adaptogenic, memory enhancing, antiparkinsonian, and antitumor properties. Several other effects such as immuno-modulation, cardiovascular protection, hypolipidemic, antibacterial, and sexual behavior, tolerance have also been studied. In conventional Unani system, enhancing immunity with immune-boosters is one of the key approaches for prevention of disease and maintenance of health. An attempt has been made in this review to explore the various dimensions of the drug *viz*; morphological, pharmacological, chemical studies and more specifically the therapeutic actions, uses and Unani perspective of *Asgand* in the time of Covid-19.

Key words: *Asgand*, *Withania somnifera*, AYUSH-Unani, medicinal plant, immune-enhancer

INTRODUCTION

Withania somnifera (L.) Dunal of family Solanaceae is one of the most valuable plants of the traditional Indian system of medicine. For centuries, the plant is widely used as a drug for the treatment of various disorders in Unani and other traditional systems of medicine. In Unani system, it is known as *Asgand* and the root of the plant is commonly used for its medicinal properties. Dioscorides (78AD) described the plant in his famous book "*Kitabul Hashaish."* The name *somnifera* is a species name which means "sleep-inducing" indicates its sedative properties.[1]

The plant is found throughout the drier parts of India, common in waste-lands, on dry soil near gardens and along the roadside. The *Asgand* plant is mainly cultivated for the medicinal root. Nowadays, except for a limited collection of roots from wild plants, most of the roots available in various markets in the country are obtained from the cultivated plants.[2,3] The cultivated plants are reported to differ from the wild ones not only in their morphological

Address for correspondence:
Dr Mohd Kashif Husain, National Research Institute of Unani Medicine for Skin Disorders (NRIUMSD- Under CCRUM), Hyderabad, Telengana, India.
E-mail: kashifptc@gmail.com

Received: 30-08-2021
Revised: 13-01-2022
Accepted: 24-01-2022

characters but also in their therapeutic action, though the same alkaloids are present in both the plants. Because of these differences, some botanists consider the cultivated plant distinct from the wild one and have given it a new specific name, *Withania ashwagandha*.[2,4]

Fresh part of *Asgand* smells like a horse that's why in Sanskrit it is known as *Ashwagandha, "Ashwa"* means horse and "*Gandha"* means smell.[5] The fresh roots of *W. somnifera* are collected usually during the months; January-March and shade dried for several days. The drug retains its therapeutic efficacy for <2 years. It is prone to decomposition and loses its potentials within 2 years. Hence, the fresh dried roots are preferred for medicinal uses. Two varieties of Asgand have been mentioned in classical Unani literature; "*Asgand Nagori"* and "*Asgand Dakhani."* Nagori is preferred for its more potential medicinal properties. The root is prone to worm and loses its potentials within 2 years.[5,6]

The commercial drug consists of the dried roots of *W. somnifera* which occur in small pieces, nearly 10.0–17.5 cm long and 6–12 mm in diameter. The bases of the stems are also present. The pieces are dark brown with a creamy interior. The stout fleshy roots when dry are cylindrical, gradually tapering down, straight and unbranched. The main roots bear fiber-like secondary roots.[2] The roots show buff to grey yellow outer color with longitudinal wrinkles. They are unbranched, straight, conical and some of them bear a crown. The root crown possesses a number of bud scars.[7] The stem bases are variously thickened, cylindrical and green and have longitudinal wrinkles. The roots have a short and uneven fracture, strong odor and mucilaginous bitter, astringent and acrid taste. Fresh roots smell similar to the urine of horses (hence ashwagandha).[7]

The powdered drug is greyish with pungent odor and acrid taste. The pharmacological activity of root is attributed to the presence of several alkaloids.[2] Fruits, seeds, leaves and roots are therapeutically used as a drug.[8] However, the dried root of the plant is used more commonly for medicinal purposes.[9]

Botanical Name

W. somnifera (L.) Dunal.

Classification

Kingdom: Plantae
Subkingdom: Tracheobionta
Superdivision: Spermatophyta – Seed plants
Division: Magnoliophyta – Flowering plants
Class: Magnoliopsida – Dicotyledons
Subclass: Asteridae
Order: Solanales
Family: Solanaceae
Genus: *Withania*
Species: *W. somnifera* (L.) Dunal.

Figure 1: a. Plant of Asgand - *Withania somnifera* (L.) Dunal; b. Dried Roots

Occurrence and Distribution

It is found throughout drier and subtropical parts of India; Madhya Pradesh, Uttar Pradesh, Punjab plains, and North-Western such as Gujrat and Rajasthan[7-10] mostly on waste places and bunds. It is extensively cultivated in Manaasaa (district Manasor) and Ganj Basodaa (district Vidisha) of Madhya Pradesh.[4] This shrub is common in Bombay and western India, occasionally met within Bengal.[11] It is also found in Sri Lanka, Afghanistan, Baluchistan, and Sindh. It is distributed in the Mediterranean regions, the Canaries, and Cape of Good Hope[10-12] and also found in Congo, South Africa, Egypt, Morocco, Jordan, Pakistan, and Afghanistan.[7]

Vernaculars

The plant is known by different vernacular names in different language, areas and traditions;[3,8,9,13-16]

Arabic: Kaknaj Hindi

Bengal: Ashvaganda, Ashvagandha, Asvagandha, Ashranda;

Bombay: Asgund, Asvagandha, Asgund, Asagandha

Cutch: Asuth

Deccan: Hindikaknuj, Natkiasgand

English: Winter Cherry

Goa: Fatarfoda

Gujarati: Ghodakun, Ghoda, Asan, Asoda, Ghodaasoda, Asundha

Hindi: Ashvagandha, Asgandh, Punir, Asgand

Marathi: Askandha, Kanchuki

Kan: Viremaddlinagadde, Pannaeru, Aswagandhi, Kiremallinagida, Amangura

Malayalam: Amukkiram, Amukirram, Pevetti, Pevette

Persian: Asgand, Kaknaj Hindi, Mehernan Barari

Punjab: Asgand, Isgand, Ak, Aksan, Asgand, Asgandnagori, Isgand Pushtu: Kutilal, Sin

Oriya: Asugandha

Rajasthan: Chirpotan

Sanskrit: Ashvagandha, Ashvakandika, Ashvaroha, Ashvavarshaka, Balada, Balaja, Gandhapatri, turangi-gandha

Siddha: Amukkura, Amkulang, Amukkuram-kilangu, Amulang-kalung

Tamil: Ashwagandhi, Achuvagandi, Amkulang-kalang, Amukaran-kizhangu, Amukkira-Kilzhangu, Amukkira, Asubam, Asuvagangi, Asuvagandi

Telugu: Pulivendram, Panneru-gadda, Panneru, Aswagandi, Dommadolu, Penneru, Vagigandha, Asvagandhi, Vajigandha, Pillivendramu, Asvagandhi, Penneroo-gadda

Unani: Asgandh, Aswagandha

Urdu: Asgand Nagori

Botanical Description

Morphology

W. somnifera is an evergreen, erect, branched undershrub 0.3–1.5 m high, thinly woolly, tomentose, with stellate tomentose hairy plant parts.[10,2] Usually clothed with mealy stellate hairy tomentum.[12]

Leaves

Leaves are simple ovate glabrous[10], those in floral region smaller and opposite.[2] They are 5–10 by 2.5–5 cm, ovate, subacute, entire[8,14] more or less minutely stellately pubescent, base acute; main nerves about 6 pairs, stout, conspecious; petioles 6–13 mm long, stellately tomentose.[12]. Leaves of *Asgand Dakni* are broad at end, long, pointed velvety and soft.

Flower

Flowers are greenish or lurid-yellow, usually about five together in a sessile or nearly sessile umbellate cymes;[9,14] pedicles 0.4 mm long;[12] axillary, sessile or shortly pedicelled, fascicled or solitary [Figure 1a], hermaphrodite.[8]

Calyx 5-mm long, stellately tomentose. Calyx campanulate, acutely 5–6 toothed,[8] Calyx-teeth short very acute; teeth 2.5 mm long, linear, acute, from a deltoid base.[12] Fruit-calyx inflated, papery, larger than the berry.[8,10]

Corolla 8 mm long, divided rather more than ½ way down; lobes lanceolate, acute, pubescent outside.[12] Corolla campanulate; lobes 3–6 and short, greenish or lurid yellow. Stamens attached near the base of the corolla.[8]

Filaments 3 mm long, slender, glabrous; anthers broadly elliptic (almost orbicular), 1.25 mm long. Ovary glabrous; style glabrous.[12] Ovary 2-celled, stigma shortly 2-fid.[8]

Berries

These are small globose, green when raw, orange-red when mature, enclosed in persistent calyx.[9] Berry red, smooth, 6 mm diameter, enclosed in the inflated calyx which reaches more than 2.5 cm diameter and is globose, slightly 5-angled, pointed with the connivent calyx-teeth and scurfy-pubescent outside.[12] Fruit ripens in spring and becomes yellow yearly.

Seed

Seeds are many, discoid, 2.5 mm in diameter, somewhat scurfy, yellow, reniform in shape.[8,9,12]

Roots

The roots are stout fleshy, slightly brownish [Figure 1b], white or buff in color with no characteristic odor, bitter and acrid in taste.[9,14]

Organoleptic Characters

The roots are slightly brownish, white or buff in color with no characteristic odor, bitter and acrid in taste.

Microscopic

The transverse section (T.S.) of root shows exfoliated cork which is non-lignified with 2–4 layers of phellogen and about 15–20 rows of phelloderm. It prominently shows parts of vascular tissue like cambium, consisting of 3–5 layers of tangentially elongated cells, phloem region with parenchyma, sieve tubes and companion cells. Secondary xylem is hard which forms a continuous vascular ring interrupted by medullary rays. The T.S. of stem base consists of pith, pericyclic fibers, xylem with tracheids, fibers, and starch grains.[7]

Cultivation

The propagation of *W. somnifera* is done by seeds, for which about 4–5 kg of seeds are required per hectare.[7] The seeds are sown in the nursery just before the onset of the rainy season. Excessive rain is harmful, as it leads to unwarranted weed growth.[9] The sowing is done in June-July, and no special arrangements are made for irrigation during growth. The plants bear flowers and fruits in December. Harvesting starts in January and continues till March. The plants from different sources vary in their morphological and therapeutic properties.[8] Nowadays, the cultivation is done at many places, including Madhya Pradesh (Manasa Plantations), where, nearly 2000 hectares of lands are under cultivation.

The entire plant is uprooted for roots, which are separated from aerial parts by cutting the stem (1–2 cm) above the crown. They are then transversely cut into smaller pieces for drying. The dried whole roots undergo cleaning, trimming and grading before dispatch. They are beaten with a club to remove adhering soil and the thin lateral rootlets. The main tap-root may be cut into transverse pieces. Based on thickness and uniformity of pieces, the entire produce is then carefully hand sorted into four grades. The fourth grade consists of

thin and wiry roots, rarely exceeding 3 mm diameter and are practically useless as a drug.[9] The dried roots, cut into smaller pieces, may be stored in air tight tin or glass containers free from moisture. Some preservative may also be used to save the roots from the attack of insects and pests.[9]

Unani Description

Mizaj (temperament)

Most of the Unani physicians have described the *Mizaj* of *Asgand* as Hot and Dry[17] in 3rd degree,[5,15,16,18,19] while a few described it to be Hot in 2nd degree and Dry in 1st degree and Hot and Dry in 1st degree.[6]

Afa'al (action)

As per the classical Unani literature, *Asgand* expels *balgham* (phlegm) and *sauda* (black bile). Various actions including *Musakkin-i-Dimagh* (sedative), *Muqawwi* (tonic); *Muhallil-e-Awarm* (anti-inflammatory), *Mufattit-i-Hasah* (lithotropic), *Muqawwi-e-Gurda* (renal tonic), *Muqawwi-e-Hawas, Mulayyan-e-Tabiyat, Taqtir al-Bawl* (dribbling of urine), *Muqawwi-e-Badan, Muqawwi-e-Bah* (aphrodisiac), *Muqawwi wa Munaqqui-e-Rahem, Muqawwi-e-Hafiza*,[5] *Mubhi, Muzayed Mani, Muzayed Sheer;*[6] *Mowallid wa Mughalliz-e-Mani* (spermatogenic, increases semen viscosity), *Musallibe Pistan wa Zakar, Nafe Aujae Mafasil, Dafe Jaryan* (spermatorrhea),[15] *Mowallid-e-Labn* (galactagogue);[16] *Mulattif* (demulcent);[6] *Muqawwi-e-Aam* (general tonic), *Moaddil, Muddir, Mufateh-e-Sudad, Musakkin-e-Asab, Dafe Sual* (cough/bronchitis) *wa Amraze Balghami*,[18] *Muqawwi-e-Kamar, Dafe Dard Kamar* (backache)[17] have been attributed to *Asgand* for which it is commonly used in clinical practices.

Istema'al (uses)

Asgand is therapeutically useful in *wajaul mafasil* (arthritis), *wajaul qutn* (lumbago), *zofe aam* (general debility), *zofe bah* (sexual debility), and *sailanur rahem*.[9] It relieves *Amraze Jigar* (hepatic disorders) and bars (leukoderma) and improves overall health of the body. It is dafe of *fasade balgham wa sauda*.[17] It relieves from morbid phlegm (*fasade balgham)* [5] and gathiya (joint pain).[19] In Indian subcontinent, it is used as substitute of Bahman Safed (*Centaurea behen* L.), that's why it is used as an important ingredient in compounds used for *taqwiyate bah.* It gives strength to the uterus and hence is used after delivery to restore the normalcy of uterine muscle.[6] In arthralgia, it can be used externally as well internally and is considered a substitute for suranjan. It is beneficial in *muzmin khansi* (choronic cough), *muzmin dama* (chronic asthma) *warm aaza* (chronic inflammatory condition of organs), (leukoderma) bars and jaryane mani, and senile debility.[5,15,16,17,19].

Decoction prepared by boiling 5 g root powder in 250 ml milk is used for the gynecological disorders at the dose of 20 g twice a day.[19] It is useful in riqqate mani. It is used in the form of tila for the treatment of inflammatory conditions.[15,16]. In menorrhagia, *Asgand*- 3 g, *Raal Safeed* - 2 g with *Misri*- 6 g is usually given with water. It relieves constipation and loosens the stool. It is also used for the treatment of renal and bladder calculi. It is beneficial in dribbling of the urine.[5] Powder of *Asgand* with cow milk is used to increase quantity of sperms (*mani)* and beautify the skin. Fresh leaves are applied to painful swelling. It is used as general tonic to increase energy. It is useful in inflammatory condition of the organs particularly *warm khusiya*. Seeds are employed to coagulate milk.[5,6,16,17]

Muzir (adverse effect)

Asgand is harmful to the individual of hot temperament *Garm Mizaj* (*Mahrooreen)*. It also harms the throat (*Halaque)*. [5,6,16,17]

Musleh (corrective)

Gond Katira and *Ghee* are used as corrective if the hot temperament person *Garm Mizaj* (Mahrooreen) is being treated with Asgand.[15,16,17,19] Gargle with *Sharbat-e-Toot* acts as corrective if *Asgand* has an adverse effect on Halaque.[6]

Badal (substitute)

Asgand may be substituted by *Bahman Safed* in the same ratio. Suranjan (*Colchicum luteum*) and Qust may also be used as the substitute of *Asgand*.[15,16,17,19]

Dose (Miqdar-e-Khurak)

- 2 g[9]
- 3–4 g[6]
- 3–5 g[15,16]
- 3–6 g[4]
- 4–6 g[17]
- 14 g.[5]

Important Unani Formulations

- Habb-e- Asgand
- Safoof-e- Asgand
- Halwa-e- Gheekawar
- Ma'joon Muqawwi-e- Rahem
- Ma'joon Pamba Dana
- Ma'joon Samagh
- Ma'joon Zanjbil
- Majoon Salab
- Sarbat Niswan

Ethnobotanical Importance

The drug *Asgand* is described in detail in ethnobotanical and scientific literature. It has sedative and hypnotic effects and works as an immune-modulatory agent. It has hypotensive,

respiratory stimulant action along with bradycardia.[7] The root is regarded as alterative, aphrodisiac, deobstruent, diuretic, tonic, narcotic, and abortifacient.[3,8,11-14] It also possesses astringent and nervine sedative properties. The root is classified as adaptogenic, tranquilizer, and anti-inflammatory. It has been found to decrease the degree of anxiety and depression and can be used as an antidepressant.[8]

Koya tribes used the root to maintain the diabetes. Its powder is given 2 times a day for 10–15 days to control diabetes. The leaves are bitter, anthelmintic and antipyretic.[8,20] It also possesses narcotic property. Bitter leaves and roots are used as a hypnotic in alcoholism and emphysematous dyspnea. The fruit possesses diuretic property. The seeds are employed to coagulate milk and they also contain poisonous properties. They also have diuretic and hypnotic properties.[8,11,20,21]

Therapeutic Uses

The root of the plant is a valuable remedy for rheumatism, senile debility, emaciation of children, general debility and loss of appetite,[12] nervous exhaustion, spermatorrhea, brain fag, loss of memory and loss of muscular energy. It is also used in hiccup, cough, dropsy, inflammation, ulcers and scabies. The paste of root is applied to the penis for toning up erectile tissues. The paste of root mixed with mother's milk is applied to sagging the breasts.[8,11,21]

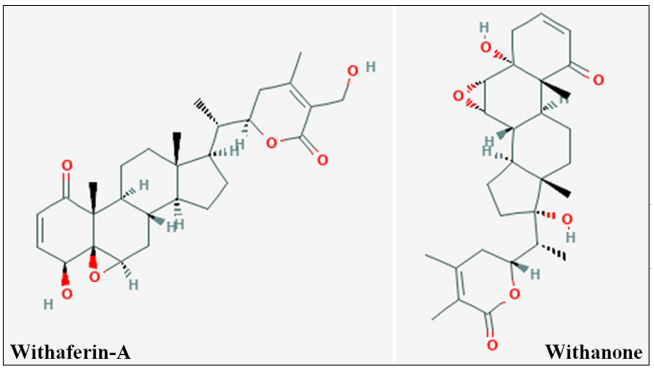
Its compound formulation *Habb-e-Asgand* is prescribed as a supporting aphrodisiac and nervine tonic.[4] The root is useful in leukorrhea, menstrual troubles, restores loss of memory; used in cases of senile debility; powder with an equal part of *ghee* and honey beneficial in impotency or seminal debility; decoction boiled with milk and *ghee* promotes nutrition.[8] Conventionally, it has been used in treatment of rheumatism, gout, hypertension, nervine, and skin diseases. This drug prevents bony degenerative changes in arthritic conditions. It has been widely used as sex stimulant and rejuvenator and is considered as a strength and vigor promoting drug especially in geriatric cases.[7]

Asgand infuses fresh energy and vigor in a system worn out due to any constitutional disease such as syphilis, rheumatic fever, or from over-work and thus prevents premature decay. As nutrient and health restorative to the pregnant and old people, a decoction of the root is recommended; or its powder with milk may be taken. The decoction boiled down with milk and with ghee added to the mixture is recommended for curing the sterility of women. Root is used as an application in obstinate ulcers and rheumatic swellings. It is therapeutically useful in asthma, cough and uterine diseases.[11]

Locally, root powder and decoction are given in debility, rheumatism, nervous complaints, and seminal disorders.[3] The root is useful in inflammations, ulcers and scabies when applied locally. In the Kuchchh district of Gujarat, roots are used as uterine tonic in sterility.[22] Root and leaves are used to relieve the emphysematous dyspnea.[8] A decoction of the root is used for cold and chills, while few administer it to tone up the uterus in women who habitually miscarry and to remove the retained conception products. Some people also take an infusion of the bark for asthma. In Punjab, it is used for lumbar pains and considered aphrodisiac. An enema of the decorticated root is given by some people to feverish infants. They regard the plant as a specific for gangrenous rectitis, using an infusion of the root as an enema. They also use the plant in treating syphilis and successfully employ the leaf in the healing of sores.[12]

In Unani system, the drug acts as an anti-inflammatory, restorative, general tonic, and aphrodisiac. It is useful for the treatment of arthritis, anxiety, insomnia, tumors, tuberculosis, asthma, leukoderma, bronchitis, backache, fibromyalgia, menstrual problems, hiccups, and chronic liver diseases, stress and nervous disorders. While in Ayurveda the tuber has been described to be useful in inflammations, psoriasis, bronchitis, asthma, consumption, ulcers, scabies and marasmus of children, insomnia and senile debility.[12] The bruised leaves and ground root are employed as a local application to painful swellings, ulcers, carbuncles and scabies. Leaves are used in fever and sore eyes.[8,12,14]

A fomentation of the leaves is used to cure sore eyes; it cures boils and swellings of the hand and feet, causing the boils to ripen and burst. In some region, the leaves are used for killing the lice. The leaves are applied to tumors and tuberculous gland. Infusion of leaves is given in fever.[12] Some people apply fresh juice of the leaf to anthrax pustules. They make an ointment for wounds and sores by boiling the leaf in fat, and administer of the root bark in asthma and other chest complaints. A paste of leaf applied to syphilitic sores, erysipelas; decoction of leaf externally and internally used in treatment of the hemorrhoids. Some apply an ointment of the leaf to bed sores. The green berries are bruised, and rubbed into ringworm in both human beings and animals. The flowers are applied to sores.[12]



Plant growing in Southern Europe is found to contain a bitter alkaloid "Somniferine" having hypnotic property; also resin, fat and coloring matters. Reducing sugar, phytosterol,

ipuranol, mixture of saturated and unsaturated acids and a small quantity of a basic substance supposed to be an alkaloid have been isolated.[11]

Roots contain the alkaloids nicotine, somnine, somniferine, somniferinine, withanine, withananine, withananinine, pseudo-withanine, tropine, pseudotropine, 3-alpha-tigloloxytropane, choline cuscuolohygrine, anaferine and its DL-form, isopelletrierine, anahygrine, withasomine and visamine. Root also contains the withanolides.[4] In addition to alkaloids they also contain starch, reducing sugars, hentriacontane, glycosides, dulcitol, withaniol (0.08%), an acid (m.p. 280-83), and a neutral compound (m.p. 294-96). The total alkaloidal content of Indian roots has been reported to vary between 0.13 and 0.31%, though much higher yields (up to 43%) have been recorded elsewhere. The wide variations in the yields might be due to factors, such as methods of isolation used, variability in species, environment, and wild or cultivated forms. The free amino acids identified in the roots include aspartic acid, glycine, tyrosine, alanine, proline, tryptophan, glutamic acid, and cysteine. The roots of South African origin yielded a small amount of a light brown, pungent volatile oil.[2] A C-28 steroid lactone isolated from roots and identified as 5,20α-dihydroxy-6α,7α-epoxy-1-oxowitha-2,24-dienolide (withanolide),[23] isolation of two new glycowithanolides sitoindoside IX and sitoindoside X from roots.[24]

Leaves contain 12 withanolides including withaferin-A, 27-deoxy withaferin A and 27-deoxy-14-alpha-hydroxywithaferin A.[4] In addition to withanolides, the leaves from Delhi region contained five unidentified alkaloids (yield, 0.09%), glycosides, glucose, many free amino acids, chlorogenic acid, condensed tannins and flavonoids. Nine new steroidal lactones-withanolides E, F, G, H, I, J, K, L and M-isolated from leaves seven of these characterized as 20-hydroxy-1-oxo-20R, 22R-witha-2,5,8(14), 24-tetraenolide (withanolide G), 20,27-dihydroxy-1-oxo-20R, 22R-witha-2,5,8(14), 24-tetraenolide (withanolide H), 20-hydroxy-1-oxo-20R, 22R-witha-3,5,8(14), 24-tetraenolide (withanolide I), 17,20-dihydroxy-1-oxo-20S, 22R-witha-2,5,8(14), 24-tetraenolide (withanolide J), 17,20-dihydroxy-1-oxo-20S, 22R-witha-3,5,8(14), 24-tetraenolide (withanolide K), 17,20-dihydroxy-1-oxo-20S, 22R-witha-2,5,14, 24-tetraenolide (withanolide L) and 17,20-dihydroxy-1-oxo-14, 15α-epoxy-20S, 22R-witha-2,5, 24-trienolide (withanolide M).[23] A new steroidal lactone (I), three new withanolides (II, III and IV), 14β-hydroxywithanone, 14α-hydroxywithanone, 14α,20-dihydroxy-1-oxowitha-2,5,16,24-tetraenolide (V) isolated.[25]

Pharmacological Studies

A number of studies on the pharmacological actions of *W. somnifera* have been carried out in recent years which clearly show that it possesses diverse pharmacological effects. Few important effects are as follows;

Antianxiety/Antistress

In a study, it has been revealed that *Asgand* produced an anti-depressant and anti-anxiety effect in rodents comparable to the anti-depressant drug imipramine and the anti-anxiety drug (Ativan) lorazepam. The anti-stress Activity of *W. somnifera* was conducted in rats using cold water swimming stress treatment, and it was found that the drug treated animals showed better stress tolerance.[26] Extracts of *W. somnifera* produced GABA-like activity, which may account for the herb's anti-anxiety effects.[27] The anxiolytic and antidepressant actions of the bioactive Glyco-Withanolides (WSG) isolated from *W. somnifera* roots, was designed to investigate in rats. WSG exhibited an antidepressant effect, comparable with that induced by imipramine, in the forced swim-induced "behavioral despair" and "learned helplessness" tests. The investigations supported the use of WSG as a mood stabilizer in clinical conditions of anxiety and depression.[28]

Antibacterial/Antifungal/Antiviral activity

Withaferin-A was found to be active against *Micrococcus pyogenes* var *aureus* and partially inhibited the activity of *Bacillus subtilis* glucose-6-phosphatedehydrogenase. Both aqueous as well as alcoholic extracts of *W. somnifera* plant (root as well as leaves) possessed strong antibacterial activity against a range of pathogenic bacteria.[29] Withaferin-A at 10 μg/ml, inhibited the growth of various Gram-positive bacteria, acid-fast, aerobic bacilli, and pathogenic fungi. The extract of *Asgand* has been found to be active against *Vaccinia* virus and *Entamoeba histolytica*. Withaferin-A inhibited the Ranikhet virus.[30] *Withania* showed the protective action against systemic *Aspergillus* infection, may be related to the activation of the macrophage function, increased phagocytosis and intracellular killing of peritoneal macrophages.[31] The lactone of Withaferin-A showed strong therapeutic Activity in experimentally induced abscesses in rabbits, the being somewhat stronger than that of *Penicillin*. It demonstrates that the *Asgand* leaves as a cure for ulcers and carbuncles in the indigenous system of medicine.

Arora *et al.* evaluated the methanol, hexane and diethyl ether extracts from both leaves and roots of *W. somnifera* for the antibacterial/synergistic activity by agar plate disc-diffusion assay against *Salmonella typhimurium* and *Escherichia coli*. Out of six extracts tested, only methanol and hexane extracts of both leaves and roots were reported to have potent antibacterial activity.[32]

Anticancer activity

A dimeric withanolide "Ashwagandhanolide," with an unusual thioether linkage isolated from the roots of *W. somnifera* displayed growth inhibition against human gastric, breast (MCF-7), central nervous system (SF - 268), colon (HCT-116), and lung (NCI H460) cancer cell lines, with IC50 values in the range 0.43–1.48 μg/ml. The dimer also inhibited the

lipid peroxidation and the enzyme cyclooxygenase-2 activity *in vitro*.[33]

In vitro and *in vivo* study on pancreatic cancer cell by Yu *et al*. revealed, *in vitro* anti-proliferative activity of withaferin against pancreatic cancer cell lines Pac-1, MiaPaCa and BxPc3 with IC50 value of 1.24, 2.93, 2.78 µ, respectively. The study also showed that withaferin-A binds to Hsp90, inhibited the chaperone activity through an ATP-independent mechanism, resulted in its client protein degradation and exhibited *in vivo* anticancer Activity against pancreatic cancer.[34] Withanolide sulfoxide (A novel bioactive compound) obtained from the methanol extract of *Asgand* roots has been shown to inhibit the nuclear transcription factor-kappa-B, cyclooxygenase and tumor cell proliferation against the human breast (MCF-7) cancer cell lines.[35]

W. somnifera extracts containing complex mixtures of different components like withferin-A, have exhibited inhibitory activities against breast, colon, prostate, colon, ovarian, lung, and brain cancer.[36] Ethanol extract of *W. somnifera* root reported to be a novel inhibitor of fatty acid synthesis in human prostate cancer cells; LNCaP and 22Rv1.[37]

Antidiabetic activity

Antidiabetic potential of leaf and root extracts of *W. somnifera* were evaluated against 3T3F442A fibroblast (3T3 adipocyte) cell line using glucose uptake assay. Leaf was found to be active on the cell line tested. Isolated fractions and standard Withaferin-A and Withanolide-A were found active at 20 µg/ml. Crude extract of *W. somnifera* have shown good antidiabetic potential indicating the synergistic effect of the extract on glucose uptake of 3T3 fibroblast in presence of insulin.[38]

Jena *et al.* explored the possibilities of using the *in vitro* and *in vivo* root and leaf extracts of *W. somnifera* for anti-diabetic and anti-hyperlipidemic effects on streptozotocin-induced diabetic rats. The study revealed that the methanolic *in vitro* root extract at the dose 300 mg/kg has more potent anti-hyperglycemic activity than the other *in vitro* and *in vivo* extracts of leaf and root on streptozotocin induced diabetic rats. They also found *in vitro* root extract effect to that of the standard drug Glibenclamide.[39]

W. somnifera root extracts (WSREt) and leaf extracts (WSLEt) were orally administered daily to Streptozotocin-induced diabetic rats for 8 weeks to examine their hypoglycemic and hypolipidemic effects. After the treatment of the diabetic rats with root and leaf extracts altered the changes and restored the blood glucose, serum enzymes and other parameters after 8 weeks of treatment. The finding indicated that the WSREt and WSLEt possess hypoglycemic and hypolipidemic properties.[40]

Antihypothyroidism

The effects of WSREt on thyroid function in female mice revealed significant increase in serum T4 while no change found in T3 levels. It also stimulated the thyroid activity indirectly through its effect on cellular antioxidant systems.[41]

Anti-inflammatory

Root powder of *W. somnifera* decreased the air pouch granuloma induced by carrageenan on the dorsum of rats. It decreased the glycosaminoglycans content in the granuloma tissue more than hydrocortisone treatment, also uncoupled the oxidative phosphorylation by significantly reducing the ADP/O ratio in mitochondria of granuloma tissue.[42] *W. somnifera* leaf water extract and one of its active chloroform fractions exhibited the anti-neuroinflammatory activity due to the combination of Withanone and Wit A as active components.[43]

Anbalagan and Sadique reported that *Asgand* (*W. somnifaera*) root extract (1 g/kg, oral) reduced Freund's complete adjuvant induced inflammation in rats. Phenylbutazone was given as a positive control. In the *Withania* group the α2-glycoprotein found only in inflamed rat serum was decreased to undetectable levels. Phenylbutazone, on the other hand, caused a considerable increase in the α2- glycoprotein in both arthritic and healthy rats.[44]

Withaferin-A, a major component of naturally occurring steroids of *W. somnifera* has shown the anti-inflammatory activity and is reported to be as effective as an anti-inflammatory drug "hydrocortisone sodium succinate."[30] A study by Al-Hindawi found *W. somnifera* inhibited the granuloma formation in cotton-pellet implantation in rats and the effect was comparable to hydrocortisone sodium succinate (5 mg/kg) treatment.[45] Oral administration of *Asgand* powder 1 h before the injection of inflammatory agent for 3 days produced anti-inflammatory responses which are comparable to hydrocortisone sodium succinate.[46]

Antioxidant/Antiageing

An *in vitro* antioxidant activity of extract of different parts of *W. somnifera* showed that leaves and tubers are the potential scavengers of radicals and protector of lipid membrane in order of; leaves >fresh tubers >dry tubers. The antioxidant activity may be due to withanolides, glycowithanolides, and sitoindosides VII-X. *Asgand* could be a natural source of safe anti-oxidative agent.[47]

Alam *et al.* evaluated the antioxidant and antibacterial activities of an 80% aqueous methanolic extract of WSREt, *W. somnifera* fruits (WSFEt) and *W. somnifera* leaves (WSLEt). Several assays were performed to determine the antioxidant properties of this herb including 1,1-diphenyl-2-picrylhydrazyl radical scavenging activity, ferric reducing antioxidant power, ferrous chelation and inhibition of

β-carotene bleaching. The findings indicated that the leaves of *W. somnifera*, possesses significant antioxidant properties.[48]

Antitumor Effect

The alcoholic extract of the dried roots of the plant as well as the active component withaferin-A isolated from the extract showed significant antitumor and radio-sensitizing effects in experimental tumors *in vivo*, without any noticeable systemic toxicity.[49] An *in vitro* study showed *W. somnifera* extracts may prevented or inhibited the tumor growth in cancer patients. The finding suggests that the plant may be a potential source for the development of new chemotherapeutic agent.[50] The chemo-preventive effect of WSREt on induced skin cancer was investigated in mice. The results revealed a significant decrease in incidence and the average number of skin lesions.[51]

Immunomodulatory Activity

Administration of *W. somnifera* was found to increase total WBC and bone marrow cells significantly indicating that the extract could stimulate the hemopoetic system.[52] Agrawal *et al.* studied the immune-modulatory activities of *Asgand* extracts namely; WST and WS2, in mice for immune inflammation. A significant increase in white blood cell counts and platelet counts was observed in animals treated with WST. A protective effect in cyclophosphamide-induced myelo-suppression was observed in animals treated with WST and WS2, revealing a significant increase in white blood cell counts and platelet counts. Cyclophosphamide-induced immune-suppression was counteracted by treatment with WS2, revealing significant increase in hemagglutinating antibody responses and hemolytic antibody responses towards sheep red blood cells.[53]

The aqueous suspension of *W. somnifera* root powder was investigated for their *in vivo* and *in vitro* immune-modulatory properties and it showed potent inhibitory activity towards the complement system, mitogen induced lymphocyte proliferation and delayed-type hypersensitivity reaction. The immune-suppressive effect of root powder, reported to be a candidate for developing as an immunosuppressive drug for the inflammatory diseases.[54]

Cardioprotective Activity

Cardioprotective effect of hydroalcoholic extract of *W. somnifera* was studied on the basis of hemodynamic, histopathological and biochemical parameters in the isoprenaline- (isoproterenol) induced myocardial necrosis in rats and was compared with vitamin E, a known cardioprotective antioxidant. Both the drugs restore the myocardial antioxidant status and maintain membrane integrity by evidently reducing the malonyldialdehyde levels. Cardioprotective effect of these drugs was also confirmed by histopathological examinations. The findings showed that *W. somnifera* (25, 50 and 100 mg/kg) exerts a strong cardioprotective effect in the experimental model of isoprenaline-induced myonecrosis in rats. Augmentation of endogenous antioxidants, maintenance of the myocardial antioxidant status and significant restoration of most of the altered hemodynamic parameters may contribute to its cardioprotective effect. Among the different doses studied, *W. somnifera* at 50 mg/kg dose produced maximum cardioprotective effect.[55]

Hypolipidemic Activity

A hypocholesteremic and antioxidant effect of *Asgand* was investigated in hypercholesteremic male albino rats. The result showed significant decreases in total lipids, cholesterol, and triglycerides in plasma, and significant increase in plasma HDL-cholesterol levels and bile acid content of liver.[56]

Neuroprotective/Anti-parkinsonism Activity

Neuroprotective effects of *W. somnifera* extract at a dose of 100, 200 and 300 mg/kg, on 6-hydroxydopamine induced Parkinsonism in rats has been reported. The findings of the results demonstrated that the *Asgand* extract significantly reversed all the parameters (glutathione content, activities of glutathione-S-transferase, glutathione reductase, glutathione peroxidase, etc.) to normal in a dose dependent manner. The extract may be helpful in protecting the neuronal injury in Parkinson's disease.[57]

DISCUSSION

Unani physicians have recommended certain single herbs and compound formulations that may possibly be used as health protecting drugs during pandemics. They have emphasized more on the use of certain drugs which are known to improve host immunity during the outbreak of epidemics and, endemics.[58] Most probably, Unani scholars were somehow aware of many drugs that they used for the promotion of health. Razi described that "people who remain physically active and exercise regularly have a lesser susceptibility to epidemic diseases."[59] During an epidemic person suffering from underlying illnesses and weak constitution, are more prone to infections.[60] Current scientific evidence has shown immune-modulatory effects of drug like *Asgand*. The preventive measures for epidemic diseases are collectively aimed toward the improvement of immunity, prevention of spread of infection, hygiene and anti-septic measures and promotion of general health. Host defenses are given particular importance.[58]

In Unani system of medicine, Asgand is mainly used for strength, vigor and rejuvenation. The drug is used as nervine tonic, aphrodisiac, stimulates sexual impulses and increases

sperm count and have sedative effect. It also relieves inflammation, pain, backache and anti-rheumatic. Several scientific studies on *Asgand* had provided the evidence related to its immune-modulatory, immune-stimulant, cardio-protective, anti-inflammatory anti-stress, antioxidant, analgesic, anticancer, adaptogenic, activity.[61] It is used as adaptogenic, antiarthritic, antispasmodic, anti-inflammatory, nervine tonic, nerve soothing, antioxidant, immune-modulator, free radical scavenger, antistress and anticancer agent.[62]

Covid-19 guidelines are recommended by the Unani officers and researchers of Ministry of AYUSH in consultation with other academia, experts and leading practitioners of Unani medicine, wherein they recommended to use 5 g of *Safoof Asgand* for prophylactic measure and as an immune-enhancer or modulator.[63]

CONCLUSION

Asgand (*W. somnifera*) is a common ingredient in many Unani compound formulations and has been in use since time immemorial to treat a wide range of indications. The drug has been subjected to quite extensive phytochemical, experimental and clinical investigations. Scientific studies have proved most of the claims of traditional medicines. These results are very encouraging and indicate this drug should be studied more extensively to confirm other potential therapeutic effects. The Ministry of AYUSH, Government of India issued specific guidelines for AYUSH-Unani practitioners to deal with Covid-19 and recommended the use of Asgand as a prophylactic measure and as an immunity enhancer. Clinical research and trials using *Asgand* for a variety of conditions should also be conducted to use it judiciously and cautiously in Unani as well as other systems of medicine.

ACKNOWLEDGMENTS

The authors would like to thank Prof. Asim Ali Khan, Director General, Central Council for Research in Unani Medicine (CCRUM), Ministry of AYUSH, Government of India, for providing the necessary infrastructure and facilities. Dr. Wasim Ahmad and Dr Mohd Kashif Husain are thankful to CCRUM, Ministry of AYUSH for the Young Scientist Awards.

CONFLICT OF INTEREST

None.

REFERENCES

1. Jadhav S, Patil M. A comprehensive review on rejuvinating herbs: *Nyctanthes arbor-tristis* Linn. and *Withania somnifera* (L) dunal. Int J Anal Pharma Biomed Sci 2016;5:26-36.
2. Anonymous. The Wealth of India a Dictionary of Indian Raw Materials and Industrial Products. Vol. X (Sp - W). New Delhi: Publication and Information Directorate, CSIR; 1976. p. 581-5.
3. Anonymous. Medicinal Plants of Gwalior Forest Division. New Delhi: Central Council for Research in Unani Medicine; 1984. p. 138.
4. Khare CP. Encyclopedia of Indian Medicinal Plants. Berlin, Heidelberg: Springer-Verlag; 2004. p. 280-2.
5. Ghani N. Khazaenul Advia. 3rd ed. New Delhi: Idara Kitabus Shifa; 2011. p. 230-1.
6. Khan SM. In: Khan JA, Nikhat S, editors. Mufradat Masihai. Deoband: Masood Publication House; 2012. p. 4.
7. Kokate CK, Purohit AP, Gokhale SB. Pharmacognosy. 26th ed. Pune: Nirali Prakashan; 2004. p. 518-20.
8. Chatterjee A, Pakrashi SC. The Treatise on Indian Medicinal Plants. Vol. 4. New Delhi: Publication and Information Directorate, CSIR; 1995. p. 208-12.
9. Anonymous. Standardization of Single Drugs of Unani Medicine. New Delhi: Part-III, Central Council for Research in Unani Medicine; 1997. p. 9-14.
10. Hooker JD. The Flora of British India. Vol. 4. Dehradun: Bishen Singh Mahendra Pal Singh; 1885. p. 239-40.
11. Nadkarni KM. Indian Materia Medica. Vol. 1., 3rd ed. Mumbai: Bombay Popular Prakashan; 1954. p. 1292-4.
12. Kirtikar KR, Basu BD, Basu LM. Indian Medicinal Plants. Allahabad: Lalit Mohan Publication; 1991.
13. Anonymous. Medicinal Plants in Folklores of Southern India. New Delhi: Central Council for Research in Unani Medicine; 2001. p. 168.
14. Anonymous. Unani Medicinal Plants and their Folklores Claims from Chamarajanagar (Wildlife Division of Karnataka). New Delhi: Central Council for Research in Unani Medicine; 2015. p. 127.
15. Kabiruddin M. Makhzanul Mufradat. Deoband: Faisal Publication; 2000. p. 75-6.
16. Tarique NA. Tajul Mufradat. New Delhi: Idara Kitabus Shifa; 2010. p. 59-61.
17. Hakim MA. Bustanul Mufradat. New Delhi: Zafar Book Depot; 1999. p. 62.
18. Ansari MY. Munafeul Mufradat. New Delhi: Ejaz Publication House; 2009. p. 112-3.
19. Nabi MG. Makhzane Mufradat wa Murakkabat. 2nd ed. New Delhi: CCRUM; 2007. p. 40.
20. Chopra RN, Nayer SL, Chopra IC. Glossary of Indian Medicinal Plants. New Delhi: Publication and Information Directorate, CSIR; 1956. p. 258.
21. Chopra RN, Chopra IC, Verma BS. Supplement to Glossary of Indian Medicinal Plants. New Delhi: Publication and Information Directorate, CSIR; 1969, p. 102.
22. Anonymous. The Wealth of India a Dictionary of Indian Raw Materials and Industrial Product. Vol. 5. New Delhi: Publication and Information Directorate, CSIR; 2004.

p. 362-4.
23. Rastogi RP, Malhotra BN. Compendium of Indian Medicinal Plants. Vol. 2. New Delhi: CDRI Lucknow and NISCAIR; 1991. p. 707-10.
24. Rastogi RP, Malhotra BN. Compendium of Indian Medicinal Plants. Vol. 4. New Delhi: CDRI Lucknow and NISCAIR; 1995. p. 765-6.
25. Rastogi RP, Malhotra BN. Compendium of Indian Medicinal Plants. Vol. 3. New Delhi: CDRI Lucknow and NISCAIR; 1993. p. 681-4.
26. Archana R, Namasivayam A. Anti-stressor effect of *Withania somnifera*. J Ethanopharmacol 1999;64:91-3.
27. Mehta AK, Binkley P, Gandhi SS, Ticku MK. Pharmacological effects of *Withania somnifera* root extract on GABAA receptor complex. Indian J Med Res 1991;94:312-5.
28. Bhattacharya SK, Bhattacharya A, Sairam K, Ghosal S. Anxiolytic-antidepressant activity of *Withania somnifera* glycol withanolides: An experimental study. Phytomedicine 2000;7:463-9.
29. Owais M, Sharad KS, Shehbaz A, Saleemuddin M. Antibacterial efficacy of *Withania somnifera* an indigenous medicinal plant against experimental murine salmonellosis. Phytomedicine 2005;12:229-35.
30. Khare CP. Indian Medicinal Plants an Illustrated Dictionary. New Delhi: First Indian Reprint, Springer (India) Pvt. Ltd.; 2007.
31. Dhuley JN. Therapeutic efficacy of Ashwagandha against experimental aspergillosis in mice. Immunopharmacol Immunotoxicol 1998;20:191-8.
32. Arora S, Dhillon S, Rani G, Nagpal A. The *in vitro* antibacterial/synergistic activities of *Withania somnifera* extracts. Fitoterapia 2004;75:385-8.
33. Babu PV, Gokulakrishnan A, Dhandayuthabani R, Ameethkhan D, Kumar CV, Ahamed MI. Protective effect of *Withania somnifera* (Solanaceae) on collagen glycation and cross -linking. Comp Biochem Physiol B Biochem Mol Biol 2007;147:308-13.
34. Yu Y, Hamza A, Zhang T, Gu M, Zou P, Newman B, *et al.* Withaferin A targets heat shock protein 90 in pancreatic cancer cells Biochem Pharmacol 2010;79:542-51.
35. Mulabagal V, Subbaraju GV, Rao CV, Sivaramakrishna C, Devitt DL, Holmes D, *et al. Withanolide sulfoxide* from Aswagandha roots inhibits nuclear transcription factor-kappa- B, cyclooxygenase and tumor cell proliferation. Phytother Res 2009;23:987-92.
36. Dutta R, Khalil R, Green R, Mohapatra SS, Mohapatra S. *Withania somnifera* (Ashwagandha) and Withaferin A: Potential in integrative oncology.Int J Mol Sci 2019;20):5310.
37. Kim SH, Singh KB, Hahm ER, Lokeshwar LB, Singha SV. *Withania somnifera* root extract inhibits fatty acid synthesis in prostate cancer cells J Tradit Complement Med 2020;10:188-97.
38. Shah RA, Khan S, Vakil M, Qureshi MT. Evaluation of antidiabetic potential of *Withania somnifera* by glucose uptake assay on 3T3 F442A fibroblast (adipocyte) cells. Int J Pharm Sci Res 2017;8:120-5.
39. Jena S, Jena RC, Bhol R, Agarwal K, Sarangi A, Sahu PK, *et al.* A comparative study of the anti-oxidative and anti-diabetic potential of *in vitro* and *in vivo* root and leaf extracts of *Withania somnifera* on streptozotocin induced diabetic rats. Int J Pharm Pharm Sci 2016;8:85-91.
40. Sarangi A, Jena S, Sarangi AK, Swain B. Anti-diabetic effect of *Withania somnifera* root and leaf extracts on streptozotocin induced diabetic rats. J Cell Tissue Res 2013;13:3597.
41. Panda S, Kar A. *Withania somnifera* and *Bauhinia pupurea* in the regulation of circulating thyroid hormone concentrations in female mice. J Ethnopharmacol 1999;67:233-9.
42. Begum VH, Sadique J. Effect of *Withania somnifera* on glycosamino glycan synthesis in carrageenin-induced air pouch granuloma. Biochem Med Metab Biol 1987;38:272-7.
43. Gupta M, Kaur G. Aqueous extract from the *Withania somnifera* leaves as a potential anti-neuroinflammatory agent: A mechanistic study. J Neuro Inflamm 2016;13:193.
44. Anbalagan K, Sadique J. Influence of an Indian medicine (Ashwagandha) on acute phase reactants in inflammation. Indian J Exp Biol 1981;19:245-9.
45. Al-Hindawi MK, Al-Khafaji SH, Abdul-Nabi MH. Anti-granuloma activity of Iraqi *Withania somnifera*. J Ethnopharmacol 1992;37:113-6.
46. Bano A, Sharma N, Dhaliwal HS, Sharma V. A systematic and comprehensive review on *Withania somnifera* (L.) Dunal an Indian Ginseng. Br J Pharm Res 2015;7:63-75.
47. Sumathi S, Padma PR, Gathampari S, Vidhya S. Free radical scavenging activity of different parts of *Withania somnifera*. Ancient Sci Life 2007;26:30-4.
48. Alam N, Hossain M, Mottalib MA, Sulaiman SA, Gan SH, Khalil MI. Methanolic extracts of *Withania somnifera* leaves, fruits and roots possess antioxidant properties and antibacterial activities. BMC Complement Altern Med 2012;12:175.
49. Devi PU, Akagi K, Ostapenko V, Tanaka Y, Sugahara T. Withaferin A. A new radio sensitizer from Indian medicinal plant *Withania somnifera*. Int J Radiation Biol 1996;69:193-7.
50. Jayaprakasam B, Zhang Y, Seeram N, Nair M. Growth inhibition of tumor cell lines by withanolides from *Withania somnifera* leaves. Life Sci 2003;74:125-32.
51. Prakash J, Gupta SK, Dinda A. *Withania somnifera* root extract prevents DMBA-induced squamous cell carcinoma of skin in Swiss albino mice. Nutr Cancer 2002;42:91-7.
52. Davis L, Kuttan G. Immunomodulatory activity of *Withania somnifera*. J Ethnopharmacol 2000;71:193-200.
53. Agarwal R, Diwanay S, Patki P, Patwardhan B. Studies on immunomodulatory activity of *Withania somnifera* (Ashwagandha) extracts in experimental immune inflammation. J Ethnopharmacol 1999;67:27-35.
54. Rasool M., Varalakshmi P. Immunomodulatory role

of *Withania somnifera* root powder on experimental induced inflammation: An *in vivo* and *in vitro* study. Vascul Pharmacol 2006;44:406-10.
55. Mohanty I, Arya DS, Dinda A, Talwar KK, Joshi S, Gupta SK. Mechanism of cardioprotective effect of *Whithania somnifera in* experimentally induced myocardial infarction. Basic Clin Pharmacol Toxicolol 2004;94:184-90.
56. Visavadiya NP, Narasimhacharya AV. Hypocholesteremic and antioxidant effects of *Withania somnifera* (Dunal) in hypercholesteremic rats. Phytomedicine 2007;14:136-42.
57. Ahmad M, Saleem S, Ahmad AS, Ansari MA, Yousuf S, Hoda MN, *et al.* Neuroprotective effects of *Withania somnifera* on 6-hydroxydopamine induced Parkinsonism in rats. Human Exp Toxicol 2005;24:137-47.
58. Rushd I. Kitab al-Kulliyat. 2nd ed. New Delhi: Central Council for Research in Unani Medicine; 1987.
59. Razi Z. Kitab al-Hawi. New Delhi: Central Council for Research in Unani Medicine; 2008.
60. Sina I. Al Qanoon Fil Tibb. Lucknow: Munshi Nawal Kishore; 1878.
61. Samadi AK. Ashwagandha: Ancient Medicine for Modern Times. J Ancient Dis Prevention Remed 2013;1:e108.
62. Verma SK, Shaban A, Purohit R, Chimata ML, Rai G, Verma OP. Immunomodulatory activity of *Withania somnifera* (L.) J Chem Pharm Res 2012;4:559-61.
63. Anonymous. Guidelines for Unani Practitioners for Covid-19. New Delhi: Ministry of AYUSH, AyushBhawan, B Block, Gpo Complex, Ina; 2020.

Source of Support: Nil. **Conflicts of Interest:** None declared.