सत्यमेव जयते
Ministry of Ayush
Government of India

SAFETY OF
ASHWAGANDHA
Withania somnifera

REPORT OF THE EXPERT COMMITTEE
Constituted by
Ministry of Ayush Govt. of India

Safety of Ashwagandha

(*Withania somnifera*)

Report of the Expert
Committee constituted by
Ministry of Ayush
Govt. of India

Title: Safety of Ashwagandha

Authors Name: Ministry of Ayush, Government of India, New Delhi

Publisher: Central Council for Research in Ayuredic Sciences, Ministry of Ayush, Government of India, New Delhi, J.L.N.C.A.H. Anusandhan Bhawan, 61-65, Institutional Area, Opp. D-Block, Janakpuri, New Delhi -110058

E-mail: dg-ccras@nic.in

Website: www.ccras.nic.in

Table of Contents

Foreword

We are pleased to introduce this Report of the Expert Committee constituted by the Ministry of Ayush, Government of India, on the Safety of Ashwagandha (Withania somnifera), an herb that has been an integral part of traditional medicine for centuries. There has been a growing global interest in Ayurveda-based herbal and natural remedies, particularly during challenging times such as the COVID-19 pandemic. The root of Ashwagandha is one such traditional medicine which has been extensively used for its adaptogenic and immune-boosting properties. There is a large set of clinical data supporting its benefits. However, like any medicine, be it allopathic, homeopathic, herbal or traditional, there could be adverse events with its use. There have been some reports about adverse events with the usage of Aswagandha in the recent past. A report by the Danish Technical University (DTU), commissioned by the Danish Veterinary and Food Administration (DVFA), assessed the safety of Withania somnifera and raised concerns about the potential risks, including abortifacient effects, stimulation of the thyroid gland and immune system, impacts on sex hormones, and adverse effects on liver (Ref.: DTU DOCX. No. 19/1030299, dated May 15, 2020).

In light of these concerns, a committee of experts including senior Endocrinologist, Pharmacologist, Gastroenterologist, Ayurveda experts and other experts was constituted by the ministry of Ayush, to address the concerns of the DTU. The committee members carefully analysed the DTU report and the published literature, including studies at molecular and cellular level, trials on experimental animals and on human beings. A critical analysis of the data on the leaves, stem and root of the plant was undertaken by a team of experts and causality assessment in relation to the adverse events was undertaken. The unbiased and collective efforts based on evidence based science of the committee members, researchers, and contributors has been compiled into this report. .

This report is a balanced document and it has taken into account all the concerns of DTU report and of the safety concerns raised in different case reports or published series. The report provides carefully analyzed scientific information that will aid in informed decision-making. Like any other medicinal preparation, be it paracetamol or antibiotics, there could be adverse events with herbal products in some individual. In light of that, adverse events reported with Ashwagandha were well within acceptable limits of medicinal usage , but do require awareness, proper documentation and warnings and pre-emptive action. In summary, the root of Ashwagandha plant in the dosages prescribed and under the vigilant eyes of the qualified practitioner, is a safe and effective preparation. This indeed is supported by its worldwide use for centuries.

We extend our heartfelt gratitude to all those involved in the preparation of this document. I hope this scientific document, will foster a greater understanding of Ashwagandha, and advance the field of herbal medicine.

Dr. Shiv Kumar Sarin
Chancellor, Institute of Liver and Biliary Sciences, New Delhi (Chairman)

Dr. Rajesh Khadgawat
Professor, Endocrinology, All India Institute of Medical Sciences, New Delhi

Dr. J.B. Gupta
Distinguished Scientist and Pharmacologist, Delhi-NCR

Dr. Vyas M Shingatgeri
Dean, Apeejay Stya University, Haryana

Prof. Bhushan Patwardhan
National Research Professor- AYUSH, Savitribai Phule Pune University, Pune

Expert Committee & Sub Committee

Expert Committee

1. Dr. Shiv Kumar Sarin – Chancellor, Institute of Liver and Biliary Sciences, New Delhi (Chairman)
2. Dr. Rajesh Khadgawat- Professor, Endocrinology, All India Institute of Medical Sciences, New Delhi
3. Dr. J.B. Gupta- Distinguished Scientist and Pharmacologist, Delhi-NCR
4. Dr. Vyas M Shingatgeri- Dean, Apeejay Stya University, Haryana
5. Prof. Bhushan Patwardhan, National Research Professor – AYUSH, Savitribai Phule Pune University, Pune

Sub Committee

1. Dr. A. Raghu, DDG (Ayush), DGHS, Ministry of Health & Family Welfare, New Delhi (Chairman)
2. Dr. N Srikanth, DDG, Central Council for Research in Ayurvedic Sciences, New Delhi
3. Dr.Galib, Associate Professor, All India Institute of Ayurveda, New Delhi
4. Dr. Sumeet Goel, OSD (T), O/o Secretary, Ministry of Ayush, New Delhi
5. Dr. Abhijit Dutta, Research Officer (H), International Cooperation Section, Ministry of Ayush, New Delhi
6. Dr. Shruti Khanduri, Research Officer (Ay.), Central Council for Research in Ayurvedic Sciences, New Delhi
7. Dr.Ramavtar Sharma, Research Officer (Ay.), DGHS, Ministry of Health & Family Welfare, New Delhi
8. Dr. Raman Kaushik, Research Officer (Ay.), Drug Policy Section, Ministry of Ayush, New Delhi
9. Dr. Azeem Ahmad, Research Officer (Ay.), Central Council for Research in Ayurvedic Sciences, New Delhi
10. Ms. Prasanthi Sampara – Expert & Industry Representative, Hyderabad

Other Contributors

Dr. Ake Nilsson, Professor Emeritus of Medicine and Gastroenterology, Lund University, Sweden
Dr. Pradeep Dua, Technical Officer, Traditional Complementary and Integrative (TCI) Medicine Unit, WHO-Hq., Geneva
Dr. Sanjay Kumar, Assistant Director (Pharm.), Central Council for Research in Ayurvedic Sciences, New Delhi
Dr. Deepak Lamba, Research Officer (Pharm.), Central Council for Research in Ayurvedic Sciences, New Delhi

Introduction

Ashwagandha (*Withania somnifera*) is a globally renowned herb known for its numerous health benefits. During the COVID-19 pandemic, its use surged as an herbal supplement, particularly valued for its adaptogenic and immune-boosting properties. *Withania somnifera* is the most widespread species in the genus, and it occurs naturally in semi-arid and drier regions stretching from the Mediterranean across tropical Africa, South Africa, and the Canary and Cape Verde Islands, as well as Afghanistan, Baluchistan, Pakistan, Sri Lanka, China, Nepal, and India. It is also grown in gardens in warmer parts of Europe and has emerged as a natural weed in South Australia and New South Wales (Paul et al 2021). Ashwagandha has been trusted for its preventive, promotive, and therapeutic applications. Ashwagandha root has been documented to be used in Indian traditional medicine since 1000–1500 BC and is recognized for its diverse pharmacological profile encompassing adaptogenic, immunomodulatory, rejuvenative, and aphrodisiac properties. It is extensively documented in Ayurvedic texts as *Rasayana*, which means beneficial for rejuvenation, immunomodulation, and longevity, and also for treating several conditions including but not limited to musculoskeletal, neurological, dermatological, respiratory, and reproductive system disorders in recent years, modern research has further validated these traditional claims.

Thousands of years of use in traditional medicine and available scientific evidence reported that Ashwagandha is well-tolerated, safe, and clinically effective. The data obtained from various studies did not demonstrate any serious adverse events of concern. However, Danish Technical University (DTU) in its report raised concerns such as the abortifacient effect, stimulation of the thyroid gland & immune system, effect on sex hormones, and adverse liver reactions.

In this respect, the Ministry of Ayush, Government of India has constituted an expert committee to address the issues raised in the DTU report. The primary goal of this technical report is to consolidate current evidence-based knowledge about Ashwagandha root, in the backdrop of observations highlighted in the DTU report. The committee has strived to include the most reliable and credible scientific information to make this document a comprehensive account of the topic, without compromising its scientific integrity.

Phytochemistry

Ashwagandha contains a varied range of bioactive compounds ranging from alkaloids, steroids, flavonoids to phenols. The active substances primarily responsible for its pharmacological effects are withanolides and alkaloids.

Withanolides are steroidal compounds of the ergostane type, with a δ-lactone functionality between the C-22 and C-26 atoms and an oxidized C-1 position. Reports indicate that more than 40 withanolides have been identified in various parts of the plant. The major withanolides include withaferin A, withanolides A-Y, withanone, withadomniferin A, and withasomniferols. Additionally, over 12 alkaloids have been reported in Ashwagandha, including anaferine, anahygrine, pseudotropine, somniferine, isopelletierine, cuseohygrine. Flavinoids such as 3-O-rutinoside, 6,8-dihydroxycemferol, quercetin and its glycosidic derivative, 3-O-rutinoside-7-O-glucoside are also present in the raw material. Moreover, withanolide glycosides, which have a structure that contains a glucose moiety at position C-27, are found in the raw material. This group of compounds includes sitoindoside IX and sitoindoside X (Paul et al., 2021; Bashir et al., 2023)

Because of unique structures and functions of these compounds, the chemical composition of the aerial parts of a plant differs from that of roots. In Ashwagandha, not all bioactive compounds are uniformly distributed across the different parts of the plant. Sahoo et al, (2024) conducted phytochemical profiling of the leaves, stems, roots, and seeds of Ashwagandha, and reported that the aerial parts (leaves and stems) exhibited a greater number of TLC bands for alkaloids, phytosterols, and triterpenoids compared to the roots and seeds. Saleem et al (2020) summarized various phytochemical studies which revealed the presence of different bioactive constituents from different plant parts as listed below.

Phytochemistry of various parts of Withania somnifera as summarized by Saleem et al., 2020

Plant Part	Phytochemicals Isolated	Nature of Extract
Roots	Withasomnine, Withanolide A	Alcoholic
	Withanosides I, II, III, IV, V, VI, and VII, Ashwagandhanolide, Pseudotropine, isopelletierine, 3α-tigloyloxtropine tropine, dl-isopelletierine-3-tropyltigloate, cuscohygrine, anaferine, hygrine, anahygrine, somniferine, mesoanaferine,choline,withanine,visamine,withananine, hentriacontane, withasomnine, along with pyrazole derivatives pseudowithanine and ashwagandhine	Methanolic
	Withasomniferol A, B, and C	Benzene, ethyl acetate
	β-sitosterol and d-glycoside	Petroleum ether, acetone
	Withanoside IV and withanoside VI	Butanol

Plant Part	Phytochemicals Isolated	Nature of Extract
Leaves	Anaferine (bis (2-piperidylmethyl) ketone), tropine, isopelletierine, 3α-tigloyloxtropine, pseudotropine, cuscohygrine, 3-tropyltigloate, anahygrine, hygrine, dl-isopelletierine, mesoanaferine, somniferine, choline, hentriacontane, withanine; withananine, withasomnine, visamine, ashwagandhine, and pseudowithanine	Methanolic
	Withanolide D, N, O, P, Withanolides G–M, F, T, U	Alcoholic
	Withanoside IV, physagulin, and withanoside VI	Butanol
Fruits	Withanamides A-I	Methanolic
	Linoleic acid, palmitic acid, tetracosanoic acid, elaidic acid, and oleic acid	Oils
Stem bark	Withasomnilide, somniferanolide, somniferawithanolide, withasomniferanolide, and somniwithanolide	Ethanolic

The differences are not only limited to the nature of phytochemicals in different plant parts but also reflected quantitatively. As observed in the table below, the concentrations of some of the phytochemicals are more in leaves than root or vice-versa (Chatterjee et al., 2010, Namdev et al., 2011, Johri et al., 2005).

Substance	Root	Leaves
Triterpenoids		
Withanone	5.54 ± 0.4mg/g (DIN)	18.42 ± 0.8mg/g CDW)
27-deoxywithanone	3.94 ± 0.4mg/g (DW)	1.63 ± 0.2mg/g CDW)
27-hyd roxywit ha none		
Steroids		
Withaferin A	0.92 ± 0.4mg/g (DW)	22.31 ± Img/g (DW)
17-hyd roxy-27-deoxyWithaferin A	0.66 ± 0.2mg/g (DW)	3.61 ± 0.5mg/g (DW)
Withanolide A	3.88 ± 0.7mg/g (DW)	2.11 ± 0.5mg/g (DW)
Withanolide B-D		
27-hydroxy Withanolide B	0.55 ± 0.2mg/g (DW)	2.78 ± 0.5mg/g (DW)
Withanoside IV	0.44 ± 0.1mg/g (DW)	1.60 ± 0.2mg/g (DW)
Withanoside VI	3.74 ± 0.2mg/g (DW)	1.90 ± 0.2mg/g CDW)
12-deoxywithastromonolide	1.90+/-O.5mg/g (DW)	2.15+/-O.5mg/g CDW)
Physagulin	Not detected	3.46 ± 0.4mg/g (DVM)

These quantitative and qualitative differences in phytochemicals are reflected in the plant's efficacy too. Kaul et al. (2016), measured the withanolides content from the root and the leaves of the same plant and reported that withaferin A concentration was much higher in leaves than in roots. They also measured the cytotoxicity against human normal fibroblasts (TIG-3) and cancerous cell lines, Osteosarcoma (U2OS), and Fibrosarcoma (HT1080), and reported that

leaf extracts showed higher toxicity to human cancer cells as compared to the root extracts. Differences are also reported in the effect of different plant parts on sperms, where in vitro incubation of fruit or stem extracts reduced sperm motility and count (Mali et al., 2008; Singh et al., 2013) whereas root extract incubation had the opposite effect (Kumar et al., 2015).

Recently Lingfa et al (2023) reported that in the MTT cytotoxicity assay, methanolic extracts of leaf and stem were more potent that roots, in HepG2 cells (IC50 values of 43.06 ± 0.615, 45.60 ± 0.3, and 314.4 ± 0.795 µg/mL respectively) and in L929 cell lines (IC50 values of 78.77 ± 0.795, 90.55 ± 0.800, and 361.70 ± 0.795 µg/mL respectively). The leaf methanolic extract was the most effective, followed by the stem methanolic extract in the HepG2 cell line.

The DTU Food Institute in its report has admitted that they have included experimental studies carried out with other plant parts than the root, as there is a coincidence of ingredients. Withanolides and alkaloids are also found in other plant parts, and therefore experimental studies with other plant parts than the root can help to shed light on possible effects of the root.

However, based on the studies cited in this document and many other similar studies, it is suggested that although some phytochemicals may be common across different plant parts, the presence of other phytochemicals and the varying concentrations of common phytochemicals in different parts result in different safety and efficacy profiles for the root compared to the aerial parts of the plant. Therefore, it is recommended to restrict usage to the time-tested and preferred part of Ashwagandha, which is the root. To quote, “Banning Ashwagandha roots based on the data on the toxicity of leaves or berries is akin to banning apples because their seeds contain amygdalin, which is a precursor to cyanide.”

Safety Profile of Ashwagandha

Thousands of years of use in traditional medicine and available scientific evidence demonstrate that Ashwagandha is well-tolerated, safe, and clinically effective. The data obtained from various studies did not demonstrate any serious adverse events of concern.

Despite of its extensive usage and clinical evidence, the report "Risk assessment of the root from Withania somnifera" prepared by DTU Food Institute (Fødevareinstituttet) and submitted to The Dietary Supplement Group (Kosttilskudsgruppen), The Danish Veterinary and Food Administration discusses safety concerns of Ashwagandha. However, the DTU report mentions that it was unable to find reports identifying the various active substances in the various plant parts. The DTU mentions that there is information about the root to be used as an abortifacient. DTU also mentions that there are animal studies that show a negative effect on sex hormones, the immune system and thus these effects could pose a potential safety risk in humans. Lastly, DTU also mentions the possible impact of Ashwagandha on the thyroid gland.

The DTU report has several methodological gaps including a lack of comprehensive search strategy, insufficient logical interpretation, and selective reporting. Moreover, it relies on only one database and uses only two search terms, selecting negative findings from a limited number of studies.

However, the evidence for the safety of Ashwagandha is further evaluated through the studies published before and after 2020 (more than 500 PubMed-indexed citations), which highlighted significant scientific limitations in the DTU report.

In the succeeding sections of this dossier, the safety concerns on liver, thyroid, sex hormones, immunomodulatory, CNS, and abortifacient activities have been addressed based on available studies.

Pre-clinical studies on the safety of Ashwagandha

There are several toxicological studies conducted to evaluate the safety of Ashwagandha root extract. These studies cover various toxicological evaluations, including acute, sub-acute, 90-day repeated dose toxicity, mutagenicity/genotoxicity, and prenatal developmental toxicity assessments. The findings consistently indicate that Ashwagandha root extracts, administered in various dosages up to 2000 mg/kg, exhibited no evidence of morbidity, mortality, or toxicologically relevant clinical signs in animal models. Thus, the root extract has proven to be safe and well-tolerated. The table below summarizes these comprehensive pre-clinical studies.

S.no	Reference	Experimental Model	Ashwagandha formulation	Conclusion
1.	**Acute Toxicity studies (Single dose studies)**			
	Khojah EY et al., 2020	Male albino mice	Root extract	No toxicity was observed even at 2000 mg/kg.
	Patel SB et al., 2016	Wistar rats	Root extract	No toxicologically significant changes were observed. NOAEL was determined to be 2000 mg/kg.
	Prabhu PC et al., 2013	Wistar rats	Hydroalcoholic root extract	No toxicity was observed even at 2000 mg/kg.
	Jain H et al., 2003	Mice	Hydroalcoholic root extract	2000 mg/kg dose is considered safe. No mortality or gross behavioral changes were observed
2.	**Sub-acute toxicity studies (Repeated dosing for 14 to 28 days)**			
	Kalaivani et al., 2024	Nulliparous and non-pregnant Wistar Albino rats	Standardized aqueous root extract	No mortality, morbidity, or toxicity. No effects on body weight, feed consumption, organ weights, or gross pathology. The extract was well tolerated up to 2000 mg/kg for 14 days.
	Langade et al., 2023	Wistar rats	Standardized aqueous root extract	No signs of intoxication. Vital liver parameters remained stable, and no abnormalities in general parameters. All hematological and biochemical parameters were within normal range, indicating safety in this 28 day study.
	Khojah EY et al., 2020	Male albino mice	Root extract	No toxicity was observed even at 2000 mg/kg in 28 days
	Patel et al., 2016	Wistar rats	Standardized root extract	No toxicologically significant changes were observed. NOAEL was determined to be 2000 mg/kg. The extract showed no adverse effects even after a 14-day recovery period following 28 days of administration.

S.no	Reference	Experimental Model	Ashwagandha formulation	Conclusion
	Prabhu PC et al., 2013	Wistar rats	Hydroalcoholic root extract	No toxic signs or mortality. No significant changes in body weights, organ weights, or haemato-biochemical parameters. NOAEL was determined to be 2000 mg/kg.
3.	**90-day Repeated Dose Toxicity study**			
	Kalaivani et al., 2023	Nulliparous and non-pregnant Wistar Albino rats	Standardized aqueous root extract	No morbidity, mortality, or clinical toxicity. No adverse effects on body weight, food consumption, blood indices, or liver histopathology. NOAEL was determined to be 2000 mg/kg.
4.	**Mutagenicity/Genotoxicity Test**			
	Kalaivani et al., 2023	Swiss Albino mice & Various in vitro genotoxicity models	Standardized aqueous root extract	The results demonstrated Ashwagandha root extract failed to show any mutagenic effects up to a dose of 5 mg/plate in the Bacterial reverse mutation test, and did not show any clastogenic activity in doses up to 2 mg/ml in chromosome aberration (CA) test with and without metabolic activation. Also, in the in vivo micronucleus test Ashwagandha root extract at doses up to 2000 mg/kg body weight showed no evidence of clastogenic activity or cytogenetic damage in the bone marrow erythrocytes of Swiss albino mice
5.	**Prenatal and Developmental Toxicity Study**			
	Prabhu PC et al., 2015	Wistar rats	Root extract	No maternal or fetal toxicity was observed. The extract did not affect body weight, number of viable fetuses, or cause malformations. NOEL was determined to be 2000 mg/kg.

Effect of Ashwagandha on Pregnancy, Fetal Development, and Female sexual health

The safety of Ashwagandha during pregnancy and fetal development has been evaluated in the following studies:

Reference	Description of the study	Study type	Nature of Evidence	Conclusions
Kalaivani et al 2023	90-days toxicity Wistar Albino rats, Root extract 2000 mg/kg/day	Controlled Pre-Clinical	90-days toxicity study	Histopathology of ovaries and uterus with cervix and vaginal cytology was observed in female animals of all the groups on day 91 and in the recovery group on day 105 in the control and high dose (2000 mg/kg/day) groups. The microscopic examination did not reveal any test item related histopathological finding in any of animals when compared with animals of control group.
Prabu et al 2015	Pregnant rats - Root extract up to 2000 mg/kg/day	Pre-clinical	Maternal & fetal toxicity	No evidence of maternal or fetal toxicity was observed. Root extract caused no changes in the body weight of parental females, number of corpora lutea, implantations, viable fetuses, external, skeletal, and visceral malformations.
Smith et al 2023	Root extract, 400 mg/day	Randomized, double-blind, placebo-controlled Clinical trial	Safety and Efficacy	Reported a slight increase in serum estradiol level, however, the estradiol remained within the normal range.
Gopal et al 2021	Perimenopausal Women Root Extract 600mg/day for 8 weeks	Randomized, double-blind, placebo-controlled Clinical trial	Safety and Efficacy	There was a reduction in MENQoL score, hot flash score, serum FSH, and serum LH, and an increase in serum estradiol level.
Ajgaonkar et al 2022	Hypoactive sexual desire disorder (HSDD) women 600mg/day	Prospective, Randomized, Placebo-controlled Clinical Study	Safety and Efficacy	Reported improvement in sexual functions.

However, the World Health Organization (2009), in its monograph on Ashwagandha, mentioned that there is a lack of safety data and cautioned its use during pregnancy or breastfeeding as cited from the American Herbal Pharmacopoeias - Ashwagandha Root Monograph and Therapeutic Compendium (2000).

Further, Roy Upton, President of American Herbal Pharmacopoeia, recently stated that "earlier cautions regarding the use of Ashwagandha in pregnancy and its claimed use as an abortifacient were based on anecdotal reports from the ethnobotanical literature that provided no indication that such an effect was evident. The misrepresentation of the AHP monograph has been repeated uncritically, resulting in the misconception that Ashwagandha root is potentially unsafe." On the contrary, he quoted that "based on a critical and comprehensive review of the traditional and modern literature, as well as the opinion of the majority of experts, there is no evidence of an abortifacient effect of Ashwagandha root." While adequate caution is warranted when using any substance during pregnancy, there is no experimental or clinical study that has reported such an effect.

The American Herbal Products Association's Botanical Safety Handbook (BSH) reclassified its safety Class from 2d to 1 based on new studies and affirmed the reproductive safety of Ashwagandha in 2022. BSH Class 1 signifies that a plant is considered safe when used appropriately.

Published preclinical and clinical studies have reported no adverse effects on female sex organs, pregnancy, or fetal development in the recommended doses.

Effect of Ashwagandha on the male reproductive system

Numerous studies have explored the potential of Ashwagandha roots in addressing reproductive system disorders, including infertility, ejaculatory dysfunction, testicular failure, and abnormalities in semen volume and/or quality. A selection of these studies is summarized below. It is important to note that the effects of the recommended part of the herb—its roots—differ from those of other plant parts. Therefore, caution should be exercised when interpreting results from studies on other parts of the plant and assuming they apply to the root.

Pre-clinical studies (on Root):

S.no	Reference	Ashwagandha Formulation with Dose	Experimental Model	Conclusions
1	Yadav A et al 2014	Purified root powder, 150 and 300 mg/kg/day for 30 days	Stressed and sexually sluggish male rats	Improvements in sexual activities, increased frequencies of erections, mounts, intromissions, and ejaculations, and positive influence on neurotransmitter and hormone levels linked to sexual desire and stress management. A dose-dependent increase in serum LH, FSH, and testosterone levels.
2	Sahin et al 2016	Root extract, 300 mg/kg/day for 8 weeks	Sprague-Dawley male rats	No effect on the weight of testes, epididymis, vas deferens, ventral prostate; Increased mounting & intromission frequency, sperm count & motility, serum testosterone; activated Nrf2/ HO-1 pathway while inhibiting NF-κB levels. No effect on testes histopathology & sperm morphology.
2	Rahmati et al2016	Root powder mixed pelleted food, 6.25% w/w (equivalent to 300 mg/kg/day) for 21 days	Morphine-addicted male rats	Morphine addiction reduces the level of testosterone, LH, and estrogen without any effect on FSH and progesterone. Ashwagandha restored testosterone, LH, and estrogen levels to normal
4	Kumar A et al2015	Root extract, 100 mg/kg body weight; for 30 days	Arsenic-induced testicular toxicity in Male Charles Foster rats	Significant ameliorative effects; improved sperm counts, sperm motility, hormonal balance, and reduced lipid peroxidation; restored testicular histology.
5	Ganu et al 2010	Root powder; up to 400 mg/kg/day for 4 weeks	Male Wistar rats	Sperm cells improved; mating behavior improved; Testes & prostate weight increased;

S.no	Reference	Ashwagandha Formulation with Dose	Experimental Model	Conclusions
6	Kiasalari et al2009	Root powder mixed pelleted food, 6.25% for 4 weeks	Streptozotocin induced diabetic male Wistar rats	WS was effective in lowering FSH serum levels in both diabetic and non-diabetic groups while increasing progesterone, testosterone, and LH levels in non-diabetic treated animals. Ashwagandha also reversed the reductive effect of diabetes on progesterone.

Pre-Clinical Studies (other plant parts)

S.No	Reference	Ashwagandha Formulation with Dose	Experimental Model	Conclusions
Stem				
1	Singh et al 2013	Stem extract, 25 and 50 mg/kg/ day for 60 days	Male & female rats	In treated males, the relative organ weight of testes, epididymis, and seminal vesicles were reduced; sperm cells and sperm motility reduced; spermatozoa formation ceased; testosterone and FSH reduced. Males were paired with fertile females and pregnancy was reduced by 71% at the highest dose level.
Fruit				
2	Mali et al 2008	Fruit extract, 50 mg/kg/day for 60 days	Male rats	Weight of testicles & seminal vesicle were lower; sperm motility and count reduced; histopathological changes in testicles which probably interfered with sperm formation
Leaves				
3	Abdel-Magied et al2001	Leaf extract, 470 mg/kg body weight for 6 days	Male Wistar rats	20 days old treated rat showed spermatogenesis which was absent in the control group; testosterone and FSH levels lowered; no effect on LH;
4	Al-Qarawi et al2000	Leaf extract; 470 mg/kg/day in 17 days or 25 days old rats for 6 days	Female immature rats	Weight gain, ovary weight, LH, and FSH were similar to control in 17 days old but in 25 days old rat's ovary weight and FSH were higher than in control; probably an early sign of sexual maturation

Clinical Studies

From the above-mentioned preclinical studies, it is obvious that root extract had positive effects on reproductive health whereas other parts of the plant mostly had negative effects. Almost similar findings were also reported in several clinical studies. The summary of the relevant studies is given below:

Condition / Reference	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events	Summary of results
Male Sexual Function and Fertility, Ambiye et al., 2013	Randomized, Double-Blind, Placebo – Controlled 12 Weeks	Infertile men / aged between 22 and 40 years Ashwagandha (n =21, 21), Placebo (n =25, 25)	225mg - Standardized Aqueous Ashwagandha Root Extract Thrice daily	Semen Parameters, Serum Testosterone, Serum Luteinizing Hormone	Ashwagandha (0) Placebo (0) There were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.	Ashwagandha is associated with significant increase in sperm concentration, semen volume, sperm motility, serum testosterone, and LH. No changes occurred in the placebo group
Male Sexual Function, Chauhan et al 2022	Randomized, Double-Blind, Placebo – Controlled 8 Weeks	Males aged between 21 and 45 years with low sexual desire Ashwagandha (n =25, 25), Placebo (n =25, 25)	300 mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	DISF-M, Serum Testosterone, PRL, SF-36	Ashwagandha (4 - Sleepiness, Mild Abdominal Pain, Low-Grade Joint Pain) Placebo (3 - Abdominal Pain, Mild Diarrhea)	Compared to the placebo, Ashwagandha was associated with significantly greater increase in Total DISF-M scores and serum testosterone levels. The reported adverse events were of mild severity and no intervention was required.
Idiopathic Maleinfertility Azgomi et al 2018a	Triple-blind, Randomised, Parallel Group, Two Arm, clinical trial. 12 Weeks	Married infertile male patients aged between 18 and 45 years Ashwagandha (n = 50, 46) Pentoxifylline (n = 50, 45)	6 capsules containing 5 g Hydroalcoholic Ashwagandha root extract once daily 6 capsules containing 800 mg Pentoxifylline once daily	Sperm parameters	Ashwagandha (1 - nausea and epigastric pain) Pentoxifylline (3 - nausea and epigastric pain) These events were resolved without any intervention and participants continued the study treatments till the end of the study.	Within group Ashwagandha markedly increased mean sperm count, progressive motility, and improved sperm morphology. However, the impacts of the two medications were not significantly different.
Seminal plasma metabolites of infertile males Gupta et al 2013	Clinical Study 12 Weeks	Infertile males aged 22–45 years Ashwagandha (n = 180) Control (n = 50)	Withania somnifera root powder (WSR) 5 g/day	Semen Profile, Testosterone, LH, FSH, PRL, IDH, LDH, ALT, AST	Ashwagandha (0) Control(0) There were no adverse events reported and Ashwagandha was well tolerated by all the participants.	Compared to the baseline, WSR normalise the disturbed concentrations of lactate, alanine, citrate, GPC, histidine, and phenylalanine in seminal plasma and recovers the quality of semen. Serum biochemistry was also improved over post-therapy.

Condition / Reference	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events	Summary of results
Mamidi et al 2011	Psychogenic erectile dysfunction Randomized, Single-blind, Placebo-controlled, parallel-group study. 8 Weeks	Patients with psychogenic erectile dysfunction aged between 18 - 60 years Ashwagandha (n = 46, 41) Placebo (n = 49, 45)	4 tablets 500mg Ashwagandha root powder - thrice daily	Semen analysis, Routine Haematological tests, Biochemical Investigations, Serum Testosterone	Ashwagandha (0) Placebo (0) Ashwagandha was well tolerated by all the participants.	Compared to the baseline there was significant improvement in International Index of Erectile Function items, but the result was insignificant when compared to placebo.
Smith et al 2023	Randomized, Double-Blind, Placebo – Controlled 12 Weeks	Healthy Adults aged between 40 and 75 years Ashwagandha (n = 60, 55), Placebo (n = 60, 56)	200 mg – Hydroalcoholic Ashwagandha root extract - twice daily	PSS, CFS PROMIS-29, Sex hormone concentrations, MDA, FG, HbA1c, TSH, HRV, Grip strength, Anthropometric measures, LFT, RFT, FBC	Ashwagandha (13 - Digestive disturbances, Mood disturbances/ changes, Headaches/migraines, Increased appetite, Increased tiredness) Placebo (15 - Digestive disturbances, Mood disturbances/ changes, Headaches/migraines, Increased appetite, Itchy Skin, Increased tiredness) There were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.	In the Ashwagandha group, there was a significant increase in the blood concentration of free testosterone and luteinizing hormone compared to the placebo group. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study.
Wankhede et al 2015	Randomized, double-blind, placebo-controlled clinical study 8-week	Healthy males aged between 18 and 50 years Ashwagandha (n = 29), Placebo (n = 28)	Standardized Aqueous Ashwagandha Root Extract 300mg twice daily	Serum Testosterone	Ashwagandha (0) Placebo (0)	The serum testosterone level was significantly increased in the Ashwagandha group as compared to the placebo control group.
Ahmad et al 2010	Prospective Clinical Study 3 Months	infertile males and matched healthy controls aged 25–40 years Ashwagandha (n = 75) Control (n = 75)	Ashwagandha root powder (5 g/ day)	Semen profile, Oxidative biomarkers, Reproductive hormone levels	Ashwagandha (0) Control (0) Ashwagandha was well tolerated by all the participants.	The treatment with Ashwagandha significantly increased serum testosterone and LH and reduced the levels of FSH and PRL

Condition / Reference	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events	Summary of results
Mahdi et al 2011	Clinical Study 3 Months	Normozoospermic but infertile men (n = 60) and Normozoospermic fertile men (n = 60) as controls	Root powder of Ashwagandha 5 g/day for 3 months	Biochemical and stress parameters including Serum testosterone (T), LH, FSH, and PRL	Not Reported	Treatment resulted in a decrease in stress, improved the level of anti-oxidants and improved overall semen quality in a significant number of individuals. The treatment resulted in pregnancy in the partners of 14% of the infertile participants

PSS - Perceived Stress Scale, GHQ- 28 - General Health Questionnaire-28, DASS - Depression Anxiety and Stress Scale, HAM-A/ HARS - Hamilton's Anxiety Rating Scale; FCQ - Food Craving Questionnaire, OHQ - Oxford Happiness Questionnaire, TFEQ - Three Factor Eating Questionnaire, BMI - Body Mass Index, PSQI – Pittsburgh Sleep Quality Index, ADHD-RS - Attention deficit hyperactivity disorder rating scale, RCMAS - Revised children's manifest anxiety questionnaire; WHOQOL-BREF - World Health Organization Quality-of-Life Scale – BREF, SOL – Sleep Onset Latency, TST – Total Sleep Time, WASO – Wake After Sleep Onset, TIB – Total Time in Bed, SE – Sleep Efficiency, CANTAB - Cambridge Neuropsychological Test Automated Battery, MoCA - Montreal Cognitive Assessment, GAD-7 - Generalized anxiety disorder scale, QOL - Quality of life, CFS - Chalder Fatigue Scale, PROMIS-29 - Patient-Reported Outcomes Measurement Information System Questionnaire, HDRS - Hamilton Depression Rating Scale, GSQS - Groningen Sleep Quality Scale, WHO-QOL - WHO-quality of life Questionnaire, BAI - Beck Anxiety Inventory, SF-36 – Short form 36 Questionnaire, FQ- Fatigue Questionnaire, VAS – Visual Analogue Scale, GRS - Global Rating Scale, DISF-M/ - Derogatis interview for sexual functioning (Male), FSFI - Female Sexual Function Index, FSDS - Female Sexual Distress Scale, SAR - Sexual Activity Records, MRS - Menopause Rating Scale, MEN-QoL- Menopause Specific Quality of life index, Hot Flash Score, Y-BOCS - Yale-Brown Obsessive Compulsive Scale, BDNF - Brain-derived Neurotrophic Factor, MDA – Malondialdehyde, GSH – Glutathione, NO - Nitric oxide, Free T3 - Serum Free triiodothyronine, Free T4 - Serum Free thyroxine, TSH - Thyroid-stimulating hormone, HbA1c - Glycated Haemoglobin, LFT – Liver Function Tests, RFT – Renal Function Test, CBC / FBC – Complete Blood Count, HRV – Heart Rate Variability, FG – Fasting Glucose, Free T3 - Serum Free triiodothyronine, Free T4 - Serum Free thyroxine, LH - Luteinizing hormone, FSH - Follicle-stimulating hormone, PRL – Prolactin, IDH - Isocitrate dehydrogenase, LDH - Lactate dehydrogenase, ALT - Alanine aminotransferase, AST - Aspartate aminotransferase, Hormone Parameters, RT-PCR - Reverse Transcription Polymerase Chain Reaction, RER - Respiratory exchange ratio.

The above mentioned studies clearly show the clinical safety and positive effects of Ashwagandha roots on the male reproductive system. On the other hand, extracts from aerial parts like stems, leaves, or fruits have either neutral or reported some adverse effects.

The reasons for these contradictory effects are difficult to explain. However, in some studies where two plant parts are compared, the differences in their effects were evident. Kaul et al. (2016), measured the withanolides content from the root and the leaves of the same plant and reported that withaferin A concentration was much higher in leaves than in roots. They further measured the cytotoxicity against human normal fibroblasts (TIG-3) and cancerous cell lines, Osteosarcoma (U2OS), and Fibrosarcoma (HT1080), and reported that leaf extracts showed higher toxicity to human cancer cells as compared to the root extracts. The reason for more cytotoxicity of the leaf over root is a matter of investigation, whether it is attributed to higher withaferin-A and withanone levels compared to withanolide-A in the leaf or to some other chemical constituents.

Sahoo et al, (2024) undertook phytochemical profiling of the leaf, stem, roots, and seeds of Ashwagandha and reported that the aerial parts (leaves and stems) exhibited a greater

number of TLC bands for alkaloids, phytosterols, and triterpenoids compared to the roots and seeds. This partly explains the reason for the differences in the effects of different plant parts. Differences are also reported in the effect of different plant parts on sperms, where in vitro incubation of fruit or stem extracts reduced sperm motility and count (Mali et al., 2008; Singh et al., 2013) whereas root extract incubation had the opposite effect (Kumar et al., 2015). To fully understand the herb's benefits and appreciate the chemical diversity in different plant parts, we must consider the unique effects of each component—fruit, leaf, and root—rather than simply extrapolating the effects of one to another.

Effect of Ashwagandha on Thyroid Hormones

Ashwagandha is reported to restore thyroid hormone levels to near normal in experimental models of hypothyroidism. The data is summarized below:

S.no	Reference	Ashwagandha Formulation with Dose	Experimental Model and Sample Size	Conclusions
1	Hosny et al 2021	Ashwagandha root extract (AE), 500 mg/kg	Propylthiouracil-induced thyroid dysfunction in male Wistar Albino rats (n=35)	Restored T3 and T4 levels, improved oxidative stress markers, reduced hippocampal TNF-α levels, and reduced nervous system complications.
2	Abdel-Wahhab et al 2019	Ashwagandha methanolic extract (AME), 500 mg/kg/day	Male albino rats with hypothyroidism induced by propylthiouracil	Improved thyroid hormones to near-normal levels, reduced oxidative stress markers, and ameliorated histopathological changes in the thyroid gland.
3	Panda and Kar, 1998	Ashwagandha root extract, 1.4g/kg/day, for 20 days	Adult healthy Swiss albino male mice (n=20)	Increased levels of T4 and T3 and antioxidant enzymes in the liver. Reduced hepatic lipid peroxidation.
4	Panda and Kar, 1999	Ashwagandha root extract (1.4 g/kg/day)	Adult healthy Swiss albino female mice (n=28)	Increased T4 but not T3 level. Decreased lipid peroxidation and increased levels of antioxidant enzymes.

Upon critical review of the published data, we found there are few recent studies, both clinical and experimental, where serum thyroid hormone levels were studied.

Preclinical studies on Thyroid Safety

In a recently published study, **Kalaivani et al. (2023),** evaluated Ashwagandha root extract, (up to 2000 mg/kg/day p.o.) in a 90-day toxicity study in 100 non-pregnant Wistar Albino rats. There was no adverse effect on thyroid hormones, including TSH, T3, and T4. Notably, no abnormalities were detected in the histopathology examination of several tissues.

This study thus adds important information to the studies by **Abdel-Wahhab et al. (2019), Panda and Kar (1998 and 1999)** that are listed in the above table. Although Ashwagandha root extract improved the thyroid hormones level, none of these studies reported serum thyroid levels beyond normal physiological ranges.

These studies suggest that although Ashwagandha has the potential to increase thyroid hormone levels, one may, however, doubt whether the findings by Panda and Kar and the

observation that Ashwagandha counteracts propylthiouracil-induced thyroid dysfunction, signal an increased risk of inducing hyperthyroidism. All changes in thyroid hormone levels were within the physiological range and there were no changes in thyroid gland histopathology findings. Furthermore, in female mice, only T4 increased but not T3 .

Clinical studies on Thyroid Safety

Vaidya VG et al. (2024), undertook a non-randomized, open-label, single-treatment clinical study conducted over 4 weeks to evaluate the safety of hydroalcoholic Ashwagandha root extract with 18 healthy male participants. Ashwagandha was administered at a dosage of 500 mg twice daily (1000mg/day). The serum thyroid hormones TSH, T3, and T4 levels after 30 days of treatment remained within normal values, leading authors to conclude that Ashwagandha root extract is safe and well-tolerated by healthy human subjects on physical, hematological, and biochemical characteristics, and no significant alterations or irregularities were observed in safety metrics like liver, kidney, and thyroid.

In another randomized, double-blind, placebo-controlled, parallel-group clinical study on 80 healthy individuals, **Verma et al. (2021)** administered Ashwagandha 600 mg/day for 8 weeks. There was no statistically significant change or abnormality observed in serum thyroid hormones. he estimated mean values for T4 hormones for the females were insignificant both in the placebo ($p = 0.26$), and the treatment ($p = 0.48$) group. For the male participants also it was insignificant for the placebo ($p = 0.33$), and the treatment group ($p = 0.67$). Similarly, the statistical evaluation for the estimated T3 hormones was also insignificant for both males ($p = 0.36$) and females ($p = 0.48$) in the treatment group. The statistical analysis of the mean estimated TSH values showed similar results for the male ($p = 0.79$) and the female ($p = 0.43$) participants in the treatment groups. In a clinical trial of 50 subjects with hypothyroidism, Sharma et al. (2018)found that Ashwagandha root extract at 600 mg/day for 8 weeks improved the serum levels thyroid hormone (TSH, T3, and T4) levels near - normal levels.

None of the subjects in these clinical studies reported the thyroid hormone levels beyond normal .

However, DTU raised concerns about Ashwagandha's safety on thyroid function mentioning that "animal studies have shown that the root or its extract can affect the hormones of the thyroid gland. There are some studies that suggest that the plant (not all studies specified the plant part used) may increase the level of these hormones in humans, which in turn may present the risk of developing increased metabolism."

DTU also cited a few human studies and case reports. DTU discusses a clinical trial of 50 subjects with hypothyroidism **(Sharma et al. (2018),** where Ashwagandha root extract 600 mg for 8 weeks improved the serum levels of thyroid hormone levels (TSH, T3, and T4) to near-normal levels. In none of the subjects did thyroid hormones increase beyond normal levels. A case report by **van der Hooft (2005)** reported thyrotoxicosis with low TSH and increased T4 level in a 32-year-old healthy female taking Ashwagandha for fatigue.

Can Ashwagandha Be Linked to Hyperthyroidism as Claimed in a Few Reports?

After the DTU report, a couple of case reports described thyroid hormone imbalances, probably linked to Ashwagandha. **Hayashi et al. (2024)** from Japan reported that a 47-year-old bodybuilder developed thyrotoxicosis after 2 months of Ashwagandha, which was reversed on discontinuation of the herb. In another case report, **Kamal et al. (2022)** from the USA reported that a 73-year-old female taking Ashwagandha for hyperthyroidism for 2 years, developed low TSH levels, but normal serum T3 and T4 levels, and increased thyroid microsomal antibodies, representing Hashimoto thyroiditis.

The central question is whether Ashwagandha has any direct or indirect effect on the thyroid gland or thyroid hormone release, and whether it can cause thyrotoxicosis as a side effect.

The 90-day repeated-dose toxicity at a high dose level of 2000 mg/kg/day did not show any changes in serum thyroid hormone levels in normal healthy rats, and the histopathology findings were normal **(Kalaivani et al., 2023).** This and other safety studies exclude an intrinsic effect of Ashwagandha on thyroid gland morphology or thyroid hormone release. In other studies, undertaken in chemically induced hypothyroid rats, Ashwagandha improved the thyroid hormone levels near-normal. None of these studies reported serum thyroid hormone levels beyond the normal range. It is well-reported that high-grade inflammation and oxidative stress are responsible for chemically induced hypothyroidism.

DTU quoted a clinical study **(Gannon et al., 2014)** where Ashwagandha extracts at a dose of 500 mg for 8 weeks in 3 patients of bipolar disorders did not affect T3 but a slight increase in the serum T4 level (7-24%). Careful evaluation of the results suggests that the baseline value of thyroid hormones was slightly abnormal, and after Ashwagandha, the values were within the normal range, and none of the subjects showed higher or lower than the normal range of thyroid hormone levels. Similarly, in another case reported by **van der Hooft (2005),** post-partum thyroiditis is not completely ruled out and the author himself reported that the relationship between the use of Ashwagandha and the change in serum thyroid hormone levels can only be considered suggestive, but does not prove a causal relationship.

Kamal et al. (2022), from the USA, reported a 73-year-old female taking Ashwagandha for hyperthyroidism for 2 years. However, they failed to confirm the chemical analysis of capsule contents. It is important to mention that Kang et al. (2013) reported that nine out of ten commercially available supplements recommended for hypothyroidism including Ashwagandha, contain amounts of T3 and T4 that exceed the doses required to treat hypothyroidism.

Thus, Ashwagandha has not been proven to influence thyroid function in healthy animals or humans. In experimental hypothyroidism induced by propylthiouracil and in humans with hypothyroidism, some increase in thyroid hormone levels has been observed. However, changes are within normal levels. Placed in a context, one should note that many plant antioxidants have been shown to either lower or raise thyroid hormones within the normal ranges. For example, flavonoids lower thyroid hormone levels **(Paunkov et al., 2019;Wu et al., 2024).** On the other hand, an extract of the herb *Bacopa monnieri*, increased the thyroid levels in propylthiouracil-induced

hypothyroidism in rats **(Vigneshwar et al., 2021).** Even dietary habits, such as adherence to a healthy Mediterranean diet have been shown to influence these levels **(Juresko et al., 2024).** The observation that Ashwagandha decreases hepatic lipid peroxidation while simultaneously increasing its effect on thyroid hormone levels should be placed in this context.

Interpreting discrete effects that do not involve lowered TSH or free T3 levels is thus complex. Thyroid hormone levels are not only influenced by the crucial feedback regulation via the TRH-TSH axis, but T4 and T3 levels are also influenced by peripheral metabolism via deiodination- and other reactions **(Kelly, 2000),** and the expression of receptors and levels of transport proteins will influence the effects. The regulation is controlled to the extent that levothyroxine, a drug for hypothyroidism rarely causes thyrotoxicosis, except in cases of massive overdose and life-threatening symptoms. Lowering of TSH to pathologically low levels that clearly signal an excess of thyroid hormone has not been reported in healthy animals or humans.

Regarding the reports of cases of thyrotoxicosis, one should consider that both hyper and hypothyroidism are common diseases. Reports of single cases of thyrotoxicosis that can be linked in time to Ashwagandha ingestion are therefore impossible to evaluate regarding causality. Both are autoimmune diseases that can be triggered by external factors, but which could also go into spontaneous remission. Even remission after withdrawal of Ashwagandha in a single case can therefore not be considered strong evidence for a causal relationship. Definite evidence would require data from large human studies with a matching control group and serial measurement of thyroid hormone levels, TSH, and thyroid antibodies. Such studies may also include patients with borderline hypothyroid function and some increase in TSH, to further explore the question, of whether Ashwagandha really improves thyroid function in some individuals, thereby avoiding an upcoming need for thyroid hormone substitution. Till then, it would not be prudent to state that Ashwagandha, causes thyrotoxicosis and thyroid hormone anomalies.

Immunomodulatory effect of Ashwagandha

Several studies have shown that Ashwagandha has an immunomodulatory effect. Immune system modulators are compounds that can increase or decrease the response of immune system to help treat a variety of diseases. These agents restore immunoregulatory pathways responsible for auto reactivity and inflammation.

Human studies

Ashwagandha modulates adaptive and innate immunity and inflammatory marker C-reactive protein (CRP). The herb is reported to decrease CRP (Afonso et al., 2023). Regarding specific immunity, a 30-day crossover clinical study (Tharakan et al., 2021) found that Ashwagandha extract caused a slight increase in IgA, IgM, and IgG subclasses as well as an increase in the cytokines such as interferon-γ and interleukin-4 (IL-4), and in lymphocyte subsets. Plant antioxidants, like dietary flavonoids, are known to cause low-grade activation of the innate immune system and tend to decrease the levels of C-reactive protein level (Kyoung et al., 2008).

Experimental studies

In a mouse model of lupus, where the body's immune system is activated, root powder had a potent inhibitory effect on proteinuria, nephritis, and other inflammatory markers such as cytokines including interleukin (IL)-6, tumor necrosis factor (TNF)-α, nitric oxide (NO), and ROS in a (Minhas et al., 2012).). However, the humoral response, was found to be impervious. Similar efficacy was observed in a complete Freund's adjuvant-induced arthritic model (Rasool and Varalakshmi, 2006).

In an in vitro study using the HaCaT human keratinocyte cell line, Ashwagandha root decreased the expression of pro-inflammatory cytokines, including interleukin (IL)-8, IL-6, TNF-α, IL-1β, and IL-12, and increased the expression of anti-inflammatory cytokines. Overall, it inhibited the NF-κB and MAPK (mitogen-activated protein kinase) pathways. Based on these results, it can be concluded that the anti-inflammatory effects of Ashwagandha could potentially be used in the prevention of skin inflammation (Sikandan et al., 2018).

Ashwagandha root powder was shown to stimulate the immune activity in immunodeficient mice. It increased the total number of white blood cells and bone marrow cells, increased the titer of circulating antibodies and antibody-producing cells, and stimulated the production of immune cells and the phagocytosis of macrophages (Davis and Kuttan, 2000).

DTU cited a study from Malik et al. (2007), who studied the effects of graded doses of root extract administered for 15 days on the immune system of SRBC-immunized BALB/c mice. Root extract stimulated cell-mediated immunity, IgM and IgG titers, and proliferation of T cells and B cells. It induced Th1 cytokines, interferon (IFN)-γ, and interleukin (IL)-2 while Th2 cytokine IL-4 observed

a moderate decline. It also activated macrophage functions ex vivo and in vitro indicated by enhanced secretion of nitrite, IL-12, and TNF-α. In contrast, IL-10 remained unchanged confirming the Th1 profile of the cytokines. The authors suggested that based on this profile, roots can be useful in the management of immune-suppressed diseases. However, DTU expressed their apprehension that this may result in an increase in Type-IV immunological reactions, which could be harmful. However, this apprehension is not supported by any studies.

It is well known that Type IV hypersensitivity is mediated by T cells and macrophages, causing diseases like multiple sclerosis and rheumatoid arthritis or graft rejection. Ashwagandha is not known to cause the exacerbation of autoimmune diseases, including rheumatoid arthritis. On the contrary, Ashwagandha restored the immune regulatory pathways and reduced the inflammatory markers in arthritis and other autoimmune disease models.

The moderate immunostimulatory (modulatory) effects of Ashwagandha have not been linked to any harmful immunopathology. Rather, they fit into the spectrum of immunomodulatory effects that have been observed for antioxidative vitamins and plant antioxidants (Cururani et al., 2022).

Effect of Ashwagandha on Acetylcholinesterase activity in CNS

Visweswari et al. (2014) reported that scopolamine-treated rats showed a significant increase in AChE activity and reduced acetylcholine concentration in various brain regions, including the cerebral cortex and cerebellum. Ashwagandha in a dose-dependent manner, brought the increased acetylcholinesterase activity to near normal levels and restored the acetylcholine concentration in various brain regions. It is important to note that in none of the treated groups was the enzyme activity inhibited below normal or the acetylcholine concentration increased above the physiological levels. Unfortunately, the investigators did not include a control group where Ashwagandha was given in the absence of scopolamine, leaving the question of whether Ashwagandha per se has any *in vivo* effect on physiological levels of acetylcholinesterase activity or acetylcholine levels unanswered.

It is important to note that this article is published in a predatory journal and is included in Beall's list of predatory journals. Predatory journals, also called fraudulent or pseudo-journals, are unethical publications where research articles are not peer-reviewed and lack transparency (Elmore and Weston, 2020). *Visweswari et al (2014) is a predatory publication and included in the DTU report.*

Besides this predatory publication, we failed to find any other evidence where the In vivo effect of Ashwagandha on acetylcholine levels was studied. Moreover, significant acetylcholinesterase inhibition is usually associated with intestinal cramps, diarrhea, vasodilation with reflex tachycardia, miosis, slurred speech, ataxia, loss of reflexes, etc. No such effects have been reported in safety studies conducted in animals and humans at very high doses. Hence the possible impact of inhibition of acetylcholinesterase inhibition is unfounded.

Ashwagandha and Liver safety

The efficacy and safety of Ashwagandha on the liver is an area of extensive investigation, both in experimental animals and humans. The findings are described below.

Hepatoprotective effect of Ashwagandha in experimental liver injury in animals

The table below lists the efficacy of Ashwagandha in experimental liver injury models. The overall conclusion is that Ashwagandha has an alleviating effect in several models.

S.No	Reference	Ashwagandha formulation with the dose	Liver Injury Model	Conclusions
1	Khalil et al 2021	Aqueous root extract; 200 and 400 mg/kg	Thioacetamide-induced hepatic encephalopathy in rats	Ashwagandha improved locomotor and cognitive deficits, decreased hepatotoxicity markers, and modulated oxidative stress and inflammatory pathways.
2	Ebithal et al 2020	Root powder; 100, 200, 300 and 400 mg/kg	CCl4-induced hepatotoxicity in male albino rats	Ashwagandha mitigated CCl4-induced hepatotoxicity, enhanced liver antioxidant activity, and reduced serum hepatic enzymes.
3	Baxla et al 2019	Root powder; 500mg/kg	Lead (Pb) Induced toxicity in Wistar albino rats.	Ashwagandha improved hematological and hepatotoxic markers, and reduced serum biomarkers (ALT, AST, ALP, BUN, creatinine).
4	Dhenge et al 2018	Root powder: 5 gm/kg with feed	Liver function in broilers.	Ashwagandha reduced SGPT and SGOT levels, enhancing growth, and immune function.
5	Shahraki et al 2016	Powder: (ROOT?) 62.5 mg/g diet	Fructose-induced liver damage in Albino- Wistar rats	Ashwagandha decreased insulin resistance, serum insulin, blood glucose, triglycerides, and liver enzymes.
6	Nabi et al 2014	Hydro-alcoholic root extract: 100 mg /kg	Liver dysfunction in geriatric dogs	Ashwagandha normalized serum ALT, AST, albumin, cholesterol, and protein levels.
7	Sabina et al2013	Powder: 500 and 1000 mg/kg	Paracetamol hepatotoxicity (rats)	Ashwagandha normalized serum liver marker enzymes and bilirubin levels.
8	Malik et al 2013	Aqueous root extract: 500 mg/kg	Paracetamol-hepatotoxicity in mice	Ashwagandha decreased AST, ALT, ALP, and bilirubin; increased total serum protein level; reduced lipid peroxidation, and enhanced antioxidant enzyme activities.

S.No	Reference	Ashwagandha formulation with the dose	Liver Injury Model	Conclusions
9	Sultana et al2012	Root extract: 500 mg/kg	Gentamicin-intoxicated Wistar albino rats	Ashwagandha root extract reduced elevated serum levels of AST and ALT induced by gentamicin.
10	Sharma et al2012	Root extract: 200, and 500 mg/kg	Lead nitrate-induced toxicity in male mice	Ashwagandha root extract ameliorated the alterations in hematological parameters and serum enzymes associated with liver function.
11	Harikrishnan et al2008	Root powder: 500 mg/kg	Hyperammonaemia induced by ammonium chloride in rats	Ashwagandha root powder reduced levels of circulatory ammonia, urea, lipid peroxidation products, and liver marker enzymes.
12	Akbarsha et al 2000	Root powder: 250 mg/kg	Carbendazim-induced liver injury in male rats	Ashwagandha root powder demonstrated a complete recovery of histopathological damage in the liver.
13	Bhattacharya et al 2000	Aqueous extract of roots: 10, 20 and 50 mg/kg	Iron overload hepatotoxicity in male rats	Ashwagandha roots decreased hepatic lipid peroxidation and serum levels of liver enzymes.

Animal studies of Ashwagandha on liver safety

Ashwagandha safety has been widely studied in healthy animals treated with Ashwagandha for various durations. These studies have used various parameters, like serum enzymes, biochemical, as well as macroscopic examination and histopathology, to assess the effect of Ashwagandha on liver health. Some of these studies are listed below. The overall conclusion is that no significant liver toxicity of Ashwagandha has been demonstrated in experimental animal studies.

Reference	Experimental Model	Ashwagandha formulation with dose	Conclusion
Langade et al., 2023	Wistar rats	Standardized aqueous root extract 200, 400, 800 mg/kg	No signs of intoxication. Vital liver parameters remained stable, and no abnormalities in general parameters. All hematological and biochemical parameters were within normal range, indicating safety. Gross necropsy examination and histopathology of the liver from some rats treated with high doses of root extract showed multifocal minimal hepatocellular infiltration of inflammatory cells. Authors suggested that the rate of occurrence of these incidences, which could be due to glycogen deposition in the cytoplasm of hepatocytes, was low and usually developed in the different laboratory animals to a certain extent, they were considered to be spontaneous/incidental in nature.

Reference	Experimental Model	Ashwagandha formulation with dose	Conclusion
Kalaivani et al., 2023	Nulliparous and non-pregnant Wistar Albino rats	Standardized aqueous root extract 500, 1000, 2000 mg/kg	No morbidity, mortality, or clinical toxicity. There were no changes in liver enzymes like SGOT, SGPT, alkaline phosphatases or in serum bilirubin. Notably, even at the highest dose, liver histopathology examinations indicated no abnormalities. No Observed Adverse Effect Level (NOAEL) determined to be 2000 mg/kg.
Patel SB et al., 2016	Wistar rats	Standardized root extract 500, 1000, 2000 mg/kg	No toxicologically significant changes were observed. Similarly, in the sub-acute group, no treatment-related microscopic changes were observed, suggesting ashwagandha safety for the liver. NOAEL was determined to be 2000 mg/kg. The extract showed no adverse effects even after a 14-day recovery period following 28 days of administration.
Prabhu PC et al., 2013	Wistar rats	Hydroalcoholic root extract 500, 1000, 2000 mg/kg	No toxic signs or mortality. No significant changes in body weights, organ weights, or haemato-biochemical parameters. NOAEL was determined to be 2000 mg/kg.

Clinical Studies on Liver Safety

Multiple clinical studies have also been conducted to evaluate the safety of Ashwagandha, and no significant alterations or irregularities were detected in several health indices and biochemical parameters, including critical safety metrics, such as liver, kidney, and thyroid functions. Details of these studies are mentioned in the table below:

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events	Summary of results
Długołęcka et al 2023 (Poland)	Randomized, double-blind, placebo-controlled Study 8-weeks	Highly qualified national team wrestlers (26) Ashwagandha (12) Placebo (14)	2x300 mg per day (2 capsules a day) for 8 weeks.,	Hematological parameters, serum levels of biochemical parameters, bone mineral content, etc.	Generally, the participants (from both PL and A group) declared good tolerability of capsules, with no adverse events. Only one participant dropped out of the study due to intolerance of Ashwagandha capsules.	The study observed that the biochemical variables remained in the normal range after the intervention with Ashwagandha, and it had no impact on liver-related parameters.
Vaidya et al 2023 (India)	A non-randomized, open-label, single-treatment clinical study 4 weeks	Healthy male participants (18), aged 18 to 60	500 mg of the WSE capsules twice daily for four weeks	vital signs, organ function tests, urine analysis, X-ray and ECG, cardiorespiratory endurance, body fat percentage, lean	During the trial, there were no adverse effects, i.e., none. All the healthy volunteers participating in the safety research demonstrated	The participant's physical, hematological, and biochemical characteristics were normal, and no significant alterations or irregularities were observed in safety

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events	Summary of results
				body weight, adverse events profile, and tolerability of the WSE capsules	tolerability to the WSE capsule at a dose of 500 mg twice daily for 30 days.	metrics like liver, kidney, and thyroid functions.
Smith et al 2023 (Australia)	Randomized, Double-Blind, Placebo – Controlled 12 Weeks	Healthy Adults aged between 40 and 75 years Ashwagandha (60, 55), Placebo (60, 56)	200 mg - Hydroalcoholic Ashwagandha root extract - twice daily	PSS, CFS PROMIS-29, Sex hormone concentrations, MDA, FG, HbA1c, TSH, HRV, Grip strength, Anthropometric measures, LFT, RFT, FBC	Ashwagandha (13 - Digestive disturbances, Mood disturbances/ changes, Headaches/migraines, Increased appetite, Increased tiredness) Placebo (15 - Digestive disturbances, Mood disturbances/changes, Headaches/migraines, Increased appetite, Itchy Skin, Increased tiredness)	The reported adverse events were of mild in severity and these events were resolved without any intervention and participants continued the study treatments till the end of the study. Ashwagandha root extract was well tolerated by all the participants. An analysis of changes in blood safety measures from baseline to week 12 demonstrated there were no statistically significant between-group differences in changes in liver function.
Verma N et al., 2021 (India)	Randomized, Double-Blind, Placebo - Controlled Study 8 Weeks	Healthy adults aged between 18 and 45 years Ashwagandha (40), Placebo (40)	Standardized Aqueous Ashwgandha Root Extract 300mg twice daily / Total daily dose of 600mg/day	Hematological parameters, Liver parameters Thyroid Parameters	Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.	Compared to the placebo, all hematological parameters, liver health parameters and thyroid parameters remained within the acceptable and normal reference range.
Raut et al 2012	Dose-related, Open-label clinical study 30 Days	Healthy adults aged 18-30 years Ashwagandha (18)	Withania somnifera extract 750 mg/day x10 days, 1000 mg/day x 10 days, 1250 mg/day x 10 days	Serum Bilirubin, Proteins, Albumin, Alanine Transaminase, Aspartate Transaminase, and Alkaline Phosphatase Serum HDL, LDL, and VLDL cholesterol	Ashwagandha 750mg (1 - Increase in appetite, libido, and hallucinogenic effects with vertigo) Ashwagandha 1000mg (0) Ashwagandha 1200mg (0)	Ashwagandha was found to be safe on hematological and biochemical organ function tests. No significant change was observed in Serum Bilirubin, Proteins, Albumin, Alanine Transaminase, Aspartate Transaminase, and Alkaline Phosphatase at all the visits in each of the volunteers and it remained within normal range.

Based on these multiple studies using biochemical, macroscopic observations, organ weight, and histopathology as studied in various preclinical and clinical studies, it is obvious to conclude that Ashwagandha has no intrinsic adverse or toxic effect on the liver or its functions.

Recent reports of liver injury cases attributed to Ashwagandha

In recent times,, few cases of clinically significant liver injury have been reported. **Bjornsson et al., 2019** reported 5 such cases from Iceland and US. A few other reports such as **Inagaki et al., 2017** from **Japan, Weber and Gerbes, 2021 and Toth et al 2022** from **Germany, Ireland et al., 2021** from the USA, **Bokan et al., 2023** from Bosnia and Herzegovina, **Lubraska et al., 2023** from Poland, and **Phillips et al., 2023** from India, have raised concerns on liver toxicity based on sporadic case reports from their respective countries. The causal relation has been classified as possible or likely based on the time of diagnosis in relation to the start of Ashwagandha intake, the exclusion of other liver diseases, and the resolution of the liver pathology after withdrawal of Ashwagandha. Most of the cases are presented as mixed cholestatic/hepatocellular damage. It is significant to note that all these cases, for which the causal relationship to Ashwagandha was classified as likely, were reversed on discontinuation of herb, and no case led to death or liver transplantation. It is difficult to establish the causal relationship as reported in a case study by **Weber and Gerbes (2021),** where the patient was on Ashwagandha for one year but reported liver injury a few weeks after changing to another formulation as well as moving to another country. In many of the other cases, no analysis of formulation was done, or doses were as high as 15-20 gm per day. Some of these individuals were on alcohol or had metabolic diseases, pre-existing liver diseases like NAFLD or NASH, or other chronic diseases. A single American case has been reported, which underwent successful liver transplantation due to liver failure caused by severe hepatocellular damage. Although there was a time relation to Ashwagandha intake, a number of complicating factors (e.g. prior cancer surgery, ingestion of progesterone in unknown dose etc.) made interpretation difficult, and the authors classified the causal relation as possible, not as likely. In the study by **Philip et al (2023),** of the 8 reported patients with suspected Ashwagandha hepatotoxicity, 5 were having underlying chronic liver disease. One patient was having non-Hodgkin lymphoma and one patient was on lithium for psychiatry disorders. Moreover, as per the publication, in some patients Ashwagandha was being taken at a dose of 10-20 g/day. Interestingly, in 3 patients, the drug was used as self-medication, and was not prescribed by an Ayurvedic practioner.

In Light of Ashwagandha Liver Safety, How Do We Explain the Liver Injury Reports?

Since Ashwagandha root extract is not hepatotoxic, neither in prescribed doses nor in much higher doses, other explanations must be considered. For example, some of the patients reported to have a possible Ashwagandha-induced liver injury had underlying diseases like cancer or metabolic diseases and were on medication known to cause liver toxicity or had prior daily exposure to alcohol. In other cases, they used formulations containing many herbs, with Ashwagandha as one of the ingredients. In fact, DTU in its report doubted **Inagaki et al. (2017)** case report from Japan and questioned if liver damage was due to Ashwagandha. Causality assessment is thus particularly difficult in most of the cases.

Unpredictable liver injuries caused by a defined chemical, usually a commonly prescribed or over-the-counter sold drug, are rare but well-known and are named drug-induced liver

injuries (DILI). Similarly, herb-induced liver injury (HILI) arises from the harmful effects of complex extracts, where one or more compounds may contribute to unpredictable hepatotoxicity. Direct or intrinsic toxic effects of a drug or herbal preparation on any organ including the liver are dose-dependent, predictable, and have a short latency period and can be reliably reproduced in animal models. In the case of Ashwagandha, we did not see any report of HILI both in clinics and animals.

However, in contrast, idiosyncratic injury is not dose-dependent, difficult to predict, and varies widely in latency, often linked to immune or allergic responses in a few susceptible individuals. It is crucial to distinguish between intrinsic and idiosyncratic liver injuries.

Based on the biochemical, hematological, gross observations, organ weight, and histopathology studied in various preclinical and clinical studies, it is safe to conclude that Ashwagandha root has no intrinsic adverse or toxic effect on the liver. The reports of liver injury may be attributed to other underlying diseases or drugs, as cited above, or at the most rarely, may be likely idiosyncratic reactions that need more investigation. These injuries were generally reversible upon discontinuation of the herb. At most, one can be cautious, and the user can be appropriately informed. In patients with comorbidities, such as cancer, immunocompromised state, polypharmacy, etc. monitoring for liver function should be done at regular intervals. However, there is no scientific evidence to proclaim Ashwagandha as liver toxic.

Summary of clinical studies conducted for evaluating the Safety of Ashwagandha Root Extract

An extensive literature search was conducted using various keywords and MeSH terms to identify relevant articles on Ashwagandha, also known as Withania somnifera (WS) and 43 randomized controlled trials focusing on Ashwagandha root as a standalone intervention were included in our review (Annexure-II). These studies were critically analyzed to assess the efficacy and safety of Withania somnifera across various medical conditions. Some of these studies are quoted below.

Vaidya et al 2023, conducted a non-randomized, open-label, single-treatment clinical study conducted over 4 weeks to evaluate the safety of hydroalcoholic Ashwagandha root extract with 18 healthy male participants ranging from 18 to 60 years of age. Ashwagandha was administered at a dosage of 500 mg twice daily (1000mg/day). Remarkably, no adverse events were reported throughout the study, indicating a favorable safety profile for the Ashwagandha root extract. All physical, hematological, and biochemical characteristics of the participants remained within normal ranges, with no significant alterations or irregularities detected in critical safety metrics such as liver, kidney, and thyroid functions.

Barbara et al 2023, conducted a randomized, double-blind, placebo-controlled, and parallel-group study on Professional athletes—specifically, highly qualified national team wrestlers—for 8 weeks. The participants were administered a standardized aqueous Ashwagandha root extract at a dose of 300 mg twice daily (600 mg/day). One of the prominent findings was that, compared to the placebo group, serum CK activity in the Ashwagandha group did not

significantly increase, suggesting improved muscle recovery. Additionally, the study observed that the biochemical variables remained in the normal range after the intervention with Ashwagandha, and it had no impact on liver parameters.

Smith et al 2023, conducted a two-arm, parallel-group, single-center, randomized, double-blind, placebo-controlled trial on 120 participants to evaluate the safety and efficacy of ashwagandha on stress, fatigue, and sex hormones in overweight or mildly obese men and women with self-reported stress and fatigue for 8 weeks. The participants were ashwagandha root extract at a dose of 200mg twice daily (400 mg/day). The authors found that compared to the placebo, there was a statistically significant reduction in fatigue symptoms and a favorable effect on heart rate variability in the Ashwagandha group. However, there was a non-significant reduction in PSS scores and other self-reported measures. In the men taking ashwagandha, there was a significant increase in the blood concentrations of free testosterone and luteinizing hormone compared to the placebo group. There were also no changes in anthropometric measures (BMI, WC, and WHR) blood pressure, and safety blood makers comprising the liver function test, full blood count, and renal function with Ashwagandha supplementation.

Verma et al 2021, conducted a randomized, double-blind, placebo-controlled, and parallel-group study on 80 healthy individuals to evaluate the safety of oral administration of Ashwagandha root extract at a dose of 300 mg twice daily for 8 weeks. The result of the study did not indicate any untoward effect in any of the treated volunteers. There was no statistically significant change observed in the parameters considered including thyroid hormonal profile in both the groups. The authors concluded that the consumption of Ashwagandha root extract for eight weeks was found to be safe in both male and female volunteers.

Gopukumar et al 2021, in a randomized, double-blind, placebo-controlled study, evaluated the effect of Ashwagandha root extract (sustained-release) capsules at 300 mg for 90 consecutive days, on cognitive function, stress level, sleep quality, overall well-being, and safety in stressed subjects [125 healthy cognitively sound adults (20–55 years of age, body mass index:18–29 kg/m2)]. The Cambridge Neuropsychological Test Automated Battery (CANTAB) reported significantly improved recall memory, and the total error rate in recalling patterns was significantly reduced at visit 4 in the Ashwagandha group as compared to the placebo group. At visit 4, significantly lower PSS-10 scores, serum cortisol levels, and Pittsburgh Sleep Quality Index (PSQI) scores with higher Oxford Happiness Questionnaire (OHQ) scores were seen in the Ashwagandha group. This suggests significantly lower stress level and significantly better psychological well-being and sleep quality in the former. No adverse events were reported during the study.

Kuchewar et al 2014, investigated ashwagandha for antioxidant potential in randomized, double-blind, placebo-controlled study, 30 healthy volunteers. The test group received 500 mg Ashwagandha root extract twice daily after food with a glass of water for 6 months. The placebo group received hard gelatin capsules filled with starch powder. All subjects completed the study and there were no adverse effects reported, and all the hematological parameters were within normal range before and after the intervention in both groups. The result of this

study indicates that intake of aqueous ashwagandha root extract at up to 1000 mg per day in divided doses is very well tolerated.

Raut et al 2012, conducted an exploratory, prospective, open-labeled study to evaluate the dose-related tolerability, safety, and activity of Withania somnifera formulation in 18 healthy volunteers. W. somnifera was given in the form of capsules (aqueous extract) daily in two divided doses with an increase in daily dosage every 10 days for 30 days (750 mg/day x10 days, 1000 mg/day x 10 days, 1250 mg/day x 10 days). All but one volunteer tolerated W. somnifera without any adverse event. One volunteer was withdrawn from the study because of the symptoms exhibited such as; increased appetite, libido, and hallucinogenic effects with vertigo at the lowest dose. No significant change was observed in Serum Bilirubin, Proteins, Albumin, Alanine Transaminase, Aspartate Transaminase, and Alkaline Phosphatase at all the visits in each of the volunteers. All values remained within the normal range. This study has also demonstrated muscle strengthening, improved quality of sleep, and lipid-lowering potential.

These studies collectively highlight the potential benefits of Ashwagandha in various health conditions, with a strong emphasis on its safety and tolerability in diverse populations.

Pharmacovigilance

To generate awareness about the possibility of adverse drug reactions associated with traditional drugs, the Ministry of Ayush, Government of India, initiated the Pharmacovigilance Program for Ayurveda, Siddha, Unani, and Homoeopathy (ASU&H) Drugs in 2017. This program features a robust three-tier system (National, Intermediary, and Peripheral centers) that has been operational since its inception, covering most states and union territories across the country. As of date, no adverse drug reactions related to the use of Ashwagandha have been reported under this program.

Conclusion

The Expert Committee Report on safety of Ashwagandha comprehensively analyses the safety concerns raised in the report by the Danish Technical University (DTU), commissioned by the Danish Veterinary and Food Administration (DVFA). Historical usage, corroborated by rigorous modern research confirms the pharmacological safety and therapeutic efficacy of Ashwagandha. This report on safety of Ashwagandha encompasses a broad spectrum of studies including those studies published after the release of DTU report. Preclinical safety assessments, clinical trials, and investigations into its benefits for the liver and thyroid, as well as its immunomodulatory effects and effects on sex hormones have been analyzed by the expert committee.

As highlighted in this report, there are glaring instances of lack of rigorous scientific scrutiny in the DTU risk assessment report including conclusions drawn from publications of predatory journals. Numerous safety studies consistently demonstrate that standardized Ashwagandha (Withania somnifera) root extract is safe for human consumption. The scientific data reveals that Ashwagandha root is well-tolerated across a wide range of doses, with no adverse outcomes reported in diverse demographic and clinical cohorts. Thus, the Expert Committee is of the strong view that current evidence supporting the safety and efficacy of Ashwagandha root is robust, allowing it to be safely recommended and integrated into global health practices. This reinforces its standing as a safe herb in both traditional and contemporary health contexts nevertheless using correctly identified species is very crucial and stringent quality control should be carried out suitably as per applicable regulatory norms. In view of its scientifically proven safety, the globally available and popular Indian herb Ashwagandha (*Withania Somnifera*) can be judiciously prescribed by the Ayurvedic physicians for its health benefits in humans.

References

- Abdel-Wahhab, K. G., Mourad, H. H., Mannaa, F. A., Morsy, F. A., Hassan, L. K., & Taher, R. F. (2019). Role of Ashwagandha methanolic extract in the regulation of thyroid profile in hypothyroidism modeled rats. *Molecular Biology Reports, 46*(4), 3637–3649. https://doi.org/10.1007/s11033-019-04721-x
- Ajgaonkar, A., Jain, M., & Debnath, K. (2022). Efficacy and safety of Ashwagandha (*Withania somnifera) root extract for improvement of sexual health in healthy women: A prospective, randomized, placebo-controlled study. Cureus, 14(10), e30787.* https://doi.org/10.7759/cureus.30787
- Akbarsha, M. A., Vijendrakumar, S., Kadalmani, B., Girija, R., &Faridha, A. (2000). Curative property of *WithaniasomniferaDunal root in the context of carbendazim-induced histopathological changes in the liver and kidney of rat. Phytomedicine, 7(6), 499-507.* https://doi.org/10.1016/S0944-7113(00)80036-7
- Ambiye, V. R., Langade, D., Dongre, S., Aptikar, P., Kulkarni, M., &Dongre, A. (2013). Clinical evaluation of the spermatogenic activity of the root extract of Ashwagandha (*Withania somnifera) in oligospermic males: A pilot study. Evidence-Based Complementary and Alternative Medicine, 2013, 571420.* https://doi.org/10.1155/2013/571420
- Andrade, C., Aswath, A., Chaturvedi, S. K., Srinivasa, M., &Raguram, R. (2000). A double-blind, placebo-controlled evaluation of the anxiolytic efficacy of an ethanolic extract of *Withania somnifera. Indian Journal of Psychiatry, 42(3), 295-301.*
- Atul, U., Charu, B., & Umesh, S. (2020). Efficacy of BrimhanaNasya and Ashwagandha (Withania somnifera (L.) Dunal) root powder in primary insomnia in elderly male: A randomized open-label clinical study. Ayu, 41(3), 159-165. https://doi.org/10.4103/ayu.AYU_177_19
- Azgomi, N. D., Nazemiyeh, H., Bazargani, H. S., Fazljou, S. M. B., Jazani, A. M., Ahmadi AsrBadr, Y., &Zomorrodi, A. (2018a). Comparative evaluation of the effects of *Withania somnifera with pentoxifylline on the sperm parameters in idiopathic male infertility: A triple-blind randomised clinical trial. Andrologia, 50(4), e13041.* https://doi.org/10.1111/and.13041
- Baishya, K., Sharma, R., & Kumar, V. (2020). A comparative clinical study to evaluate the efficacy of AshwagandhaGhrita on growth and development of infants. *Journal of Ayurveda and Integrative Medicine, 1(1), 31-36.* https://doi.org/10.21760/jaims.5.1.7
- Barbara, D., Ewa, J., Jadwiga, K., & Dariusz, G. (2023). Effects of Ashwagandha (*Withania somnifera) supplementation on body composition and blood health indices in professional wrestlers. Polish Journal of Sport and Tourism, 30*, 26-32. https://doi.org/10.2478/pjst-2023-0022
- Bashir, A., Nabi M., Tabassum N., Afzal S. and Ayoub M. An updated review on phytochemistry and molecular targets of Withania somnifera (L.) Dunal (Ashwagandha). Front. Pharmacol., 29 March 2023, 1. https://doi.org/10.3389/fphar.2023.1049334
- Baxla, S. L., Gora, R. H., &Kerketta, P. (2019). Effect of *Withania somnifera powder against lead-induced toxicity in albino rats. International Journal of Engineering Research & Technology (IJERT), 8(5S), 327-329.*
- *Bhattacharya, A., Ramanathan, M., Ghosal, S., & Bhattacharya, S. K. (2000). Effect of Withaniasomniferaglycowithanolides on iron-induced hepatotoxicity in rats. Phytotherapy Research, 14(7), 568-570.* https://doi.org/10.1002/1099-1573(200011)14:7
- Chandrasekhar, K., Kapoor, J., &Anishetty, S. (2012). A prospective, randomized double-blind, placebo-controlled study of safety and efficacy of a high-concentration full-spectrum extract of ashwagandha root in reducing stress and anxiety in adults. *Indian Journal of Psychological Medicine, 34*(3), 255-262. https://doi.org/10.4103/0253-7176.106022

- Chauhan, S., Srivastava, M. K., & Pathak, A. K. (2022). Effect of standardized root extract of Ashwagandha (*Withania somnifera) on well-being and sexual performance in adult males: A randomized controlled trial. Health Science Reports, 5(4), e741.* https://doi.org/10.1002/hsr2.741
- Chatterjee S, Srivastava S, Khalid A, Singh N, Sangwan RS, Sidhu OP, Roy R, Khetrapal CL, Tuli R. Comprehensive metabolic fingerprinting of Withania somnifera leaf and root extracts. Phytochemistry. 2010 Jul;71(10):1085-94
- Chopra, A., Srikanth, N., Patwardhan, B., & AYUSH CCRAS Research Group. (2021). *Withania somnifera as a safer option to hydroxychloroquine in the chemoprophylaxis of COVID-19: Results of interim analysis. Complementary Therapies in Medicine, 62, 102768.* https://doi.org/10.1016/j.ctim.2021.102768
- Choudhary, B., Shetty, A., &Langade, D. G. (2015). Efficacy of Ashwagandha (*Withania somnifera [L.] Dunal) in improving cardiorespiratory endurance in healthy athletic adults. Ayu, 36(1), 63-68.* https://doi.org/10.4103/0974-8520.169005
- Choudhary, D., Bhattacharyya, S., & Bose, S. (2017a). Efficacy and safety of Ashwagandha (*Withania somnifera [L.] Dunal) root extract in improving memory and cognitive functions. Journal of Dietary Supplements, 14(6), 599-612.* https://doi.org/10.1080/19390211.2017.1284970
- Choudhary, D., Bhattacharyya, S., & Joshi, K. (2017b). Body weight management in adults under chronic stress through treatment with Ashwagandha root extract: A double-blind, randomized, placebo-controlled trial. *Journal of Evidence-Based Complementary & Alternative Medicine, 22*(1), 96-106. https://doi.org/10.1177/2156587216658737
- Cooley, K., Szczurko, O., Perri, D., Mills, E. J., Bernhardt, B., Zhou, Q., & Seely, D. (2009). Naturopathic care for anxiety: A randomized controlled trial ISRCTN78958974. *PLOS One, 4(8), e6628.* https://doi.org/10.1371/journal.pone.0006628
- Cururani et al in Immunomodulators and Human Health, Chapter "Antioxidants and immunomodulation" 2022; pp 101-121
- Davis L., Kuttan G. Immunomodulatory activity of *Withania somnifera*. J. Ethnopharmacol. 2000;71:193–200
- Dhenge, S. A., et al. (2018). Effect of dietary supplementation of Ashwagandha (*Withaniasomnifera) and Kalmegh (Andrographispaniculata) on growth performance and immune status in broilers. International Journal of Agriculture Sciences, 10(24), 7634-7636.*
- Długołęcka, Barbara, Jówko, Ewa, Kotowska, Jadwiga and Gierczuk, Dariusz. "Effects of Ashwagandha (Withania Somnifera) Supplementation on Body Composition and Blood Health Indices in Professional Wrestlers" Polish Journal of Sport and Tourism, vol.30, no.4, 2023, pp.26-32. https://doi.org/10.2478/pjst-2023-0022
- Dongre, S., Langade, D., & Bhattacharyya, S. (2015). Efficacy and safety of Ashwagandha (*Withania somnifera) root extract in improving sexual function in women: A pilot study. BioMed Research International, 2015, 284154.* https://doi.org/10.1155/2015/284154
- Fuladi, S., Emami, S. A., Mohammadpour, A. H., Karimani, A., Manteghi, A. A., &Sahebkar, A. (2020). Assessment of *Withania somnifera root extract efficacy in patients with generalized anxiety disorder: A randomized double-blind placebo-controlled trial. Current Clinical Pharmacology*. Advance online publication. https://doi.org/10.2174/1574884715666200413120413
- Gómez Afonso, A., Fernandez-Lazaro, D., Adams, D. P., Monserdà-Vilaró, A., & Fernandez-Lazaro, C. I. (2023). Effects of Withania somnifera (Ashwagandha) on Hematological and Biochemical Markers, Hormonal Behavior, and Oxidant Response in Healthy Adults: A Systematic Review. *Current nutrition reports*, *12*(3), 465–477. https://doi.org/10.1007/s13668-023-00481-0
- Gopal, S., Ajgaonkar, A., Kanchi, P., Kaundinya, A., Thakare, V., Chauhan, S., &Langade, D. (2021). Effect of an Ashwagandha (*Withania somnifera) root extract on climacteric symptoms in women during peri-*

menopause: A randomized, double-blind, placebo-controlled study. Journal of Obstetrics and Gynaecology Research. Advance online publication. https://doi.org/10.1111/jog.15030

- Gopukumar, K., Thanawala, S., Somepalli, V., Rao, T., Thamatam, V. B., & Chauhan, S. (2021). Efficacy and safety of Ashwagandha root extract on cognitive functions in healthy, stressed adults: A randomized, double-blind, placebo-controlled study. *Evidence-Based Complementary and Alternative Medicine*, 2021, 8254344. https://doi.org/10.1155/2021/8254344
- Gupta, A., Mahdi, A. A., Shukla, K. K., Ahmad, M. K., Bansal, N., Sankhwar, P., &Sankhwar, S. N. (2013). Efficacy of *Withania somnifera on seminal plasma metabolites of infertile males: A proton NMR study at 800 MHz. Journal of Ethnopharmacology, 149(1), 208-214.* https://doi.org/10.1016/j.jep.2013.06.026
- Harikrishnan, B., Subramanian, P., & Subash, S. (2008). Effect of *Withania somnifera root powder on the levels of circulatory lipid peroxidation and liver marker enzymes in chronic hyperammonemia. E-Journal of Chemistry, 5, 2090-9063.*
- *Homoeopathic Pharmacopoeia of India. vol. 10, 1*stedn. New Delhi, India: Government of India, Ministry of Health and Family Welfare, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (Ayush); 2013; p. 224-225.
- Hosny, E. N., El-Gizawy, M. M., Sawie, H. G., Abdel-Wahhab, K. G., &Khadrawy, Y. A. (2021). Neuroprotective effect of Ashwagandha extract against the neurochemical changes induced in rat model of hypothyroidism. *Journal of Dietary Supplements, 18(1), 72–91.* https://doi.org/10.1080/19390211.2020.1713959
- Hosseini, N., Moharari, F., Soltanifar, A., Poor, A. M., Hosseini, A., &Zahedian, F. (2019). Evaluation of the effectiveness of *Withania somnifera root extract on the anxiety symptoms among children with ADHD in Mashhad. Journal of Medical and Health Sciences, 13(1).*
- Indian Pharmacopoeia. Volume III. 8th ed. Ghaziabad, India: The Indian Pharmacopoeia Commission; 2018; p. 3743-3745
- Jain, H., Parial, S. D., Jarald, E., Daud, A. S., & Ahmad, S. (2010). Extraction of Ashwagandha by conventional extraction methods and evaluation of its anti-stress activity. *International Journal of Green Pharmacy, 4(3), 183-185.*
- *Johri S., Jamwal U., Rasool S., Kumar A., Verma V., Qazi G.N. Purification and characterization of peroxidases from Withania somnifera (AGB 002) and their ability to oxidize IAA. Plant Sci. 2005; 169: 1014–1021.*
- *Kalaivani, P., Siva, R., Gayathri, V., &Langade, D. (2024). Two weeks dose range finding study of KSM-66 Ashwagandha root extract by oral route in Wistar rats – A toxicity study. International Journal of Medical and Pharmaceutical Research, 5(1), 153-164.*
- *Kalaivani, P., Siva, R., Gayathri, V., &Langade, D. (2023). Ninety-day repeated dose toxicity of Ashwagandha (Withania somnifera) root extract in Wistar rats. Toxicology Reports, 11, 189–198.* https://doi.org/10.1016/j.toxrep.2023.09.004
- Kalaivani, P., Siva, R., Gayathri, V., &Langade, D. (2023). Mutagenicity and safety evaluation of Ashwagandha (*Withania somnifera) root aqueous extract in different models. Toxicology Reports, 12, 41–47.* https://doi.org/10.1016/j.toxrep.2023.12.005
- Kelgane, S. B., Salve, J., Sampara, P., ... &Langade, D. (2020). Efficacy and tolerability of Ashwagandha root extract in the elderly for improvement of general well-being and sleep: A prospective, randomized, double-blind, placebo-controlled study. *Cureus, 12*(2), e7083. https://doi.org/10.7759/cureus.7083
- Khalil, H., Eliwa, H. A., El-Shiekh, R. A., Al-Mokaddem, A. K., Hassan, M., Tawfek, A. M., & El-Maadawy, W. H. (2021). Ashwagandha (*Withania somnifera) root extract attenuates hepatic and cognitive deficits in thioacetamide-induced rat model of hepatic encephalopathy via induction of Nrf2/HO-1 and mitigation of NF-κB/MAPK signaling pathways. Journal of Ethnopharmacology, 277, 114141.* https://doi.org/10.1016/j.jep.2021.114141

- Kyoung C. Sang-Jin C. Kate C and Won S., Serum C-Reactive Protein Concentrations Are Inversely Associated with Dietary Flavonoid Intake in U.S. Adults. J. Nutr. 138, 2008, 753-760.
- Langade, D., Kanchi, S., Salve, J., Debnath, K., &Ambegaokar, D. (2019). Efficacy and safety of Ashwagandha (*Withania somnifera) root extract in insomnia and anxiety: A double-blind, randomized, placebo-controlled study. Cureus, 11*(3), e5797. https://doi.org/10.7759/cureus.5797
- Langade, D., Thakare, V., Kanchi, S., &Kelgane, S. (2021). Clinical evaluation of the pharmacological impact of Ashwagandha root extract on sleep in healthy volunteers and insomnia patients: A double-blind, randomized, parallel-group, placebo-controlled study. *Journal of Ethnopharmacology, 251*, 113276. https://doi.org/10.1016/j.jep.2020.113276
- Langade, D., Dawane, J., &Dhande, P. (2023). Sub-acute toxicity of Ashwagandha (*Withania somnifera) root extract in Wistar rats. Toxicology Reports, 11, 389–395.* https://doi.org/10.1016/j.toxrep.2023.10.009
- Mahdi AA, Shukla KK, Ahmad MK, Rajender S, Shankhwar SN, Singh V, Dalela D. Withaniasomnifera Improves Semen Quality in Stress-Related Male Fertility. Evid Based Complement Alternat Med. 2009 Sep 29;2011:576962. doi: 10.1093/ecam/nep138.
- Majeed, M., Nagabhushanam, K., &Mundkur, L. (2023). A standardized Ashwagandha root extract alleviates stress, anxiety, and improves quality of life in healthy adults by modulating stress hormones: Results from a randomized, double-blind, placebo-controlled study. *Medicine, 102(41), e35521.* https://doi.org/10.1097/MD.0000000000035521.
- Majeed, M., Nagabhushanam, K., Murali, A., Vishwanathan, D. T., Mamidala, R. V., &Mundkur, L. (2023). A standardized *Withania somnifera (Linn.) root extract with piperine alleviates the symptoms of anxiety and depression by increasing serotonin levels: A double-blind, randomized, placebo-controlled study. Journal of Integrative and Complementary Medicine. Advance online publication.* https://doi.org/10.1089/jicm.2023.0279
- Malik, T., Pandey, D. K., & Dogra, N. (2013). Ameliorative potential of aqueous root extract of *Withania somnifera against paracetamol-induced liver damage in mice. Pharmacologia, 4, 89-94.*
- *Mamidi, P., &Thakar, A. B. (2011). Efficacy of Ashwagandha (WithaniasomniferaDunal. Linn.) in the management of psychogenic erectile dysfunction. Ayu, 32(3), 322-328.* https://doi.org/10.4103/0974-8520.93914
- Minhas U, Minz R, Das P, Bhatnagar A. Therapeutic effect of *Withania somnifera* on a pristane-induced model of SLE. Inflammopharmacology. 2012;20:195–205
- Mishra, R. K., Trivedi, R., & Pandya, M. A. (2010). A clinical study of Ashwagandhaghrita and Ashwagandha granules for its brumhana and balya effect. *Ayu, 31(3), 355-360. https://doi.org/10.4103/0974-8520.77164*
- *Nabi, S. U., Wani, A. R., & Dey, S. (2014). Therapeutic effect of ashwagandha (Withania somnifera L.) in liver dysfunction of old dogs. Applied Biological Research, 16(2), 232-236.*
- *Narra, K., Naik, S. K., &Ghatge, A. S. (2023). A study of efficacy and safety of Ashwagandha (Withania somnifera) lotion on facial skin in photoaged healthy adults. Cureus, 15(3), e36168.* https://doi.org/10.7759/cureus.36168
- Patel, S. B., Rao, N. J., &Hingorani, L. L. (2016). Safety assessment of *Withania somnifera extract standardized for withaferin A: Acute and sub-acute toxicity study. Journal of Ayurveda and Integrative Medicine, 7(1), 30-37.* https://doi.org/10.1016/j.jaim.2015.08.001
- Panda S, Kar A. Changes in thyroid hormone concentrations after administration of ashwagandha root extract to adult male mice. J Pharm Pharmacol. 1998 Sep;50(9):1065-8. doi: 10.1111/j.2042-7158.1998.tb06923.x. PMID: 9811169.
- Panda S, Kar A. Withania somnifera and Bauhinia purpurea in the regulation of circulating thyroid hormone concentrations in female mice. J Ethnopharmacol. 1999 Nov 1;67(2):233-9. doi: 10.1016/s0378-8741(99)00018-5. PMID: 10619390.
- Paul, S., Chakraborty, S., Anand, U., Dey, S., Nandy, S., Ghorai, M., Saha, S. C., Patil, M. T., Kandimalla, R., Proćków, J., & Dey, A. (2021). Withania somnifera (L.) Dunal (Ashwagandha): A comprehensive review

on ethnopharmacology, pharmacotherapeutics, biomedicinal and toxicological aspects. *Biomedicine & pharmacotherapy = Biomedecine&pharmacotherapie, 143, 112175.* https://doi.org/10.1016/j.biopha.2021.112175

- Prabu, P. C., & Panchapakesan, S. (2015). Prenatal developmental toxicity evaluation of *Withania somnifera root extract in Wistar rats. Drug and Chemical Toxicology, 38(1), 50-56.* https://doi.org/10.3109/01480545.2014.900073
- Prabu, P. C., Panchapakesan, S., & Raj, C. D. (2013). Acute and sub-acute oral toxicity assessment of the hydroalcoholic extract of *Withania somnifera roots in Wistar rats. Phytotherapy Research, 27(8), 1169-1178.* https://doi.org/10.1002/ptr.4854
- Rasool M., Varalakshmi P. Immunomodulatory role of *Withania somnifera* root powder on experimentally induced inflammation: An in vivo and in vitro study. Vascul. Pharmacol. 2006;44:406–410
- Raut, A. A., Rege, N. N., Tadvi, F. M., Solanki, P. V., Kene, K. R., Shirolkar, S. G., Pandey, S. N., Vaidya, R. A., & Vaidya, A. B. (2012). Exploratory study to evaluate tolerability, safety, and activity of Ashwagandha (*Withania somnifera) in healthy volunteers. Journal of Ayurveda and Integrative Medicine, 3*(3), 111-114. https://doi.org/10.4103/0975-9476.100168
- Sabina, E. P., Rasool, M., Vedi, M., Navaneethan, D., Ravichander, M., Poornima, P., & Thella, S. R. (2013). Hepatoprotective and antioxidant potential of *Withania somnifera against paracetamol-induced liver damage in rats. International Journal of Pharmacy and Pharmaceutical Sciences, 5(2), 648-651.*
- *Saleem, S., Muhammad, G., Hussain, M. A., Altaf, M., & Bukhari, S. N. A. (2020). Withania somnifera L.: Insights into the phytochemical profile, therapeutic potential, clinical trials, and future prospective. Iranian journal of basic medical sciences, 23(12), 1501–1526.* https://doi.org/10.22038/IJBMS.2020.44254.10378
- Salve, J., Pate, S., Debnath, K., ... & Singh, S. (2019). Adaptogenic and anxiolytic effects of Ashwagandha root extract in healthy adults: A double-blind, randomized, placebo-controlled clinical study. *Cureus, 11*(12), e6466. https://doi.org/10.7759/cureus.6466
- Sandhu, J. S., Shah, B., Shenoy, S., Chauhan, S., Lavekar, G. S., &Padhi, M. M. (2010). Effects of *Withania somnifera (Ashwagandha) and Terminalia arjuna (Arjuna) on physical performance and cardiorespiratory endurance in healthy young adults. International Journal of Ayurveda Research, 1(3), 144-149.* https://doi.org/10.4103/0974-7788.76788
- Shahraki, M. R., Dadpisheh, S., Shahraki, A. R., &Mirshekari, H. (2016). The effects of *Withania somnifera on blood sugar, serum insulin, lipid profile, and liver enzymes in fructose drinking water male rats. Journal of Chemical and Pharmaceutical Research, 8(4), 1328-1334.*
- *Sharada, A. C., Solomon, F. E., & Devi, P. U. (1993). Toxicity of Withania somnifera root extract in rats and mice. International Journal of Pharmacognosy, 31(3), 205–212.* https://doi.org/10.3109/13880209309082943
- Sharma, V., Sharma, S., &Pracheta. (2012). Protective effect of *Withania somnifera roots extract on hematoserological profiles against lead nitrate-induced toxicity in mice. Indian Journal of Biochemistry & Biophysics, 49(6), 458-462.*
- *Sharma, A. K., Basu, I., & Singh, S. (2018). Efficacy and safety of Ashwagandha root extract in subclinical hypothyroid patients: A double-blind, randomized placebo-controlled trial. Journal of Alternative and Complementary Medicine, 24(3), 243-248.* https://doi.org/10.1089/acm.2017.0183
- Shenoy, S., Chaskar, U., Sandhu, J. S., &Paadhi, M. M. (2012). Effects of eight-week supplementation of Ashwagandha on cardiorespiratory endurance in elite Indian cyclists. *Journal of Ayurveda and Integrative Medicine, 3(4), 209-214.* https://doi.org/10.4103/0975-9476.104431
- Sikandan A., Shinomiya T., Nagahara Y. Ashwagandha root extract exerts anti-inflammatory effects in HaCaT cells by inhibiting the MAPK/NF-κB pathways and by regulating cytokines. Int. J. Mol. Med. 2018;42:425–434
- Singh, B., Saxena, A. K., Chandan, B. K., Gupta, D. K., Bhutani, K. K., & Anand, K. K. (2001). Adaptogenic activity of a novel, withanolide-free aqueous fraction from the roots of *Withania somnifera Dun. Phytotherapy Research, 15(4), 311-318.* https://doi.org/10.1002/ptr.858

- Smith, S. J., Lopresti, A. L., & Fairchild, T. J. (2023). Exploring the efficacy and safety of a novel standardized Ashwagandha (*Withania somnifera) root extract (Witholytin®) in adults experiencing high stress and fatigue in a randomized, double-blind, placebo-controlled trial. Journal of Psychopharmacology, 37*(11), 1091-1104. https://doi.org/10.1177/02698811231200023
- Sultana, N., Shimmi, S. C., Parash, M. T., & Akhtar, J. (2012). Effects of ashwagandha (*Withania somnifera) root extract on some serum liver marker enzymes (AST, ALT) in gentamicin intoxicated rats. Journal of Bangladesh Society of Physiology, 7, 1-7.*
- *Suprabha, K., & Mamatha, K. V. (2017). A clinical trial to evaluate the effect of RasayanaAvaleha during pregnancy with special reference to the fetal outcome. Indian Journal of Health Sciences and Biomedical Research, 10, 74-79.*
- The Ayurvedic Pharmacopoeia of India. Part I, vol. VIII. 1stedn. New Delhi, India: Government of India, Ministry of Health and Family Welfare, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (Ayush); 2011; p. 28-32.
- The Siddha Pharmacopoeia of India. Part I, vol. I. 1stedn. New Delhi, India: Government of India, Ministry of Health and Family Welfare, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (Ayush); 2008; p. 1-4.
- The Unani Pharmacopoeia of India. Part I, vol. I, 1stedn. New Delhi, India: Government of India, Ministry of Health and Family Welfare, Department of Ayurveda, Yoga & Naturopathy, Unani, Siddha and Homoeopathy (Ayush); 2007; p. 7-8.
- Tiwari, S., Gupta, S. K., & Pathak, A. K. (2021). A double-blind, randomized, placebo-controlled trial on the effect of Ashwagandha (*WithaniasomniferaDunal.) root extract in improving cardiorespiratory endurance and recovery in healthy athletic adults. Journal of Ethnopharmacology, 279, 113929.* https://doi.org/10.1016/j.jep.2021.113929
- Wankhede, S., Langade, D., Joshi, K., Sinha, S. R., & Bhattacharyya, S. (2015). Examining the effect of *Withania somnifera supplementation on muscle strength and recovery: A randomized controlled trial. Journal of the International Society of Sports Nutrition, 12, 43.* https://doi.org/10.1186/s12970-015-0104-9
- Vaidya, V. G., Gothwad, A., Ganu, G., Girme, A., Modi, S. J., &Hingorani, L. (2023). Clinical safety and tolerability evaluation of *Withania somnifera (L.) Dunal (Ashwagandha) root extract in healthy human volunteers. Journal of Ayurveda and Integrative Medicine, 15(1), 100859. Advance online publication.* https://doi.org/10.1016/j.jaim.2023.100859
- Verma, N., Gupta, S. K., Patil, S., & Mishra, A. K. (2023). Effects of Ashwagandha (*Withania somnifera) standardized root extract on physical endurance and VO2 max in healthy adults performing resistance training: An eight-week, prospective, randomized, double-blind, placebo-controlled study. F1000Research, 12, 335.* https://doi.org/10.12688/f1000research.121534.1
- Verma, N., Gupta, S. K., Tiwari, S., Mishra, A. K., & Patil, S. (2023). Effect of Ashwagandha root extract on serum testosterone and muscle recovery in strength training. *International Journal of Health Sciences, 4(5), 371-381.* https://doi.org/10.12669/pjms.39.1.6731
- Verma, N., Gupta, S. K., Tiwari, S., & Mishra, A. K. (2021). Safety of Ashwagandha root extract: A randomized, placebo-controlled study in healthy volunteers. *Complementary Therapies in Medicine*, 57, 102642. https://doi.org/10.1016/j.ctim.2020.102642
- Yadav, S. (2014). Effect of Ashwagandha (*Withania somnifera) consumption on the selected physical fitness variables of male sprinters. Turkish Journal of Sport and Exercise, 16(3), 45-47.*
- *Yerram, C., Jillela, A., & Reddy, V. (2023). Effects of Ashwagandha (Withania somnifera) root extract serum application on hair health in healthy adults: A prospective, double-blind, randomized, parallel, placebo-controlled study. Journal of Ayurveda and Integrative Medicine. Advance online publication.* https://doi.org/10.1016/j.jaim.2023.100859

Annexure I – AHP Press Release

AMERICAN HERBAL PHARMACOPOEIA®

Standards of Identity, Analysis, and Quality Control

AHP PRESS RELEASE

FOR IMMEDIATE DISTRIBUTION
June 25, 2024

AHP Responds to Claims of Ashwagandha Abortifacient Effects

In May of 2020, Danish Food Authorities issued a risk assessment of ashwagandha recommending against its use due to purported abortifacient activity. Other European countries followed, calling for independent risk assessments that have called into question the safety of the herb when used in pregnancy. As their primary reference, the Danish authorities cited an ashwagandha monograph of the World Health Organization (WHO) (2009) that in turn cited the American Herbal Pharmacopoeia (AHP) *Ashwagandha Root Monograph and Therapeutic Compendium* (2000). However, the WHO monograph, in an example of what is known in medical literature as *citation distortion*, did not fully articulate the AHP review which stated the following:

"There are conflicting reports regarding the use of ashwagandha in pregnancy. Large but undefined doses have been reported to possess abortifacient activity (Chadha 1976; Svoboda 1992). Of several ayurvedic practitioners consulted, none reported having observed an abortifacient activity clinically. Conversely, ashwagandha has, traditionally and in modern ayurvedic practice, been used to prevent miscarriage and stabilize the fetus (Tirtha 1998)."

Misrepresentation of the AHP monograph has been repeatedly uncritically resulting in the misconception that ashwagandha root is potentially unsafe. A potential for an abortifacient effect was similarly reported in the first edition of the *Botanical Safety Handbook* (BSH; McGuffin et al. 1997), which provides a safety classification for ashwagandha of 2b: Not to be used in pregnancy unless otherwise recommended by a qualified health care practitioner, and a "Notice" as an abortifacient. The 2b classification remained in the second edition of BSH but the Notice as an abortifacient was removed due to the lack of documentation that such an action existed.

Since the earlier publications of both AHP and BSH, a comprehensive review of the traditional and scientific literature and all accessible citations that made any mention of ashwagandha as an abortifacient was conducted. Additionally, the opinion of experienced Ayurvedic medicine practitioners from India and North America was solicited. Neither the Expert Advisory Council for the revision of BSH (third edition), nor experts involved in the AHP revision, found any traditional or scientific documentation that ashwagandha possesses an abortifacient activity. The earlier cautions regarding the use of ashwagandha in pregnancy and its claimed use as an abortifacient were based on anecdotal reports from the ethnobotanical literature that provided no indication such an effect was evident. Furthermore, when such reports were made, the overwhelming majority referred to above-ground parts, which in Ayurveda were rarely used internally, not the root, the portion used almost exclusively. Similarly, a review of the traditional and scientific data reveals no pharmacological mechanisms that would indicate an abortifacient effect.

The BSH safety classification was revised to the current safety classification of 1: Herbs that can be safely consumed when used appropriately. An upcoming revision of the AHP *Monograph and Therapeutic Compendium* will reflect this as well.

In addition, subsequent to safety concerns raised in the European Union, the Ministry of AYUSH (Government of India) released a Safety Dossier (2.0; 2024) noting the lack of abortifacient activity of ashwagandha root and citing all clinical and pre-clinical data that have investigated the use of ashwagandha and its preparations in pregnancy. One toxicity investigation in rats demonstrated a No Observed Adverse Effect Level of ashwagandha root extract of 2,000 mg/kg. The available human trials reported no maternal or fetal toxicity in pregnant women using ashwagandha preparations. No other clinical or pre-clinical investigations revealed an abortifacient activity.

While adequate caution when using any substance during pregnancy is warranted, based on a critical and comprehensive review of the traditional and modern

literature, as well as the opinion of the majority of experts, there is no evidence of an abortifacient effect of ashwagandha root.

For more information regarding this press release contact:

Roy Upton, President
American Herbal Pharmacopoeia
roy@herbal-ahp.org
1-831-461-6317

ABOUT AMERICAN HERBAL PHARMACOPOEIA
AHP is a non-profit 501(c)(3), non-governmental, educational organization committed to advancing knowledge about the quality and understanding of herbal medicine worldwide. Our work is made possible by a global network of experts, including botanists, chemists, herbalists, pharmacists, pharmacologists, and physicians, as well as experts in Ayurveda and traditional Chinese and Persian medicine. AHP believes our medicines of the past are our medicines of the present and future. To learn more about AHP, visit https://herbal-ahp.org/.

CONTACT US	ABOUT US
American Herbal Pharmacopoeia® PO Box 66809, Scotts Valley, CA. 95067 Email: ahp@herbal-ahp.org Website: www.herbal-ahp.org Call Us: 831-461-6318 Fax: 831-438-2196	The American Herbal Pharmacopoeia® is a non-profit 501(c)(3) educational organization.

Annexure II - Clinical Studies on Ashwagandha

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
Stress, Sleep, and Anxiety						
Stress and Anxiety / Chandrasekhar et al2012 (India)	Randomized, Double-Blind, Placebo – Controlled 8 Weeks	Healthy adults / Aged between 18 and 54 years experiencing high-stress Ashwagandha (32, 30), Placebo (32, 31)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	PSS, GHQ-28, DASS, Serum Cortisol	Ashwagandha (6 - Nasal congestion, Constipation, Cough and cold, Drowsiness, Decreased appetite, Placebo (5 - Dryness of mouth, tiredness, fever, headache, abdominal pain, diarrhea, tremor in legs)	Compared to placebo, Ashwagandha was associated with significantly greater improvements in PSS, GHQ-28 total and subscale scores, DASS total and subscale scores, and serum cortisol. Mild Adverse events were seen and were comparable in the two groups. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The study concluded that the Ashwagandha root extract is safe, and well tolerated by all the participants.
Stress and Weight Management / Choudhary et al 2017b (India)	Randomized, Double-Blind, Placebo – Controlled 8 Weeks	Adults aged between 18 and 60 years with symptoms of chronic work stress Ashwagandha (26, 25), Placebo (26, 25)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	PSS, FCQ, OHQ, TFEQ Serum Cortisol, Body weight, BMI	Ashwagandha (1) Placebo (1) Giddiness, Heaviness of head, Blurring of vision, hyperacidity	Compared to placebo, Ashwagandha associated with significantly greater improvements in PSS, FCQ-T (planning, positive reinforcement, negative reinforcement, lack of control, emotion, and environment scores), OHQ, TFEQ (uncontrolled eating and emotional eating scores), serum cortisol, body weight, and BMI The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The study concluded that the Ashwagandha root extract is safe, and well tolerated by all the participants.
Stress, Sleep and Anxiety / Salve et al 2019 (India)	Randomized, Double-Blind, Placebo – Controlled 8 Weeks	Adults aged between 18 and 55 years experiencing high stress Ashwagandha 250mg (20, 19),	125mg and 300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	PSS, HAM-A, Serum Cortisol, Sleep quality	Ashwagandha (0) Placebo (0)	Compared to placebo, Ashwagandha associated with significantly greater reductions in PSS (both doses), HAM-A (600 mg), sleep quality rating (both doses), and serum cortisol (both doses).

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
		Ashwagandha 600mg (20,20), Placebo (20, 19)				Trends suggested greater efficacy with the higher Ashwagandha dose The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Insomnia and Anxiety / Langade et al2019 **(India)**	Randomized, Double-Blind, Placebo – Controlled 10 Weeks	Adults aged between 18 and 60 years with insomnia Ashwagandha (40, 39), Placebo (20, 19)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	Sleep actigraphy - SOL, TST, WASO, TIB, SE, Sleep log, PSQI, HAM-A, Sleep Quality, Mental alertness on rising score	Ashwagandha (0) Placebo (0)	Compared to placebo, Ashwagandha associated with significantly greater improvements in sleep actigraphy measurements of sleep onset latency and sleep efficiency, PSQI sleep quality scores, HAM-A scores, and sleep quality scores. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Anxiety Symptoms among children with ADHD / Hosseini et al 2019 **(Iran)**	Randomized, Double-Blind, Placebo – Controlled 6 Weeks	Children aged 7-12 years Ashwagandha (16, 14) Placebo (15, 14)	Ashwagandha Root Extract 10mg / day	RCMAS, ADHD-RS	Ashwagandha (0) Placebo (0)	Ashwagandha root extract reduces the symptoms of physiological anxiety, sensitivity, social concerns, and an overall score of RCMA among children with ADHD and comorbid anxiety disorders. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Elderly and General Wellbeing / Kelgane et al2020 **(India)**	Randomized, Double-Blind, Placebo - Controlled Study 12 Weeks	Healthy older-age adults aged between 65 and 80 years Ashwagandha (25, 19), Placebo (25, 20)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	WHO-QOL-BREF, Sleepiness scale, Mental alertness on rising, Sleep quality scale	Ashwagandha (0) Placebo (0)	Compared to placebo, Ashwagandha is associated with significantly greater improvements in WHOQOL-BREF scores (total score and global, physical, psychological, and environment domain), mental alertness on waking rating, and sleep quality rating, but not on the sleep scale scores The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
Primary insomnia in elderly males / Atulet al2020 **(India)**	Simple Randomized, Two-arm Open-label 4 Weeks	Male patients from the age group of 60–70 years Ashwagandha (only) (30, 27) BrimhanaNasya + Ashwagandha (30, 28)	Ashwagandha root powder - 6 g orally with 100 ml of milk / day BrimhanaNasya + 6g Ashwagandha Root Powder with 100ml of milk / day	PSQI	Ashwagandha (only) (0) BrimhanaNasya + Ashwagandha (0)	The result of the study indicates that BrimhanaNasya and Ashwagandha root powder group patients got more significant results in all components of PSQI compared to Ashwagandha root powder group patients. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Generalized Anxiety Disorder / Fuladi et al 2020 **(Iran)**	Randomized, Double-Blind, Placebo – Controlled 6 Weeks	Healthy Adults Ashwagandha (18, 18) Placebo (22, 22)	Withania somnifera Root Extract 1g/day	HAM-A, GAD level	Ashwagandha (0) Placebo (0)	Compared to the placebo, the change in the Hamilton anxiety rating scores (HAM-A) revealed a significantly ameliorated situation by decreasing HAM-A score in the treatment group. Moreover, there was a significant difference in the treatment group in the second week and sixth week in the reduction of Generalized Anxiety Disorder. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Sleep, Insomnia and Anxiety / Langade et al2021 **(India)**	Randomized, Double-Blind, Placebo – Controlled 8 Weeks	Heathy adults and insomnia patients aged between 18 and 50 years Healthy - Ashwagandha (20,20), Placebo (20, 20); Insomnia - Ashwagandha (20,20), Placebo (20, 20)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	Sleep actigraphy, parameters - SOL, TST, WASO, TIB, SE; PSQI, HAM-A, Mental Alertness on rising, Sleep quality	Ashwagandha (0) Placebo (0)	Compared to the placebo, Ashwagandha root extract supplementation resulted in a significant improvement in both healthy participants and insomnia patients. There was a statistically significant improvement in SOL, HAM-A outcomes, mental alertness, and sleep quality. Although both healthy and insomniac subjects reported significant improvement in sleep parameters, it was more significant in the latter group. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
Stress and Cognitive Functions / Gopukumar et al2021 **(India)**	Randomized, Double-blind, Parallel-group, Two-arm, Placebo-controlled 12 Weeks	Healthy Cognitively sound adults aged 20–55 years Ashwagandha (65, 62) Placebo (65, 63)	300mg - Hydroalcoholic Ashwagandha root extract - once daily	CANTAB, OHQ, PSQI PSS, MoCA Serum Cortisol, BDNFlevels	Ashwagandha (0) Placebo (0)	Compared to the placebo, the CANTAB reported significantly improved recall memory, and the total error rate in recalling patterns significantly decreased in the Ashwagandha SR group. Also, lower PSS-10 score, serum cortisol levels, and Pittsburgh Sleep Quality Index (PSQI) score but higher Oxford Happiness Questionnaire (OHQ) scores were seen in Ashwagandha SR suggesting significantly lower stress levels and significantly better psychological well-being and sleep quality in the former. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Stress and Anxiety / Majeed et al 2023 **(India)**	Randomized, Double-Blind, Placebo - Controlled 8 Weeks	Adult participants aged 21 to 54 years Ashwagandha (27, 25), Placebo (27, 25)	500 mg - Hydroalcoholic Ashwagandha root extract with 95% piperine-5 mg - once daily	PSS, GAD-7, QOL CANTAB, Salivary Cortisol, Serotonin, Dopamine, NO, GSH, MDA	Ashwagandha (8 - Nausea, Headache, Diarrhoea) Placebo (4 - Headache, Nausea)	Compared to placebo, the PSS, GAD-7, and QOL scores improved significantly in all the participants taking ARE. The CANTAB analysis revealed a significant improvement in multitasking, concentration, and decision-making time in ARE compared to placebo. ARE was also associated with a greater reduction in the morning salivary cortisol and an increase in urinary serotonin compared to placebo. Serum levels of NO, GSH, and MDA were not significantly different. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
Stress and Fatigue / Smith et al 2023 **(Australia)**	Randomized, Double-Blind, Placebo – Controlled 12 Weeks	Healthy Adults aged between 40 and 75 years Ashwagandha (60, 55), Placebo (60, 56)	200 mg - Hydroalcoholic Ashwagandha root extract - twice daily	PSS, CFS PROMIS-29, Sex hormone concentrations, MDA, FG, HbA1c, TSH, HRV, Grip strength, Anthropometric measures, LFT, RFT, FBC	Ashwagandha (13 - Digestive disturbances, Mood disturbances/changes, Headaches/ migraines, Increased appetite, Increased tiredness) Placebo (15 - Digestive disturbances, Mood disturbances/changes, Headaches/ migraines, Increased appetite, Itchy Skin, Increased tiredness)	Compared to the placebo, there was a statistically significant reduction in fatigue symptoms and a significant increase in heart rate variability in the Ashwagandha group. However, there was non- significant reduction in PSS score and other self-report measures. In the men taking ashwagandha, there was a significant increase in the blood concentrations of free testosterone and luteinizing hormone compared to the placebo group. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Anxiety, Depression, and Serotonin Levels / Majeedet al2023 **(India)**	Randomized, Double-Blind, Placebo – Controlled 12 Weeks	Healthy adults aged between 18 and 60 years Ashwagandha (34, 34), Control (36, 36)	500 mg - Ashwagandha root extract with piperine-5 mg - once daily	HDRS, HARS, GSQS, WHO-QOL, Serum serotonin	Ashwagandha (18 - Nausea, Diarrhea, Drowsiness, Fever, Headache, Stomach Pain) Placebo (16 - Nausea, Diarrhea, Drowsiness, Fever, Headache, Stomach Pain, Back Pain)	Compared to the placebo, the HARS, HDRS, GSQS, and QOL scores improved significantly in the Ashwagandha group. Serum levels of serotonin increased in ARE, but showed a decrease in placebo. Biochemical and hematological parameters remained in the normal range in all participants. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
Anxiety in Adults / Cooley et al2009 **(Canada)**	Randomized, Controlled, Pragmatic trial 12 Weeks	Adults aged 18 - 65 years Ashwagandha (41, 36) Placebo (40, 39)	Withania somnifera root (Swiss ashwagandha); 300-mg supplements twice daily	BAI, SF-36, FQ, VAS	Ashwagandha (Gastrointestinal upset, Overstimulation, Feeling warm, increased frequency of nocturnal night cramps, mild hair loss) Placebo (Gastrointestinal upset, Overstimulation, Rash, Feeling warm, increased frequency of nocturnal night cramps, mild hair loss)	Compared to the placebo, the Ashwagandha group caused a significant decrease in anxiety levels and an improvement in quality of life measures. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The safety of Ashwagandha root was confirmed as there were no adverse events reported and Ashwagandha root was well tolerated by all the participants.
Anxiety in Adults / Andrade et al 2000 **(India)**	Double-blind, Placebo-controlled, Dose-ranging study 6 Weeks	Adults with GAD, aged between 18 - 70 years Ashwagandha (20, 17) Placebo (19, 16)	Ethanolic extract of Ashwagandha Two 250-mg tablets, twice daily - Ten tablets a day.	HAM-A, GRS	Ashwagandha (17 - Drowsiness (2), Heaviness of head (4), Increased frequency of migraine (1), Fatigue (1), Withdrawal fatigue (1), Itching (1), Numb hands (1), Bitter taste (1), Decreased appetite (1), Increased appetite (1), Decreased sleep (2), Gastritis (2), Heaviness in stomach (1)). Placebo (16 - Giddiness (2), Dullness (1), Heaviness of head (1), Fatigue (1), Chest pain (1), Chest infection (1),	Compared to the placebo, there was a trend for the anxiolytic superiority of drugs at week 2, and a statistically significant at week 6 with Ashwagandha.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
					burning eyes (1), Burning urine (1), Multiple somatic complaints (1), Heat in body (1), Increased appetite (1), Gastritis (1), Heaviness in stomach (1), Diarrhea (1), Menstrual irregularities (2), Worsening of obsessive-compulsive disorder (1)).	
Subclinical Hypothyroidism						
Subclinical Hyperthyroidism / Sharma et al 2018 **(India)**	Randomized, Double-Blind, Placebo – Controlled 8 Weeks	Adults aged between 18 and 50 years with elevated TSH (4.5 to 10µIU/L) Ashwagandha (25, 25), Placebo (25, 25)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	TSH, Free T3, Free T4	Ashwagandha (1) Placebo (3) Fever, Asthenia, cough and headache	Compared to placebo, Ashwagandha associated with significantly greater increases in T3, T4, and reduction in TSH. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The study concluded that the Ashwagandha root extract is safe, and well tolerated by all the participants.
Sexual Health in Men / Male sexual function						
Male Sexual Function and Fertility / Ambiye et al2013 **(India)**	Randomized, Double-Blind, Placebo – Controlled 12 Weeks	Infertile men / aged between 22 and 40 years Ashwagandha (21, 21), Placebo (25, 25)	225mg - Standardized Aqueous Ashwagandha Root Extract Thrice daily	Semen Parameters, Serum Testosterone, Serum Luteinizing Hormone	Ashwagandha (0) Placebo (0)	Ashwagandha is associated with significant increases in sperm concentration, semen volume, sperm motility, serum testosterone, and LH. No changes occurred in the placebo group The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
Male Sexual Function / Chauhan et al 2022 **(India)**	Randomized, Double-Blind, Placebo – Controlled 8 Weeks	Males aged between 21 and 45 years with low sexual desire Ashwagandha (25, 25), Placebo (25, 25)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	DISF-M, Serum Testosterone, PRL, SF-36	Ashwagandha (4 - Sleepiness, Mild Abdominal Pain, Low Grade Joint Pain) Placebo (3 - Abdominal Pain, Mild Diarrhea)	Compared to the placebo, Ashwagandha was associated with significantly greater increases in Total DISF-M scores and serum testosterone levels. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The study concluded that the Ashwagandha root extract is safe, and well tolerated by all the participants.
Idiopathic Male infertility / Azgomi et al 2018a **(Iran)**	Triple-blind, Randomised, Parallel Group, Two Arm, clinical trial. 12 Weeks	Married infertile male patients aged between 18 and 45 years Ashwagandha (50, 46) Pentoxifylline (50, 45)	6 capsules containing 5 g Hydroalcoholic Ashwagandha root extract once daily 6 capsules containing 800 mg Pentoxifylline once daily	Sperm parameters	Ashwagandha (1 - nausea and epigastric pain) Pentoxifyline (3 - nausea and epigastric pain)	Compared to the baseline the administration of Ashwagandha markedly increased mean sperm count, progressive motility, and improved sperm morphology.The results showed that both WS and pentoxifylline meaningfully improve sperm parameters in idiopathic male infertility. However, the impacts of the two medications were not significantly different. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Seminal plasma metabolites of infertile males / Gupta et al 2013 **(India)**	Clinical Study 12 Weeks	Infertile males aged 22–45 years Ashwagandha (180) Control (50)	Withania somnifera root powder (5 g/day)	Semen Profile, Testosterone, LH, FSH, PRL, IDH, LDH, ALT, AST	Ashwagandha (0) Control (0)	Compared to the baseline, Ashwagandha supplementation repairs the disturbed concentrations of lactate, alanine, citrate, GPC,histidine, and phenylalanine in seminal plasma and recovers the quality of semen. Serum biochemistry was also improved over post-therapy in infertile men. The safety of Ashwagandha was confirmed as there were no adverse events reported and Ashwagandha was well tolerated by all the participants.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
Psychogenic erectile dysfunction / Mamidi et al 2011 **(India)**	Randomized, Single-blind, Placebo-controlled, parallel-group study. 8 Weeks	Patients with psychogenic erectile dysfunction aged between 18 - 60 years Ashwagandha (46, 41) Placebo (49, 45)	4 tablets 500mg Ashwagandha root powder - thrice daily	Semen analysis, Routine Hematological tests, Biochemical Investigations, Serum Testosterone	Ashwagandha (0) Placebo (0)	Compared to the baseline there was significant improvement in IIEF items, but the result was insignificant when compared to placebo. The safety of Ashwagandha was confirmed as there were no adverse events reported and Ashwagandha was well tolerated by all the participants.
Sexual Health in Women / Female sexual function						
Sexual Function and Fertility in Women / Dongre et al 2015 **(India)**	Randomized, Double-Blind, Placebo – Controlled 8 Weeks	Females aged between 21 and 50 years with female sexual dysfunction Ashwagandha (25, 25), Placebo (25, 25)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	FSFI, FSDS, SAR	Ashwagandha (0) Placebo 0)	Compared to placebo, Ashwagandha associated with significantly greater increases in FSFI scores (total, arousal, lubrication, orgasm, satisfaction), FSDS, but not SAR The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Sexual Health in Women / Ajgaonkar et al 2022 **(India)**	Randomized, Double-Blind, Placebo – Controlled 8 Weeks	Females aged between 18 and 50 years with a Female Sexual Function Index (FSFI) Ashwagandha (40, 37), Placebo (40, 35)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	FSFI, FSDS SAR, GHQ-28	Ashwagandha (3) Placebo (3) Nausea, Drowsiness	Compared to placebo, Ashwagandha associated with significantly greater increases in FSFI scores (total, arousal, lubrication, orgasm, satisfaction), FSDS, and Successful Sexual encounters. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The study concluded that the Ashwagandha root extract is safe, and well tolerated by all the participants.
Perimenopause						
Climacteric symptoms in Perimenopausal Women / Gopal et al2021 **(India)**	Randomized, Double-Blind, Placebo - Controlled Study 8 Weeks	Healthy women with perimenopausal symptoms aged 40 - 60 years Ashwagandha (40, 40), Placebo (40, 40)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	MRS, MEN-QoL, Hot Flash score, Hormonal Parameters	Ashwagandha (3 - Abdominal Discomfort, Abdominal Pain, Nausea) Placebo (4 - Abdominal Discomfort, Abdominal Pain, Insomnia, Nausea)	Compared to placebo, Ashwagandha administration resulted in a significant reduction in MEN-QoL score, hot flash score, serum FSH, LH, and testosterone. 41.7% reported treatment with Ashwagandha as "excellent" compared to the placebo i.e.,23.9% The reported adverse events were of mild severity and no intervention was required.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
						These events were resolved without any intervention and participants continued the study treatments till the end of the study. The study concluded that the Ashwagandha root extract is safe, and well tolerated by all the participants.
Personal Care / Hair and Skin Health						
Healthy Skin in Adults / Narra et al 2023 **(India)**	Randomized, Double-Blind, Placebo-Controlled study 8 Weeks	Healthy men and women aged between 18 and 60 years with Fitzpatrick phototype III-VI skin grade Ashwagandha (28, 27), Placebo (28, 26)	1 mL of skin lotion on the face until it was well absorbed	Physician Global Assessment Scores (Wrinkles, pores, hydration & pigmentation), Melanin Index Transepidermal, Water Loss Skin Elasticity, Skin Hydration	Ashwagandha (4 - Local Swelling, Erythema) Placebo (5 - Local Swelling, Erythema, Local Irritation)	Compared to placebo, Ashwagandha was associated with significant improvement in wrinkles, pores, hydration, pigmentation, and elasticity. A significant reduction was seen in TEWL and Melanin index The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The study concluded that the Ashwagandha root extract is safe, and well tolerated by all the participants.
Healthy Hair in Adults/ Yerram et al2023 **(India)**	Randomized, Double-Blind, Placebo-Controlled study 75 Days	Healthy adults between 18 and 45 years of age with mild to moderate hair loss including androgenic alopecia Ashwagandha (34, 30), Placebo (34, 31)	1-2 drops of the serum were taken and then applied to the hair once a day	Body fat percentage, Trichoscan hair analysis, Hair pull test, Hair-specific skindex-29	Ashwagandha (0) Placebo (0)	Compared to placebo, Ashwagandha was associated with a significant reduction in hair shedding, and an improvement in hair density, growth, and thickness. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Strength, Endurance and Recovery						
Muscle Strength and Endurance / Vermaet al 2023 **(India)**	Randomized, Double-Blind, Placebo - Controlled study 8 Weeks	Healthy adults aged between 18 and 45 years Ashwagandha (40, 40), Placebo (40, 40)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	Muscle strength (1- RM load for bench press and leg extension exercises),Muscle size	Ashwagandha (0) Placebo (0)	Compared to the placebo group Ashwagandha root extract supplementation demonstrated an improvement in chest press, leg press, and a significant improvement in endurance as compared to the placebo group. Also, significant improvements in muscle girth for the arm, and chest, were seen, and there was non significant increase in the muscle girth for thigh.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
				(arm, chest, and upper thigh), Body fat percentage, VO2 Max		The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Health Indices in Professional Wrestlers / Barbara et al 2023 **(Poland)**	Randomized, Double-Blind, Placebo-Controlled study 8 Weeks	Professional athletes – highly qualified national team wrestlers Ashwagandha (12, 11), Placebo (14, 10)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	Hematological parameters, Biochemical parameters, Body composition, Creatine kinase (CK) activity	Ashwagandha (0) Placebo (0)	Compared to the placebo, serum CK activity in the Ashwagandha group did not increase significantly, thus indicating improved muscle recovery. At the end of the study, the values of biochemical variables remain in the normal range after the Ashwagandha intervention. It was observed that Ashwagandha did not affect the liver parameters, it was well tolerated by all the participants with no reported adverse events. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Cardiorespiratory Endurance and Recovery / Tiwari et al 2021 **(India)**	Randomized, Double-Blind, Placebo - Controlled study 8 Weeks	Healthy adults aged between 18 and 45 years with BMI range 18.5-24.9 kg/m2 Ashwagandha (25, 25), Placebo (25, 25)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	WHO-QOL-BREF, Sleepiness scale, Mental alertness on rising, Sleep quality scale	Ashwagandha (1 - Mild Ear pain) Placebo (3 - Diarrhoea, Low Grade Fever)	Compared to placebo, Ashwagandha is associated with statistically significant improvements in VO2 max, TRQ, DALDA, and RESTQ scores. In the Ashwagandha group, a majority of subjects (56%) showed good improvement, and 36% showed moderate improvement. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study. The study concluded that the Ashwagandha root extract is safe, and well tolerated by all the participants.
Muscle Strength and Recovery / Wankhede et al 2015 **(India)**	Randomized, Double-Blind, Placebo - Controlled study 8 Weeks	Healthy males aged between 18 and 50 years with little experience in resistance training Ashwagandha (29, 25), Placebo (28, 25)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	Muscle strength (1- RM load for bench press and leg extension exercises), Muscle size	Ashwagandha (0) Placebo (0)	Compared to placebo, Ashwagandha is associated with greater increases in muscle strength (bench press and leg extension), muscle size (arm and chest), and serum testosterone; and greater reductions in creatine kinase and Body fat Percentage.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
				(arm, chest, and upper thigh), Body fat percentage, Muscle recovery, Serum Testosterone		The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Cardiorespiratory Endurance / Choudhary et al 2015 **(India)**	Randomized, Double-Blind, Placebo - Controlled study 12 Weeks	Healthy athletic adults / aged between 20 and 45 years Ashwagandha (25, 25), Placebo (25, 24)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	VO2 max, WHOQOL	Ashwagandha (0) Placebo (0)	Mean change in VO2max and WHO-QOL subscale scores (physical health, psychological, social relationships, and social relationships, and environmental) was significantly greater in Ashwagandha compared to placebo. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Cardiorespiratory endurance in elite Indian cyclists / Shenoy et al 2012 **(India)**	Randomized, Placebo-controlled study 8 Weeks	Adults (stated level medal winners) aged between 18-27 years Ashwagandha (20, 18) Placebo (20, 19)	500mg - Aqueous Ashwagandha root extract powder - Twice daily	VO2 max, RER	Ashwagandha (0) Placebo (0)	Compared to the baseline, there was a significant improvement in all parameters including VO2 max and time for exhaustion on treadmill. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Muscle Strength, Safety and Tolerability / Raut et al 2012 **(India)**	Dose-related, Open-label clinical study 4 Weeks	Healthy adults aged 18-30 years Ashwagandha (18, 18)	Withania somnifera extract 750 mg/day x10 days, 1000 mg/day x 10 days, 1250 mg/day x 10 days	Exercise tolerance (by Cycle Ergometer), Muscle strength , Body fat percentage and lean body weight, LFT, Serum HDL, LDL, and VLDL cholesterol	Ashwagandha 750mg (1 - Increase in appetite, libido, and hallucinogenic effects with vertigo) Ashwagandha 1000mg (0) Ashwagandha 1200mg (0)	Ashwagandha found to be safe on hematological and biochemical organ function tests. This study has also demonstrated muscle strengthening, lipid lowering, and improved quality of sleep in view of its traditional use as balya.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
Physical performance and cardio-respiratory endurance / Sandhu et al 2010 **(India)**	Randomized, Placebo-controlled study 8 Weeks	Healthy adults aged 18 - 25 years Ashwagandha (10,10) Terminalia Arjuna (10, 10) Ashwagandha + Terminalia Arjuna (10, 10) Placebo (10, 10)	500mg - Aqueous Ashwagandha root extract powder - Once daily	Maximum velocity, Average absolute and average relative power of the lower limbs, 20-second wobble board test, Maximum oxygen consumption, Blood pressure, BMI	Ashwagandha (0) Terminalia Arjuna (0) Ashwagandha + Terminalia Arjuna (0) Placebo (0)	Compared to the placebo and Terminalia Arjuna, Ashwagandha increased velocity, power, and VO2 max. The safety of Ashwagandha was confirmed as there were no adverse events reported and Ashwagandha was well tolerated by all the participants.
Memory and Cognitive Performance						
Cognitive Performance / Choudhary et al2017a **(India)**	Randomized, Double-Blind, Placebo - Controlled Study 8 Weeks	Adults over the age of 35 with mild, subjective symptoms of memory impairment Ashwagandha (25, 25), Placebo (25, 25)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	Weschler Memory Scale III, Shepard Mental Rotation Task, Wisconsin Card Sort Test, Eriksen Flanker Task, Trail Making Test, Mackworth Clock Test	Ashwagandha (0) Placebo (0)	Mean scores on tests/subtests associated with immediate memory, general memory, executive function, and attention and information processing speed, were significantly better in the Ashwagandha group compared to placebo The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Cognitive Functions and Stress / Gopukumar,et al 2021 **(India)**	Randomized, Double-blind, Parallel-group, Two-arm, Placebo-controlled 12 Weeks	Healthy Cognitively sound adults aged 20–55 years Ashwagandha (65, 62) Placebo (65, 63)	300mg - Hydroalcoholic Ashwagandha root extract - once daily	CANTAB, OHQ, PSQI PSS, MoCA Serum Cortisol, BDNF levels	Ashwagandha (0) Placebo (0)	Compared to the placebo, the CANTAB reported significantly improved recall memory, and the total error rate in recalling patterns significantly decreased in the Ashwagandha SR group. Also, lower PSS-10 score, serum cortisol levels, and Pittsburgh Sleep Quality Index (PSQI) score but higher Oxford Happiness Questionnaire (OHQ) scores were seen in Ashwagandha SR suggesting significantly lower stress levels and significantly better psychological well-being and sleep quality in the former. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
Elderly Health and Wellbeing						
Elderly and General Wellbeing / Kelgane et al2020 **(India)**	Randomized, Double-Blind, Placebo - Controlled Study 12 Weeks	Healthy older-age adults aged between 65 and 80 years Ashwagandha (25, 19), Placebo (25, 20)	300mg - Standardized Aqueous Ashwagandha Root Extract Twice daily	WHO-QOL-BREF, Sleepiness scale, Mental alertness on rising, Sleep quality scale	Ashwagandha (0) Placebo (0)	Compared to placebo, Ashwagandha is associated with significantly greater improvements in WHOQOL-BREF scores (total score and global, physical, psychological, and environment domain), mental alertness on waking rating, and sleep quality rating, but not on the sleep scale scores The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
COVID-19						
Chemoprophylaxis of COVID-19 / Chopraet al2021 **(India)**	Randomized, Prospective, Open-label, Parallel efficacy, Two arm, Multi-centre study 8 Weeks (Interim Analysis)	High risk health care workers (HCW) Ashwagandha (80, 34), Comparator (HCQ) (80, 36)	2 tablets of 250 mg Withania somnifera dried roots standardized aqueous extract - twice daily	Failure of prophylaxis' as confirmed COVID-19 by RT-PCR	Ashwagandha (27) Comparator (HCQ) (40)	The interim analysis suggests that WS is not inferior to HCQ. The results show non-inferiority for both symptomatic COVID-19 with RT-PCR and asymptomatic COVID-19 with RT-PCR and also for all RT-PCR positives. The reported adverse events were of mild severity and no intervention was required. These events were resolved without any intervention and participants continued the study treatments till the end of the study.
Obsessive-compulsive disorder						
Obsessive-compulsive disorder / Jahanbakshet al2016 **(Iran)**	Randomized, Double-blind, Placebo-controlled trial 6 Weeks	Adults with OCD Ashwagandha (15, 15) Placebo (15, 15)	Withania somnifera Root Extract 120mg / day	Y-BOCS	Ashwagandha (0) Placebo (0)	Compared to the placebo group, there was significant reduction in Yale-Brown Obsessive-Compulsive Scale score in Ashwagandha group. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Children studies						
Brumhana and Balya effect / Mishra et al 2010 **(India)**	Randomized, Placebo-controlled study 6 Weeks	Children between 3 years and 12 years AshwagandhaGhrita (51, 41) Ashwagandha Granules (36, 36) Placebo (34, 34)	AshwagandhaGhrita - 2.5 – 4 gm for age 3-7 years, and 6 - 8gm for 8 -12 years Ashwagandha Granules - 2.5 – 4 gm for age 3-7 years, and 6 - 8gm for 8 -12 years	Muscular strength, Endurance Neck and abdomen circumferenceSkin fold thickness measurement	AshwagandhaGhrita (0) Ashwagandha Granules (0) Placebo (0)	Compared to placebo and Ashwagandha granules, the Ashwagandhaghrita group demonstrated a more significant improvement in all the parameters. The safety of Ashwagandha was confirmed as there were no adverse events reported and Ashwagandha was well tolerated by all the participants.

Condition / Reference (Country)	Design & Duration	Participants	Intervention	Outcome Measures	Adverse events (Ashwagandha vs Placebo/ Control group)	Summary of results
Anxiety Symptoms among children with ADHD / Hosseini et al 2019 **(Iran)**	Randomized, Double-Blind, Placebo – Controlled 6 Weeks	Children aged 7-12 years Ashwagandha (16, 14) Placebo (15, 14)	Withania somnifera Root Extract 10mg / day	RCMAS, ADHD-RS	Ashwagandha (0) Placebo (0)	Withania somnifera root extract reduces the symptoms of physiological anxiety, sensitivity, social concerns, and an overall score of RCMA among children with ADHD and comorbid anxiety disorders. The safety of Ashwagandha root extract was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.
Growth and Development in Infants /KoushikBaishya et al 2020.	Comparative Clinical Study 4 weeks	Infants upto 1 year Ashwagandha (20, 18) Placebo (20, 16)	AshwagandhaGrita - 0.5 ml/kg/day with milk	Anthropometrical Parameters	Ashwagandha (0) Placebo (0)	AshwagandhaGhrita enhances growth and development in the infant. The safety of Ashwagandhaghrita was confirmed as there were no adverse events reported and Ashwagandha root extract was well tolerated by all the participants.

Abbreviations

ADHD-RS - Attention Deficit Hyperactivity Disorder rating scale

ALP - Alkaline Phosphatase

ALT - Alanine Aminotransferase

API - Ayurvedic Pharmacopeia of India

AST - Aspartate Aminotransferase

ASU&H – Ayurveda, Siddha, Unani and Homeopathy

BAI - Beck Anxiety Inventory

BDNF - Brain-derived Neurotrophic Factor,

BMI - Body Mass Index

CANTAB - Cambridge Neuropsychological Test Automated Battery

CBC / FBC – Complete Blood Count,

CFS - Chalder Fatigue Scale

CNS - Central Nervous System

DASS – Depression Anxiety Stress Scale

DISF-M/ - Derogatis interview for sexual functioning (Male)

DILI- Drug-induced Liver Injury

DTU - Danish Technical University

EU - European Union

FCQ - Food Craving Questionnaire

FDA - Food and Drug Administration

FG – Fasting Glucose

FQ- Fatigue Questionnaire

FSH - Follicle-Stimulating Hormone

FSFI – Female Sexual Function Index

FSDS – Female Sexual Distress Scale

GAD-7 - Generalized anxiety disorder scale

GMP - Good Manufacturing Practices

GHQ – 28 – General Health Questionnaire- 28

GSH – Glutathione

GRS - Global Rating Scale

GSQS - Groningen Sleep Quality Scale

HaCaT- Human Epidermal Keratinocyte line

HAM-A/ HARS - Hamilton's Anxiety Rating Scale

HbA1c - Glycated Haemoglobin

HILI - Herb-induced Liver Injury

HPA - Hypothalamic-Pituitary-Adrenal

HRV – Heart Rate Variability

IDH - Isocitrate dehydrogenase

LDH - Lactate dehydrogenase

LFT – Liver Function Tests

LH - Luteinizing Hormone

MoCA - Montreal Cognitive Assessment

MDA – Malondialdehyde

MENQOL - Menopause-Specific Quality of Life

MRS – Menopause Rating Scale

NO - Nitric oxide

NOAEL - No Observed Adverse Effect Level

OHQ - Oxford Happiness Questionnaire

PRL – Prolactin

PROMIS-29 - Patient-Reported Outcomes Measurement Information System Questionnaire

PSQI – Pittsburgh Sleep Quality Index

PSS - Perceived Stress Scale

QC - Quality Control

QOL - Quality of life

RCMAS - Revised children's manifest anxiety questionnaire

RER - Respiratory exchange ratio.

RFT – Renal Function Test

RT-PCR - Reverse Transcription Polymerase Chain Reaction

SAR - Sexual Activity Records

SE – Sleep Efficiency

SF-36 – Short form 36 Questionnaire

SGOT - Serum Glutamic-Oxaloacetic Transaminase

SGPT - Serum Glutamic-Pyruvic Transaminase

SOL – Sleep Onset Latency

T3 – Triiodothyronine

T4 – Thyroxine

TFEQ - Three Factor Eating Questionnaire

TIB – Total Time in Bed

TSH - Thyroid Stimulating Hormone

TST – Total Sleep Time

TLC - Thin Layer Chromatography

USP - United States Pharmacopeia

VAS – Visual Analogue Scale

WASO – Wake After Sleep Onset

WHO – Hq - World Health Organization – Head Quarters

WHO-QOL – World Health Organization -quality of life Questionnaire

WS - Withania somnifera

Y-BOCS - Yale-Brown Obsessive-Compulsive Scale

Glossary

Adaptogenic - Substances that help the body adapt to stress and exert a normalizing effect upon bodily processes.

Antioxidant - A substance that inhibits oxidation, especially one used to counteract the deterioration of stored food products or remove potentially damaging oxidizing agents in a living organism.

Immunomodulatory - Capable of modifying or regulating one or more immune functions.

Neuroprotective - Capable of protecting neurons from injury or degeneration.

Phytochemicals - Chemical compounds produced by plants, generally to help them thrive or thwart competitors, predators, or pathogens.

Rasayana - A term in Ayurveda that refers to the science of lengthening lifespan and rejuvenation.

Thyrotoxicosis - The condition that occurs due to excessive thyroid hormone of any cause and therefore includes hyperthyroidism

www.ayush.gov.in

www.facebook.com/moayush

www.twitter.com/moayush

Ministry of Ayush
Ayush Bhawan, B Block, GPO Complex,
INA, New Delhi - 110023