

Can *Ashwagandha* Leaf be Replaced with its Root in Therapeutics? A Review through Published Literature

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ABSTRACT

Introduction: *Ashwagandha* (*Withania somnifera* Linn. Dunal) is an important and frequently used herb in Ayurvedic therapeutics. Its numerous parts, including flowers, leaves and roots, are said to have wide range of health-encouraging properties. Although *Ashwagandha*'s root have been used traditionally, it necessitates sacrificing the whole plant. So, there is a need to explore bio-activities in other parts of the plant. *Ashwagandha* leaf is traditionally used as an ethnomedicine in various regions of India. Leaves of *Ashwagandha* are least considered in the classical literature and hardly there are references for their therapeutic utilities. Considering this, it has been planned to gather evidences against the therapeutic efficacies of *Ashwagandha* leaf. **Materials and Methods:** PubMed indexed articles published till 12th September 2022 were reviewed using the search strategy "*Ashwagandha*", "*Withania somnifera*", "*Ashwagandha* AND leaf", "*Withania* AND leaf". **Results:** Searching by using the keyword "*Ashwagandha* AND leaf" yielded 252 results, while the search "*Withania* AND leaf" resulted in 245 results. Out of these 245/252; the free full texts were only 42 that have been considered in this review. The plant leaf is extensively used in folklore practice for various disease conditions. The leaf is preferred using both internal and external routes. Pre-clinical, clinical studies have been established diversified therapeutic benefits of *Ashwagandha* leaf. **Conclusion:** *Ashwagandha* leaf studies shows numerous bioactive compounds as present in its root. It can become a lead for the anticancer, neurodegenerative, anti- microbial and anti-inflammatory purpose and can be used as widely as its roots.

Keywords: *Ashwagandha*, *Ashwagandha* leaf, Ethnomedicine, Folklore, *Withania somnifera*.

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Received: 07-Oct-2022 ; **Revised:** 29-Oct-2022 ; **Accepted:** 09-Nov-2022

INTRODUCTION

For numerous concerns, traditional medicines have gained more popularity in the present era. Traditional medicines are widely accessible, relatively safe and have high level of public trust, thus World Health Organization (WHO) also supports, recommends and promotes it in national health programs. People in South-East Asia nations and other parts of world have employed traditional medical systems for healthcare for generation and industrial production is also environmentally friendly.^[1]

Ayurveda, the Indian traditional medicine is a science developed by the experiences and wisdom of Indian ancestors. Ayurveda has given exigent contribution in global health care. The potential of Ayurveda in providing primary health care has received global attention leading to its globalization at a fast pace. To sustain the present momentum and to meet the ensuing globalization,

it is necessary to have a strong institutional framework with the capacity to generate the resources in a sustainable and economical manner.

Ayurveda uses natural resources in therapeutics after converting them into formulations. Researches and reviews published in recent years on Ayurveda formulations have helped in creating a conceptual interface between Ayurveda and Modern Science. Preliminary studies with Ayurveda formulations provided certain leads, emphasizing on their therapeutic impact on patients suffering from various infectious and non-infectious diseases by preventing complications and amending the quality of life.^[2-7]

Ashwagandha (*Withania somnifera* Linn. Dunal), one such important and frequently used herb in Ayurvedic therapeutics. Its numerous parts, including flowers, leaves and roots, are said to have wide range of health-encouraging properties. *Ashwagandha* is trusted to enhance the body's resilience to stress so, it works as a powerful adaptogen. *Ashwagandha* works on following body systems -(i) the nervous system, by improving functions of brain and memory, (ii) the reproductive system by maintaining a healthy sexual and reproductive balance, (iii) improve the cell-mediated immunity and boost the body's resistance to illness and (iv) acts as anticancer, anti-inflammatory anti-arthritis



DOI: 10.5530/097484900286

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agent. Preliminary investigations suggested that, constituents of *Ashwagandha* offer a range of therapeutic effects with slight or no associated toxicity. These results are quite positive, so this plant should further researched in order to confirm the findings and elucidate additional possible therapeutics effects. The available information supports the therapeutic values of *Ashwagandha* as a promising *Rasayana* (regenerative tonic), due to its diversified pharmacological actions.^[8,9]

Although *Ashwagandha*'s root have been used traditionally, it necessitates sacrificing the whole plant. So, there is a need to explore bio-activities in other parts of the plant. The leaves of *Ashwagandha* are least considered in the classical literature and hardly there are references for their therapeutic utilities. However, there are works that have generated evidence against the use of *Ashwagandha* leaf in different pathological conditions. Chemical constituents identified in *Withania somnifera* leaf are given in Table 1. Considering this, it has been planned to compile available information on the therapeutic efficacies of *Ashwagandha* leaf.

MATERIALS AND METHODS

PubMed indexed articles published till 12th September 2022 were reviewed using the search strategy "*Ashwagandha*", "*Withania somnifera*", "*Ashwagandha* AND leaf", "*Withania* AND leaf". In addition, information on folklore claims against the use of *Ashwagandha* leaf in different pathologies was also compiled.

RESULTS

Withania somnifera is the most widely distributed species in the genus. Thus the search was limited to *Withania somnifera*. Searching by using the keyword "*Withania somnifera*" yielded 1413 results and the search using the keyword "*Ashwagandha*" yielded 1503 results. When the search was narrowed down to "*Ashwagandha* AND leaf", the results were reduced to 252, while the search "*Withania* AND leaf" resulted in 245 results. Out of these 245/252; the free full texts were only 42 that have been considered in this review as enlisted in Table 2. The remaining articles were related to phytochemical analysis etc. that are not compiled in this attempt.

Although *Ashwagandha* leaf is traditionally used as an ethnomedicine in various regions of India as enlisted in Table 3 and Figure 1. But, there is no direct reference towards its use as a medicine in the classical literature, except in a couple of references for its recommendation as a topical medicament. It's paste is indicated in the management of *Granthi* (~glandular swellings/cyst), *Gandamala* (~tubercular lymphadenitis) and *Apachi* (~cervical lymphadenopathy); and *Vedanahara* (~analgesic) property is attributed to it.^[10-12]

Table 1: Chemical constituents identified in *Withania somnifera* leaf.

Chemical constituents	Possible activity	References
Withaferin (Steroidal lactone)	Anticancer properties	[42,43]
Withaferin A (Steroidal lactone)	Anticancer properties Inhibits experimental angiogenesis Antibacterial Immunomodulatory Anti-inflammatory	[44-49]
Triethylene glycol	Triethylene glycol is a sleep-inducing molecule Active anticancer component.	[50,51]
Withanolide D (Steroidal lactone)	Improves apoptosis in the bone marrow of leukemia	[52,53]
Withanolide E (Steroidal lactone)	Antibacterial Immunosuppressive	[54]
Withanone (Steroidal lactone)	Withanone is found to be efficient in ameliorating human-like pathological responses induced in humanized zebrafish by SARS-CoV-2 recombinant spike (S) protein Withanone may serve as a potential neuroprotective agent.	[52, 55, 56, 57]
Withanolide Z (Novel)	In Leishmaniasis – Exert inhibitory activity against <i>L. donovani</i> topoisomerase I.	[58]
Withanolide B	-	[58, 52]
7-hydroxywithanolide	-	[58]
3 α -methoxy-2,3-dihydro	-	[43]
27-deoxywithaferin A (Steroidal lactone)	-	[59, 52]
4 β ,17 α -dihydroxy-1-10xo	-	[60]

Chemical constituents	Possible activity	References
2, 24-dienolide (steroidal lactone) Trienolide (steroidal lactone)	-	[59, 61]
4 β -dihydroxy-5 β , 6 β -epoxy	-	[54]
1-oxo-22R-with a-2,14-24	-	[55]

DISCUSSION

In Ayurveda, the root of *Ashwagandha* is used in most of formulations as a medicine. References against the use of *Ashwagandha* leaf as medicine in classical texts of Ayurveda are rare, however, the leaves are extensively used in folklore practices that can be witnessed at Table 4. Its use is even observed in traditional practices in various parts of Pakistan and Bangladesh.^[10]

The warm leaf is advised to be tied over the inflamed joints for managing pain. Topical application of leaf to counter manifestations associated with inflammation is also observed

Table 2: Published evidences against the usefulness of *Withania* leaves.

Activity	Intervention	Model	Results	Reference
Neuroprotective activities against oxidative stress	Alcoholic and water extracts of leaves and their bioactive components	Cell line study: Glioblastoma and Neuro blastoma cells	<i>Ashwagandha</i> leaf-derived bioactive compounds have neuro-protective potential and may serve as a supplement for brain health	[62]
Neuro-degenerative diseases	Alcoholic extract (iExtract) and its component Withanone	<i>In vivo</i> : Scopolamine-induced amnesia. (Male Swiss albino strain mice) <i>In vitro</i> -Brain cell culture (IMR32, neuronal and C6, glioma)	Scopolamine induced memory loss may be associated with oxidative stress and <i>Ashwagandha</i> i-extract, and withanone may serve as potential preventive and therapeutic agents.	[63]
Neuro-degenerative diseases	Aqueous extract (ASH-WEX) and a chloroform fraction (fraction IV (FIV))	β -amyloid and lipo-polysaccharide (LPS)-stimulated primary microglial cells and BV-2 microglial cell line.	ASH-WEX and FIV - suppress the proliferation and migration of activated microglia. ASH-WEX and FIV were screened and found to possess Withaferin A and Withanone as active phytochemicals. FIV seems to contain more quantity of Wit A and Withanone than ASH-WEX. Thus, FIV is higher effective than the ASH-WEX in the current results.	[64]
Parkinson's disease	Leaf extract (A-Extract)	PD model mouse (Male Swiss albino mice)	Treatment with A-Extract significantly improved the levels of Glutathione and Glutathione peroxidase in the Parkinson's mouse brain. The extract could be a potential drug in treating oxidative damage and physiological abnormalities in PD.	[65]

Activity	Intervention	Model	Results	Reference
Amnesia	i-Extract (alcoholic extract of leaf)	Scopolamine-induced amnesic mice (Adult Swiss albino male mice)	The spine density and mushroom-shaped morphology that was regained if pre-treated with i-Extract. The ARC (activity-regulated cytoskeleton-associated protein) helps in the polymerization of F-actin and subsequent changes in the morphology of dendritic spines. i-Extract attenuates down regulation of Arc Protein Expression in Amnesic Mice	[66]
Insomnia	Alcoholic extract Aqueous extract Cyclo dextrin-assisted aqueous extract	Male C57BL/6 mice weighing 24–30 g	Both aqueous and cyclodextrin extracts increased NREM (non-rapid eye movement) sleep significantly as compared to vehicle administration. TEG (the active component of leaves) may be a potent sleep-inducing molecule.	[67]
Obesity induced cognitive dysfunction	Dry leaf powder (ASH - 1 mg/g of body weight)	Wistar albino young female rats grouped into 4 Low fat diet (LFD) High fat diet (HFD) Low fat diet extract (LFDE) high fat diet extract (HFDE)	ASH-treated rats showed significant improvement in their working memory and loco-motor coordination during behavioural studies as compared to high fat diet rats. ASH could be a key regulator in maintaining the synaptic plasticity in HFD-induced obesity and can serve as a nootropic candidate against obesity-induced cognitive impairments	[68]
Glio-protective Effects against Lead-induced Toxicity	Aqueous Extract (ASH-WEX)	<i>In vitro</i> -C6 Glioma Cell <i>In vivo</i> -Wistar strain young male albino rats	ASH-WEX plays neuro-modulatory role to rescue the glial cells against lead toxicity by suppression of stress response and upregulation of plasticity marker proteins such as GFAP and NCAM	[69]
In Methoxy-acetic acid (MAA) induced toxicity	Leaf derived Withanone	Normal human fibroblasts	Withanone protects human normal cells against the toxicity of MAA.	[70]
Anti-cancer Activity	Aqueous Extract (ASH-WEX)	<i>In vitro</i> -Nude mice - subcutaneous xenograft and tail vein metastasis models. <i>In vivo</i> -Human normal (TIG-1, WI-38 and MRC5) and tumor derived (U2OS, MCF7 and HT1080) cells	ASH-WEX has considerable anti-cancer activity <i>in vitro</i> and <i>in vivo</i> . It is cytotoxic to cancer cells selectively and causes tumour suppression <i>in vivo</i> . Its active anticancer component was identified as trimethylene glycol (TEG). Activation of tumor suppressor proteins (p53 and pRB) and down-regulation of MMP-3 and MMP-9.	[71]

Activity	Intervention	Model	Results	Reference
Anti-cancer	i-Extract, Withanone and Withaferin A	Human normal fibroblasts, breast carcinoma, colon carcinoma, Mouse packaging cells.	Bioinformatics on the selected gene targets revealed the involvement of p53, apoptosis and insulin/ IGF signaling pathways linked to the ROS signaling. Leaf extract and Withanone cause selective killing of cancer cells by induction of ROS-signaling. Thus, could be recruited for ROS-mediated cancer chemotherapy.	[72]
Apoptosis, inhibition of invasion, and osteo-clastogenesis activity	A 20 mmol/L solution of Withanolide prepared with DMSO	<i>In vitro</i> –KBM-5 (human chronic myeloid leukemia), A293 (human embryonic kidney carcinoma), MCF-7 (human breast adenocarcinoma), and RAW 264.7 (murine monocytic cell) cells	Withanolides inhibit activation of NF-kappaB and NF-kappaB-regulated gene expression, which may explain the ability of withanolides to enhance apoptosis and inhibit invasion and osteoclastogenesis.	[73]
Hypo-glycaemic and Hypo-lipidaemic effects	Alcoholic extracts of root (WSREt) and leaf (WSLEt).	Alloxan-induced diabetes mellitus in Albino Wistar strain rats	Flavonoids have hypo-glycaemic, hypo-lipidaemic and hypo-cholesterolaemic effects. Root and leaf extracts possess anti-diabetic and anti-hyperlipidaemic activities. Root extract contained more flavonoids than leaf extract.	[74]
Diabetes mellitus (DM) type 1	Extracts of root (WSREt) and leaf (WSLEt)	Alloxan-induced diabetic rats.	The presence of phenolic compounds including flavonoids in root and leaf extracts and their antioxidant activity may play a vital role in the reduction of blood glucose level.	[75]
Anti-malarial activity	Leaf and root bark	Rodent malaria parasite, <i>Plasmodium berghei</i> inoculated-Swiss albino mice	Extracts of the leaves and root barks showed parasite suppressive effect and a protective effect on PCV drop (at higher doses), both in dose-related fashions.	[76]
Anti-malarial efficacy	Chloroform fraction, methanolic extract and raw leaf powder	<i>In silico</i> -Molecular docking, Pharmacokinetic profiling of the withaferin A	Based on molecular docking and pharmacokinetic profiling, withaferin A could be a suitable therapeutic adjunct for preclinical investigation of antimalarial potentiality in artemisinin-resistant malaria.	[77]

Activity	Intervention	Model	Results	Reference
Anti-inflammatory	Herbal extract of mixture of dry powder of leaves of <i>W. somnifera</i> and stem of <i>T. cordifolia</i>	Wistar strain female albino rats Three groups: (1) Control (2) (IF-DR) Intermittent fasting-dietary restriction (3) IF-DR and herbal extract (DRH) group in	DRH regimen reduced anxiety-like behavior in middle age female rats and associated neuroinflammation by ameliorating key inflammatory cytokines and modulated stress response. The present data may provide scientific validation for the anxiolytic and anti-inflammatory potential of herbal intervention combined with short term IF-DR regimen	[78]
Platelet aggregation and Inflammation	Aqueous and ethanolic (1:1) leaf extract	<i>in vitro</i> -Indirect haemolytic activity using <i>Naja naja</i> venom. <i>in silico</i> -Molecular docking was performed by the ligand fit method using molegro software package	The extracts have the inhibitory potential on inflammatory enzymes and platelet aggregation. Can serve as a newer, safer and affordable medicine for inflammatory diseases.	[79]
Free Radical Scavenging Activity	Aqueous extract of different parts of <i>Withania somnifera</i> viz. fresh tubers, dry tubers and leaves.	1) DPPH assay. 2) <i>in vitro</i> -Determining percentage inhibition of lipid peroxidation using single cell suspension from liver cells from goat.	The extract of different parts are potential scavengers of radicals and protect membrane lipids in the order: leaves > fresh tubers > dry tubers. The antioxidant activity may be attributed to the presence of various active principles like Withanolides, Glyco-withanolides, Sitoindosides vii-x.	[80]
Anti-oxidant activity	Ethanolic extract of leaf and fruit of <i>Physalis minima</i> , <i>Withania somnifera</i> , <i>Datura innoxia</i> , <i>Solanum nigrum</i> and <i>Kigelia africana</i>	DPPH free radical scavenging assay	The percentage of antioxidant activity of leaves extracts was found in order: <i>P. minima</i> > <i>W. somnifera</i> > <i>S. nigrum</i> > <i>K. africana</i> > <i>D. innoxia</i> and fruits extracts was in order: <i>W. somnifera</i> ≥ <i>D. innoxia</i> > <i>P. minima</i> > <i>K. africana</i> > <i>S. nigrum</i> respectively.	[81]
Antioxidant and anti-bacterial activities	80% aqueous methanolic extract of roots (WSREt), fruits (WSFEt) and leaves (WSLEt).	Antioxidant properties- 1. DPPH scavenging activity, 2. Ferric reducing antioxidant power (FRAP) 3. Ferrous chelation and inhibition of β-carotene bleaching. Anti-bacterial activities- The agar well diffusion method and five pathogenic Gram-negative bacteria: <i>Escherichia coli</i> , <i>Salmonella typhi</i> , <i>Citrobacter freundii</i> , <i>Pseudomonas aeruginosa</i> and <i>Klebsiella pneumoniae</i> .	Leaves have remarkable anti-oxidant properties and have the highest ascorbic acid and anthocyanin content. Leaves possess significant anti-bacterial properties against Gram-negative organisms, particularly against <i>S. typhi</i> .	[82]

Activity	Intervention	Model	Results	Reference
Cognitive and psychomotor performance	Standardized dried aqueous extract of roots and leaves	(CTRI/2013/04/003537) Double-blind, multi-dose, placebo-controlled, crossover study. Participants- 20 healthy male. Two capsules (250 mg each) twice daily or a matching placebo period of 14 days	Significant improvement was observed in reaction time with simple reaction, choice discrimination, digit symbol substitution, digit vigilance, and card sorting tests with the extracts compared to placebo. The extracts can improve cognitive and psychomotor performance.	[83]

Table 3: Folk uses of *Withania somnifera* leaf.

Place and State	Local name	Ethno-medicinal use against	Form used	Route of administration	Reference
Morigaon, Assam	<i>Achagandha</i>	Leprosy	Paste	Topical	[13]
Chhattisgarh	<i>Aswagandha</i>	Rheumatism Bed sores Haemorrhoids Abscesses Smallpox Poorly healing open wounds Blood purification	Dry powder or paste of leaf are used to cure burns and wound. The ointment processed from the leaves is used to treat wounds and bed sores. To heal ulcers, the leaf ash is used topically. Leaves are used as blood purifier. Leaves are used to alleviate general body pain, when given as purgative. When leaf or root powder heated with fat, it might be used to cure smallpox, abscesses and haemorrhoids. Poultice prepared with fresh leaves and roots is used for rheumatic limbs. To cure open wounds that are not healing properly, preparations made from leaves and root are employed. Rashes and injuries formed due to belt, are treated using a paste made from fruits, stem and leaves.		[14]
Mahendergarh, Haryana	<i>Ashgandh</i>	Boils Swellings Rheumatic pains	The warm leaf of the plant with latex of <i>C. procera</i> is applied and tied over boils, swellings and rheumatic pains.	Topical	[15]
Karnal, Haryana	<i>Asgand, Ashwagandha</i>	Swelling of joints	Decoction prepared with leaves of <i>Ashwagandha</i> is applied on swollen joints.	Topical	[16]

Place and State	Local name	Ethno-medicinal use against	Form used	Route of administration	Reference
Jind, Haryana	<i>Bambhol</i>	Painful swellings, Boils and Rheumatic pains	The warm leaves are to be tied over painful swelling, boils, and rheumatic pains.	Topical	[17]
Hamirpur, Himachal Pradesh	<i>Ashvagandha</i>	Diabetes	Leaf infusion is prescribed as a medicine to cure diabetes	Oral	[18]
Mandi, Himachal Pradesh	<i>Ashwagandha</i>	Joint pains	Poultice of leaves applied to cure joint pains	Topical	[19]
Udhampur, Jammu and Kashmir	<i>Asgandh</i>	Obesity, Memory enhancer	Fresh leaves	Oral, chewing on an empty stomach	[20]
Gulbarga, Karnataka	<i>Ashwagandha</i>	Ulcers, swellings, Carbuncles, Scabies	Leaf paste	Topical	[21]
		Obesity	Leaf	-	
Bijapur, Karnataka	<i>Ashwagandha</i>	Insomnia, anxiety, amnesia and mental stress	20 g of dried, leaf and root powder, with goat milk	Oral, twice a day, for 45 days	[22]
Tumkur, Mysore Karnataka	<i>Ashwagandha</i>	Ulcers, Painful swellings and Sore eyes	Leaf paste	Topical	[23]
Gadag, Karnataka	<i>Ashwagandha</i>	Cough with sputum	Decoction prepared from crushed young leaves is advised to take orally twice a day for 3-5 weeks.		[24]
		Tuberculosis (Kshaya)	About 3 g of plant leaves are made into a fine powder, mixed into an equal amount of water and milk to prepare a decoction. This is advised to take orally thrice a day, for 1-2 months.		
		All types of ulcers	Topically, leaves are covered on the affected region and tied with the cloth until cure.		
Anuppur, Madhya Pradesh	<i>Ashwagandha</i>	Asthma	A teaspoonful paste of leaf added with a cup of cow's milk	Oral, once daily in the morning before breakfast for 21 days	[25]
Nanded, Maharashtra	<i>Dhorgunj, Askand</i>	Cough	Leaf extract along with boiled milk	Oral	[26]
Sundargarh, Orissa	<i>Aswagandha</i>	Asthma; Cold and Cough	Leaf tea	Oral; every morning	[27]
Dhenkanal, Orissa	<i>Ashwagandha</i>	Tuberculosis	-	Oral	[28]
Salem, Tamil Nadu	<i>Amukkara kizhangu</i>	Anthelmintic	Leaf decoction is taken as a remedy for anthelmintic activity.	Oral	[29]

Place and State	Local name	Ethno-medicinal use against	Form used	Route of administration	Reference
Salem, Tamil Nadu	Amukkira	Joint pains	Paste of dried leaves	Topical	[30]
Virudhunagar, Tamil Nadu	Amukkuran	Diabetes	Leaf juice	Oral	[31]
Vellore, Tamil Nadu	Amukkara	Stress, Nerves disorder	-	Oral	[32]
Dindigul, Tamil Nadu	Amukkara	Sedative, Diuretic, Analgesic	-	Oral	[33]
Hathras, Uttar Pradesh	<i>Ashwagandha</i>	Anti-cancer, Anti-oxidant; asthma,	-	Oral	[34]
		Leaves are used as a hypnotic and for the treatment of asthma, anti-cancer and antioxidant activity. Roots, leaves and bark of <i>Ashwagandha</i> has a potential role in the treatment of cancer. It has anticarcinogenesis, anti-oxidative and chemoprotective activity. Leaves are used as a tonic and to cure the conditions like memory loss, hormonal imbalance, mental problem, arthritis, depression etc			
Shahjahanpur, Uttar Pradesh	<i>Ashwagandha</i>	Body pain, inflammation	Paste of leaves along with <i>Boerhavia</i> leaves is applied in body pain and inflammation	Topical	[35]
Vindhya region, Uttar Pradesh	<i>Ashwagandha</i>	Rheumatic pain, Fever, Tuberculosis	Decoction of leaf	Oral	[36]
Dehradun, Uttarakhand	<i>Ashwagandha</i>	Insomnia, Urinary disorders, Fever	Leaf juice	Oral	[37]
Haridwar, Dehradun and Pauri, Uttarakhand	<i>Talwaada</i>	Boils	The leaves and stem is burnt and ash is mixed with mustard oil; this paste is applied on boils.	Topical	[38]
Bageshwar, Uttarakhand	<i>Asgandha</i>	Intestinal worm infestation	Decoction of the leaf is administered	Oral	[39]
Kedarnath valley, Uttarakhand	<i>Ashwagandha</i>	Insomnia, Scrofula	Juice	Oral	[40]
Paschim Medinipur, West Bengal	<i>Ashwagandha</i>	Wound and burn	-	Topical	[41]

in the practice. Using pastes, decoctions, and ashes as dusting powders is in practice to manage wounds, bed sores, and other skin lesions.

Oral administration of leaf infusion is said to be beneficial in the management of diabetes. Chewing fresh leaves is believed to be useful in controlling obesity and improving memory.

Table 4: Use of *Ashwagandha* leaf in folklore practices.

Routes of usage	Diseases managed	Dosage forms	States where it is used
Topical	Leprosy, Bed sores, Abscess, Open wounds, Haemorrhoids, Scabies	Warm leaf, Paste, Ashes (as dusting), Decoction (irrigation)	Assam, Chhattisgarh, Haryana, Himachal Pradesh, Jammu and Kashmir, Karnataka, Madhya Pradesh, Maharashtra, Orissa, Tamil Nadu, Uttar Pradesh, West Bengal
Internal	Rheumatism, Diabetes, Obesity, Memory enhancer, Insomnia, Psychological stress, Anxiety, Amnesia, Productive cough, Asthma, Tuberculosis, Anthelmintic, Anti-cancer	Raw leaf for chewing, Juice, Infusion, Decoction,	

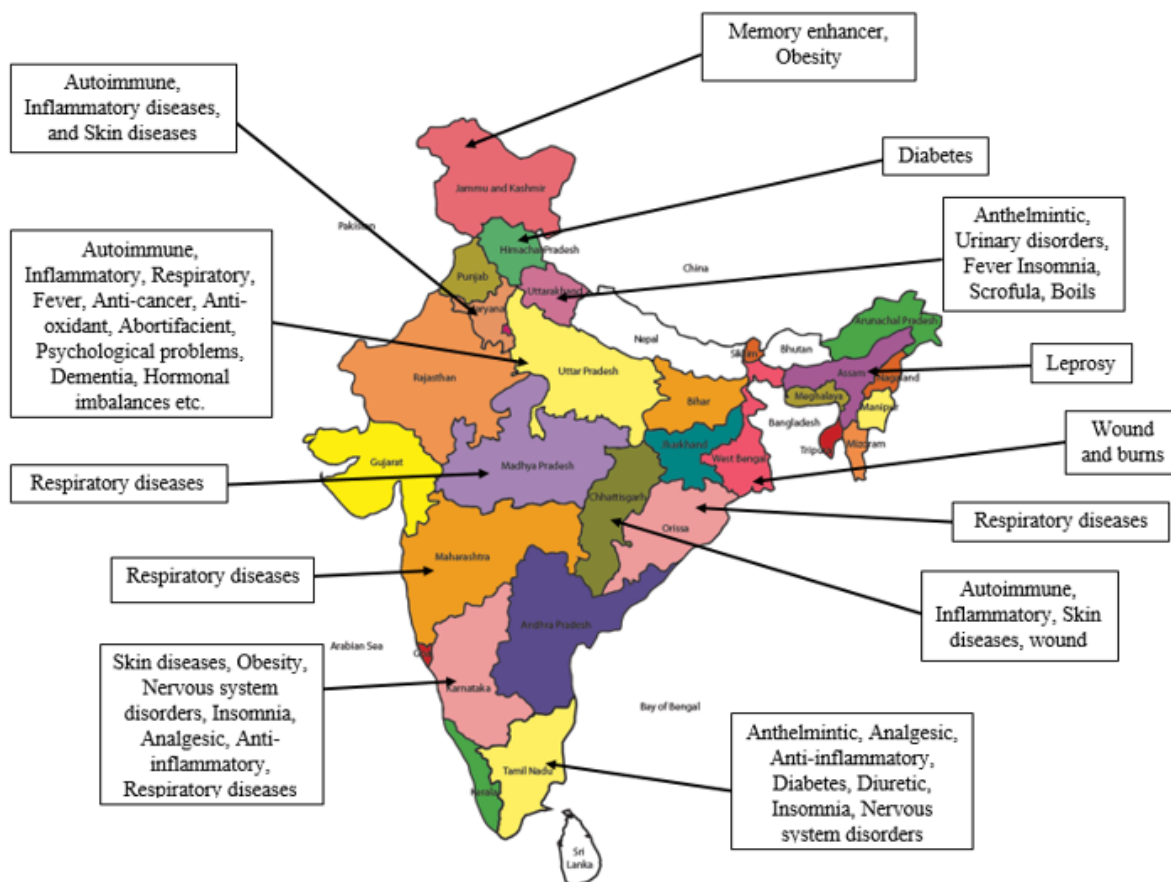


Figure 1: Ethnomedicinal uses of *Ashwagandha* leaf in India.

The decoction made out of the leaves is said to be useful in the management of productive cough, and asthma. It is even said to be beneficial in the management of tuberculosis. In the management of psychological stress, insomnia and anxiety also the leaf and its different dosage forms were used.

A number of chemical constituents have been identified in leaves that may be beneficial as anti-cancerous, anti-bacterial, anti-inflammatory, neuro-protective, and immuno-stimulatory agents. Experimental studies have established neuro-protective activity (against Glioblastoma, Neuroblastoma, Parkinsonism), anti-cancer activity of leaf extract. The aqueous extracts are reported to be beneficial in lead induced toxicity. The extracts are also found to be useful as Anti-malarial, Anti-inflammatory, Antioxidant, Anti-bacterial, Hypo-glycemic, Hypo-lipidemic and Anti-diabetic agents. Standardized dried aqueous extracts were found to improve psychomotor and cognitive performance in a multi-dose, double-blind, crossover, placebo-controlled study suggesting an effective supplemental therapy for illnesses linked to cognitive impairment. These studies infer that *Ashwagandha* leaf has a great potential in therapeutics and can be explored in wider studies.

CONCLUSION

Though folklore practices are observed against the use of leaves in varied pathologies, the actual role in the maintenance of health, specifically with regard to protecting against various chronic, non-communicable diseases are not established systematically. This review highlights the potential health benefits of easily available plant part. Further, the studies on *Ashwagandha* leaf reported much similar bioactive compounds as present in roots, inferring the possibility of using leaf in place of root.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. WHO. Quality control methods for medicinal plant material. Geneva: World Health Organization; 1998.
2. Available from: https://www.cochranelibrary.com/cdsr/doi/10.1002/central/doi/10.1002/central/CN-01905191&doi=10.1002/central/CN-01905191&p_p_id=scolariscontentdisplay_WAR_scolariscontentdisplay&_scolariscontentdisplay_WAR_scolariscontentdisplay_action=related-content&p_p_lifecycle=0&p_p_mode=view&type=central&contentLanguage=en [cited 8/10/2022].
3. Available from: https://www.cochrane.org/CD008288/ENDOC_ayurvedic-treatments-for-diabetes-mellitus [cited 8/10/2022].
4. Available from: https://www.cochranelibrary.com/content?templateType=related&urlTitle=/central/doi/10.1002/central/CN-01905191&doi=10.1002/central/CN-01905191&p_p_id=scolariscontentdisplay_WAR_scolariscontentdisplay&_scolariscontentdisplay_WAR_scolariscontentdisplay_action=related-content&p_p_lifecycle=0&p_p_mode=view&type=central&contentLanguage=en [cited 8/10/2022].
5. Available from: <https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02185946/related-content> [cited 8/10/2022].
6. Kessler CS, Pinders L, Michalsen A, Cramer H. Ayurvedic interventions for osteoarthritis: a systematic review and meta-analysis. *Rheumatol Int*. 2015 Feb;35(2):211-32. doi: 10.1007/s00296-014-3095-y. PMID 25062981.
7. Available from: <https://www.frontiersin.org/articles/10.3389/fphar.2022.821810/full> [cited 8/10/2022].
8. Singh N, Bhalla M, de Jager P, Gilca M. An overview on ashwagandha: a Rasayana (rejuvenator) of Ayurveda. *Afr J Trad Compl Alt Med*. 2011;8(55):208-13. doi: 10.4314/ajtcam.v8i55.9. PMID 22754076, PMCID PMC3252722.

9. Mishra LC, Singh BB, Dagenais S. Scientific basis for the therapeutic use of *Withania somnifera* (*Ashwagandha*): a review. *Altern Med Rev*. 2000 Aug;5(4):334-46. PMID 10956379.
10. Paul S, Chakraborty S, Anand U, Dey S, Nandy S, Ghori M et al. *Withania somnifera* (L.) Dunal (*Ashwagandha*): A comprehensive review on ethnopharmacology, pharmacotherapeutics, biomedical and toxicological aspects. *Biomed Pharmacother*. 2021 Nov;143:112175. doi: 10.1016/j.biopha.2021.112175. PMID 34649336.
11. Nighantu adarsha vol. 1 Vaidy BG, editor. Varanasi: Kantakaryadi varga, Chaukhamba Bharati Academy. p. 135.
12. Divya Aushadhi Vijyan. By M. Choudhari. Delhi: Choukhmba Orientalia. p. 28.
13. Ghosh G, Narayan B, Bengal W. Traditional use of plants against leprosy in India: a review of the recent literature. *J Innov Pharm Biol Sci*. 2017;4(4):55-64.
14. Husain N, Trak TH, Panday B. Ethnomedicinal significance of two important shrubs, viz *Withania somnifera* (L.) and *Datura metal* (L.) (Family solanaceae) of Chhattisgarh, India. *Indian J Sci Res*. 2018;9(1):37-9.
15. Yadav SS, Bhandoria MS. Ethnobotanical exploration in Mahendergarh district of Haryana (India). *J Med Plants Res*. 2013;7(18):1263-71. doi: 10.5897/JMPRI 2.774.
16. Kaur Ravinder VBD. Ethnobotanical studies on Karnal District, Haryana, India. *Int Res J Biol Sci*. 2014;3(8), 46-55.
17. Rani J. Ethnobotanical survey and traditional uses of medicinal plants in jind district of Haryana, India. *Plant Arch*. 2019;19(1):1241-7.
18. Kumar N, Jakhar AK, Choyal R. Traditional uses of some medicinal plants of Hamirpur district of Himachal Pradesh for the treatment of diabetes. *Int J Adv Res*. 2014;2:131-9.
19. Suresh K. Ethnobotanical uses of some medicinal plants of district Mandi, Himachal Pradesh (India). *J Biol Chem Chron*. 2015;2(1):34-7.
20. Bhatia H, Sharma YP, Manhas RK, Kumar K. Ethnomedicinal plants used by the villagers of district Udhampur, J&K, India. *J Ethnopharmacol*. 2014 Feb 3;151(2):1005-18. doi: 10.1016/j.jep.2013.12.017. PMID 24365639.
21. Ghatapanadi SR, Johnson N, Rajasab AH. Documentation of folk knowledge on medicinal plants of Gulbarga district, Karnataka. *Indian J Nat Prod Resour*. 2011;10(2):349-53.
22. Laddimath A, Rao S. Ethno-medicinal plants used to treat some psychological (mental) disorders by traditional practitioners of Vijayapur (Bijapur) district of Karnataka, India. *J Ethnobiol Ethnomed*. 2016;3(1):1-7.
23. Shiddamallayya N, Yasmeen A, Gopakumar K. Hundred common forest medicinal plants of Karnataka in primary healthcare. *Indian J Tradit Knowl*. 2010;9(1):90-5.
24. Shivakumar HM, Parashurama TR. Phyto-ethno-medicinal knowledge of folklore people in Kappathgudda Region of Gadaga District, Karnataka, South India. *Int J Sci Technol*. 2014;3:3080-91.
25. AHIRWAR RK. Ethnomedicinal investigations among the Baiga tribes, district Anuppur, Madhya Pradesh, India, Nelumbo. 2017;59(2):181-6.
26. Shaikh RU, Dukare DD, Sarwade KP, Sarwade PP. Ethnobotanical study of folk medicinal plants used by villagers in Nanded district of Maharashtra (India), *Int J. Ayur Herb. Med*. 2014;4:1585-95.
27. Mallick SN, Ram JP, Parida N. Study of ethnomedicinal values of some shrub in Rourkela steel city and its surroundings, Sundergarh, Odisha. *Int J Appl Biol Pharm Tech*. 2014;5:123-30.
28. Mohanty N, Panda T, Sahoo S, Rath SP. Herbal folk remedies of Dhenkanal district, Odisha, India. *Int J Herb Med*. 2015;3(2):24-33.
29. Alagesaboopathi C. Ethnomedicinal plants and their utilization by villagers in Kumaragiri hills of Salem district of TamilNadu, India. *Afr J Tradit Complement Altern Med*. 2009;6(3):222-7. doi: 10.4314/ajtcam.v6i3.57157, PMID 20448846.
30. Vaidyanathan D, Sisubalan N. Ghouse Basha M. survey of ethnomedicinal plants and folklore studies on Malayali tribals of Vellakadai village A part of Shervaroy range in Eastern Ghats, Tamil Nadu. *Int J Recent Sci Res*. 2014;5(7):1368-80.
31. Aadhan K, Anand SP. Survey of medicinal plants used for the treatment of diabetes by the Paliyar's Tribe in Sadhuragiri hills, Tamil Nadu, India. *Int J Herb Med*. 2017;5(3):17-25.
32. Tariq NPM, Iffham S. Ethnobotanical survey of medicinal plants in Yelagiri Hills of Tamil Nadu. *Res J Pharm Technol*. 2013;6(6):652-4.
33. Sundaram SS, Suresh K. Potential of medicinal plants for curing human ailments in Natham, Dindigul district, Tamil Nadu, India. *Pharma. Innov J*. 2019;8(4):512-4.
34. Kumar S, Singh BS, Singh RB. Ethnomedicinal plants uses to cure different human diseases by rural and tribal peoples of Hathras district of Uttar Pradesh. *J Pharm Phytochem*. 2017;6(2):346-8.
35. Sharma J, Painuli RM, Gaur RD. Plants used by the rural communities of district Shahjahanpur, Uttar Pradesh. *Indian J Tradit Knowl*. 2010;9(4):798-803.
36. Singh A, Singh P, Singh G, Pandey AK. Plant used in primary health practices in Vindhya region of eastern Uttar Pradesh, India. *Int J Herb Med*. 2014;2(2):31-7.
37. Bhatt VP, Negi GCS. Ethnomedicinal plant resources of Jaunsari tribe of Garhwal Himalaya, Uttaranchal. *Indian J Tradit Knowl*. 2006;5(3):331-5.
38. Sharma J, Gaur RD, Gairola S, Painuli RM, Siddiqi TO. Traditional herbal medicines used for the treatment of skin disorders by the Gujjar tribe of Sub Himalayan tract, Uttarakhand. *Indian J Tradit Knowl*. 2013;12(4):736-8.

39. Pandey NC, Bhatt D, Arya D, Chopra N, Upreti BM, Joshi GC, et al. Diversity of ethno-medicinal plant: a case study of Bageshwar district Uttarakhand. *J Med Plants Stud.* 2017;5(2):11-24.
40. V.P. Bhatt, D.P. Vashishtha, Indigenous plants in traditional healthcare system in Kedarnath valley of western Himalaya, *Indian J. Tradit. Knowl.* (2008);7(2):300-10.
41. Hota S, Chatterjee A. Traditional and indigenous uses of plants for treatment of skin diseases by the tribes in Paschim Medinipur district of West Bengal. *J Med Plants Stud.* 2016;4(5):175-80.
42. Hranush, H & Arakelyan, Hayk. *Ashwagandha (Withania somnifera)* and Withaferin. (2021)
43. Anjaneyulu ASR, Satyanarayana Rao D (1997) new withanolides from the roots of *Withania somnifera*. *Indian J Chem.* 36:424-433
44. Vibhavari Sail, M. Kyle Hadden Chapter Eighteen - Notch Pathway Modulators as Anticancer Chemotherapeutics, *Annual Reports in Medicinal Chemistry.* 2012;47:267-80.
45. Royce Mohan, Paola Bargagna-Mohan Chapter Eight - The Use of Withaferin A to Study Intermediate Filaments, *Methods in Enzymology.* 2016;568:187-218.
46. Kurup PA. The antibacterial principle of the leaves of *Withania somnifera*. *Curr Sci Bangalore.* 1956;25:57-8.
47. Sethi PD, Sharma KB, Subramanian Sankara S. Antibacterial activity of some C28 steroidal lactones. *Indian J Pharm* 1947;36:122-3
48. Ziauddin M, Phansalkar N, Patki P, Diwanay S, Patwardhan B. Studies on the immunomodulatory effects of *ashwagandha*. *J Ethnopharmacol.* 1996;50.
49. Budhiraja RD, Sudhir S. Review of biological activity of Withanolides. *J Sci Ind Res.* 1987;46:488-91.
50. Kaushik MK, Kaul SC, Wadhwa R, Yanagisawa M, Urade Y (2017) Triethylene glycol, an active component of *Ashwagandha (Withania somnifera)* leaves, is responsible for sleep induction. *PLoS ONE* 12(2): e0172508. doi:10.1371/journal.pone.0172508
51. Wadhwa, R., Konar, A., Kaul, S.C., Nootropic potential of *Ashwagandha* leaves: Beyond traditional root extracts, *Neurochemistry International* (2015), doi: 10.1016/j.neuint.2015.09.001.
52. Narayan Das Chaurasiya et al., Analysis of Withanolides in Root and Leaf of *Withania somnifera* by HPLC with Photodiode Array and Evaporative Light Scattering Detection, *Phytochem. Anal.* 19: 148-154 (2008)
53. Sayantan G, Sujata L. Withanolide D of *Ashwagandha* improves Apoptosis in the Bone Marrow of Leukemic Murine Model. *J Biomed Res Environ Sci.* 2021 June 02; 2(6): 431-438. doi: 10.37871/jbres1255, Article ID: JBRES1255
54. Glotter E, Kirson I, Abraham A, Lavis D (1973) Constituents of *Withania somnifera* (Dunal) XIII The Withanolides of chemotype III. *Tetrahedron Lett* 29:1353-64
55. Dhalla NS, Gupta KC, Sastry MS, Malhotra CL (1961) Comparative studies of *Withania somnifera*. *Indian J Pharmacol* 23:126
56. Balkrishna A, Pokhrel S, Singh H, Joshi M, Mulay VP, Haldar S, Varshney A. Withanone from *Withania somnifera* Attenuates SARS-CoV-2 RBD and Host ACE2 Interactions to Rescue Spike Protein Induced Pathologies in Humanized Zebrafish Model. *Drug Des Devel Ther.* 2021 Mar 11;15:1111-1133. doi: 10.2147/DDDT.S292805. PMID: 33737804; PMCID: PMC7961299.
57. Dar, N.J., Bhat, J.A., Satti, N.K. et al. Withanone, an Active Constituent from *Withania somnifera*, Affords Protection Against NMDA-Induced Excitotoxicity in Neuron-Like Cells. *Mol Neurobiol* 54, 5061-5073 (2017) <https://doi.org/10.1007/s12035-016-0044-7>
58. Pramanick S, Roy A, Ghosh S, Majumder H, Mukhopadhyay S (2008) Withanolide Z, a New Chlorinated Withanolide from *Planta Medica* 74(14):1745-1748
59. Kirson I, Glotter E, Abraham A, Lavis D (1970) Constituents of *Withania somnifera*. Dunal XI the structure of three new withanolides. *Tetrahedron* 26:2209-2215
60. Lavie D, Glotter E, Shvo Y (1965) Constituents of *Withania somnifera* Dun. Part IV. The structure of withaferin A *J Chem Soc* 30:7517-7531
61. Lavie D, Kirson I, Glotter E (1968) Constituents of Dun. Part X the structure of Withanolide D. *Israel J Chem* 6(5):671-678
62. Shah N, Singh R, Sarangi U, Saxena N, Chaudhary A, Kaur G, et al. Combinations of *ashwagandha* leaf extracts protect brain-derived cells against oxidative stress and induce differentiation. *PLOS ONE.* 2015;10(3):e0120554. doi: 10.1371/journal.pone.0120554, PMID 25789768.
63. Konar A, Shah N, Singh R, Saxena N, Kaul SC, Wadhwa R, et al. Protective role of *Ashwagandha* leaf extract and its component withanone on scopolamine-induced changes in the brain and brain-derived cells. *PLOS ONE.* 2011;6(11):e27265. doi: 10.1371/journal.pone.0027265, PMID 22096544.
64. Gupta M, Kaur G. Aqueous extract from the *Withania somnifera* leaves as a potential anti-neuroinflammatory agent: a mechanistic study. *J Neuroinflammation.* 2016;13(1):193. doi: 10.1186/s12974-016-0650-3, PMID 27550017.
65. Raja Sankar S, Manivasagam T, Surendran S. *Ashwagandha* leaf extract: A potential agent in treating oxidative damage and physiological abnormalities seen in a mouse model of Parkinson's disease. *Neurosci Lett.* 2009;454(1):11-5. doi: 10.1016/j.neulet.2009.02.044, PMID 19429045.
66. Gautam A, Kaul SC, Thakur MK Alcoholic Extract of *Ashwagandha* Leaves Protects Against Amnesia by Regulation of Arc Function. *Mol Neurobiol.* 2016;53(3):1760-9. doi: 10.1007/s12035-015-9117-2. PMID 25744565.
67. Kaushik MK, Kaul SC, Wadhwa R, Yanagisawa M, Urade Y. Triethylene glycol, an active component of *Ashwagandha (Withania somnifera)* leaves, is responsible for sleep induction. *PLOS ONE.* 2017;12(2):e0172508. doi: 10.1371/journal.pone.0172508, PMID 28207892.
68. Manchanda S, Kaur G. *Withania somnifera* leaf alleviates cognitive dysfunction by enhancing hippocampal plasticity in high fat diet induced obesity model. *BMC Complement Altern Med.* 2017;17(1):136. doi: 10.1186/s12906-017-1652-0, PMID 28253924.
69. Praveen K et al. Glioprotective effects of *Ashwagandha* leaf extract against lead induced toxicity. *Hindawi publishing corporation. BioMed Res Int;*2014;15:Article ID 182029.
70. Priyandoko D, Ishii T, Kaul SC, Wadhwa R. *Ashwagandha* leaf derived withanone protects normal human cells against the toxicity of methoxyacetic acid, a major industrial metabolite. *PLOS ONE.* 2011;6(5):e19552. doi: 10.1371/journal.pone.0019552, PMID 21573189.
71. Wadhwa R, Singh R, Gao R, Shah N, Widodo N, Nakamoto T, et al. Water extract of *Ashwagandha* leaves has anticancer activity: identification of an active component and its mechanism of action. *PLOS ONE.* 2013;8(10):e77189. doi: 10.1371/journal.pone.0077189, PMID 24130852.
72. Widodo N, Priyandoko D, Shah N, Wadhwa R, Kaul SC. Selective killing of cancer cells by *Ashwagandha* leaf extract and its component withanone involves ROS Signaling. *PLOS ONE.* 2010;5(10):e13536. doi: 10.1371/journal.pone.0013536, PMID 20975835.
73. Ichikawa H, Takada Y, Shishodia S, Jayaprakasam B, Nair MG, Aggarwal BB. Withanolides potentiate apoptosis, inhibit invasion, and abolish osteoclastogenesis through suppression of nuclear factor-kappaB (NF-kappaB) activation and NF-kappaB-regulated gene expression. *Mol Cancer Ther.* 2006;5(6):1434-45. doi: 10.1158/1535-7163.MCT-06-0096, PMID 16818501.
74. Udayakumar R, Kasthuriangan S, Mariashibu TS, Rajesh M, Anbazhagan VR, Kim SC et al. Hypoglycaemic and hypolipidaemic Effects of *Withania somnifera* Root and Leaf Extracts on alloxan-Induced Diabetic Rats. *Int J Mol Sci.* 2009;10(5):2367-82. doi: 10.3390/ijms10052367, PMID 19564954.
75. Udayakumar R, Kasthuriangan S, Vasudevan A, Mariashibu TS, Rayan JJ, Choi CW et al. Antioxidant Effect of Dietary Supplement *Withania somnifera* L. Reduce blood glucose Levels in alloxan-induced Diabetic Rats. *Plant Foods Hum Nutr.* 2010;65(2):91-8. doi: 10.1007/s11130-009-0146-8, PMID 20186490.
76. Dikasso D, Makonnen E, Debella A, Abebe D, Urga K, Makonnen W et al. Anti-malarial activity of *Withania somnifera* L. Dunal extracts in mice. *Ethiop Med J.* 2006;44(3):279-85. PMID 17447395.
77. Pradhan D, Biswasroy P, Sahu DK, Ghosh G, Rath G. Isolation and structure elucidation of a steroidal moiety from *Withania somnifera* and in silico evaluation of antimalarial efficacy against artemisinin resistance *Plasmodium falciparum* kelch 13 protein. *J Biomol Struct Dyn.* 2022;1-14. doi: 10.1080/07391102.2022.2077448 [Epub ahead of print]. PMID 35585777.
78. Singh H, Kaur T, Manchanda S, Kaur G. Intermittent fasting combined with supplementation with Ayurvedic herbs reduces anxiety in middle aged female rats by anti-inflammatory pathways. *Biogerontology.* 2017;18(4):601-14. doi: 10.1007/s10522-017-9706-8, PMID 28478492.
79. M M, Zameer F, Naidu A, M N NP, Dhananjaya BL, Hegdekatte R. Evaluating the inhibitory potential of *Withania somnifera* on platelet aggregation and inflammation enzymes: An *in vitro* and *in silico* study. *Pharm Biol.* 2016;54(9):1936-41. doi: 10.3109/13880209.2015.1123729, PMID 26704448.
80. Sumathi Setal, Padma PR, Gathampari S, Vidhya S. Free radical scavenging activity of different parts of *Withania somnifera*. *Anc Sci Life.* 2007;26(3):30-4. PMID 22557238.
81. Fatima I, Hussain T, Rafay M, Akram M, Bano S, Shabbir S. Evaluation of antioxidant activity of leaves and fruits extracts of five medicinal plants. *Pak J Pharm Sci.* 2017;30(5):1625-8. PMID 29084682.
82. 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. doi: 10.1186/1472-6882-12-175, PMID 23039061.
83. Usharani P et al. Effect of standardized aqueous extract of *Withania somnifera* on tests of cognitive and psychomotor performance in healthy human participants. *Pharmacogn Res.* 2014;6(1). doi: 10.4103/09748490.122912.