



Document prepared by Nerve Center of TFORD, Venture Center, Pune
Task Force on Repurposing of Drugs (TFORD) for COVID19
 S&T Core Group on COVID19 constituted by PSA to Gol

Medicinal Herb Briefs: *Withania somnifera*

Ref: TFORD/MHB/003 **Date:** 26 May 2020

About this document: This document summarizes information available on medicinal herb candidates for COVID19. One Medicinal Herb Brief document covers one candidate at a time.

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1. Summary Information on *Withania somnifera*

Information About the Herb for Reported Indication(s)	
Common Name	Indian Ginseng. Indian Winter cherry
Botanical Name (Family)	<i>Withania somnifera</i> (Ashwagandha) Solanaceae
Type of Plant/Source of Herbal Ingredients	Perineal Shrub Source – Roots http://www.ayurveda.hu/api/API-Vol-1.pdf
TKDL Information	20 mentions for this Herb on TKDL
Indian Pharmacopeia Information	Herbal Drug Monograph available in Indian Pharmacopeia 2018
Reported Pharmacological Effects	Adaptogen/Anti-stress, Diuretic, Sedative, Anti-inflammatory, Anti-cancer, Anxiolytic, Anti-arthritis https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3252722/pdf/AJT085S-0208.pdf https://www.sciencedirect.com/topics/nursing-and-health-professions/withania-somnifera
Reported Therapeutic Target(s)	Glucocorticoid Receptor (GR), JNK, p38MAPK, NFκB https://www.sciencedirect.com/science/article/pii/S0968089619302329 https://www.frontiersin.org/articles/10.3389/fpls.2015.01031/full
Reported Mode of Action	Modulation of Acetylcholinesterase and Butyrylcholinesterase activity, inhibition of Calcium ion influx, blockade of GABA receptors, modulation of 5-HT1 and 5-HT2 receptors, regeneration of neuritis http://www.phcogrev.com/article/2007/1/1-13
Herb is reported to be beneficial for which conditions?	<ul style="list-style-type: none"> • Anti-stress agent to improve reaction time, treatment of Bronchitis, Dyspepsia, Impotency, Scabies and Ulcers • Also used as a dietary supplement and general tonic increase energy, improve overall health and prevent disease in athletes and the elderly The Ayurvedic pharmacopoeia of India. Part I, Vol. I, https://www.ncbi.nlm.nih.gov/pubmed/10956379 http://cms.herbalgram.org/herbalgram/issue99/hg99-herbprofile.html
Is the herb or its extract form used for clinical purposes?	Yes – Both
Prescribed Dose	3-6 g of the drug in powder form

	Orally as an Anti-stress agent: 250 mg twice daily The Ayurvedic pharmacopoeia of India. Part I, Vol. I, https://www.who.int/medicines/areas/traditional/SelectMonoVol4.pdf
Route of Administration	Oral
Safety Profile (dose range in which it has been tested to be safe in humans)	Data not available
Adverse events/Side effects reported at the current prescribed dose	Nausea, vomiting and diarrhoea. Abortifacient properties have been reported for Ashwagandha. Withania somnifera. In: American herbal pharmacopeia
Reported Drug-Herb interactions	The crude drug may potentiate the effects of Barbiturates and reduce the effects of Diazepam and Clonazepam. Caution prescribed with Anti-diabetes drugs, Anti-hypertensive drugs, Immunosuppressants, Sedative medications. WHO Monograph on selected medicinal plants Withaniasomnifera. In: American herbal pharmacopeia
Link to Datasheet	Data not available
Regions where Herb is found	Local Distribution: Maharashtra, Karnataka, Kerala, Tamil Nadu, Assam, Gujarat, Madhya Pradesh, Rajasthan Global Distribution: Mediterranean, Canary Islands Cape of Good Hope https://indiabiodiversity.org/species/show/231468 http://www.ayurveda.hu/api/API-Vol-1.pdf
Is the Herb or Extract being sold in India?	Yes – Both
Indian Manufacturer(s)	Herbochem, Arjuna natural, All Season Herbs
International Manufacturer(s)	Data not available
Cost of the Herb and Extract products in India	100-1000/- per kg based on root powder/ extract
Information About the Major Bioactive for Reported Indication(s)	
NOTE – THIS INFORMATION IS ONLY FOR THE MAJOR BIOACTIVE IN THE HERB	
What is the Major Bioactive in the Herb?	No Major Bioactives reported Constituents reported -Steroidal lactones collectively known as “Withanolides” include: Withaferin A, 27-Deoxywithaferin A, Withanolide D, Withanosides I–XI, and Withasomniferols A–C, Alkaloids, saponins including Sitoindosides VII–X http://www.researchtrends.net/tia/article_pdf.asp?in=0&vn=12&tid=24&aid=5710
Is the Major Bioactive, in isolated form used for clinical purposes?	Data not available
Drug Bank ID	Data not available
Reported Pharmacological effects	Data not available
Reported Therapeutic Target	Data not available
Reported Mode of Action	Data not available
Bioactive is reported to be beneficial for which conditions?	Data not available
Prescribed Dose	Data not available
Route of Administration	Data not available
Safety Profile (dose range in which it has been tested to be safe)	Data not available

in humans)	
Adverse events/Side effects reported at the current prescribed dose	Data not available
Reported Drug-Bioactive interactions	Data not available
Link to Datasheet for Bioactive	Data not available
Is the Bioactive being sold in India?	Data not available
Indian Manufacturer(s)	Data not available
International Manufacturer(s)	Data not available
Cost of the Bioactive in India	Data not available
Information About the Candidate for COVID-19	
Repurposing Claim	Prophylaxis; New Indication (COVID-19) + New Dose (not confirmed)
Rationale for Repurposing for COVID19/MoA? –	<ul style="list-style-type: none"> Anti-viral activity: Reported for a formulation made using <i>W.somnifera</i> against Chikungunya induced arthralgia in a mouse model - effective in reducing viral load, morbidity and arthralgia. The herb is also a potent inducer of Nitric Oxide, which has been shown to have both anti-viral (Infectious Bursal Disease Virus) in-vitro and protective effects against viral infections. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5871050/ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5759882/ https://www.ncbi.nlm.nih.gov/pubmed/12551750 A review article by an Ayurvedic research group suggest <i>W.somnifera</i> could be considered for evaluation as a prophylactic and add on therapy for COVID-19 https://www.liebertpub.com/doi/10.1089/acm.2020.0129
Proposed use as Primary or Adjuvant?	Primary
Pre-Clinical Data available for COVID-19	No published data. A pre-print article based on molecular docking studies show that Withanone, a constituent of <i>W.somnifera</i> docks in the binding interface of AEC2-RBD complex. Authors report that Withanone significantly decreased electrostatic component of binding free energies of ACE2-RBD complex and that such a interruption of electrostatic interactions between the RBD and ACE2 would block or weaken SARS-Cov-2 entry and its subsequent infectivity. https://orcid.org/0000-0001-8509-0882
Status of Clinical Trials	1 ongoing trial in India
Trial Details	See details below

Trial ID/Link	Type of Trial	Form used	No. of patients	Drug Combination/Dose/ Stage of Disease	Primary and Secondary Measures	Has data from the trial been published?
CTRI/20/20/05/025069 (Prophylaxis)	Interventional Single arm	Herb	1324	Ashwagandha Dose: 500 mg two times before meal with water for 1 month Total duration of therapy is 1 month	Primary: Incidence of COVID 19 positive cases (as confirmed by hospital by standard investigation (real-time polymerase chain reaction test) among Ayurveda users Secondary: 1) Incidence of severe COVID 19	No

					<p>positive cases among Ayurveda users</p> <p>2) Incidence of mortality due to COVID 19 among Ayurveda users.</p> <p>3) Incidence of any other ailment like cough, fever, sore throat etc during this study</p> <p>4) Change in appetite, bowel habit, sleep among the users.</p> <p>5) ADR/AE due to use of any particular Ayurveda advocacies</p>	
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Key Data from Clinical Trials	Data not available	
IP Status	Status/ Molecule	<i>Withania Somnifera</i>
	Approved and Active applications	<p>236009 Title: A kit containing a vaccine and an immunological adjuvant Assignee: Serum Institute Of India Ltd. Filing date: 08/12/2003 Grant date: 15/09/2009 Expected Expiry date: 08/12/2023</p>
	Pending applications	<p>201731038204 Title: A herbal formulation for treating disease and complications caused by the malaria parasite Inventor: Dropadi Devi Filing date:27/10/2017 Status: Published: 03/05/2019 3280/CHE/2013 Title: Pharmaceutical formulation exhibiting antiviral activity Assignee: Sri Ramachandra Unviersity Filing date:23/07/2013 Status: Published: 30/01/2015 3943/MUM/2014 Title: An herbal composition Inventor: Wankhedkar Mahalaxmi Kamlakar Filing date: 09/14/2014 Status: Published: 10/06/2016 201841032445 (No link on WIPO site) Title: An anti-tumour and antibacterial formulation and a method there of Assignee: Mahatma Gandhi University Filing Date: 30/08/2018 Status: Published: 06/03/2020 201611025617 Title: A novel synergistic medicinal composition for antioxidant and treatment for anti-stress related disorder Inventor: Dr. Sandhya Singh Filing Date: 27/07/2016 Status: Published: 09/08/2016 201641016138 Title: Endosymbiotic pathogenic archaea in chronic diseases and treatment with natural antioxidant antibiotics derived from crude plants extracts Assignee: Ravikumar Kurup, Parameswara AchuthaKurup Filing Date: 09/05/2016 Status: Published: 10/11/2017 201641001114 Title: Novel dietary supplementary immune system stimulator formulation and method of preparation thereof Inventor: Dr. Abdulsubahan Abdul Rahman</p>

	<p>Filing Date: 12/01/2016 Status: Published: 14/07/2017 201841030180 (No link on WIPO site) Title: Poly-herbal composition and a process for its preparation Assignee: SRM Institute of Science & Technology Filing Date: 10/08/2018 Status: Published: 14/02/2020 201821004538 Title: Stable synergistic ayurvedic composition for higher energy and alertness Assignee: Triquetrus Essentials Pvt. Ltd. Filing Date: 07/02/2018 Status: Published: 03/01/2020 201941004860 Title: Poly-herbal formulation Assignee: SRM Institute of Science & Technology Filing Date: 07/02/2019 Status: Published: 15/02/2019, Request for Examination Date -07/02/2019 201841039628 (No link on WIPO site) Title: <i>WithaniaSomnifera</i> composition, method of preparation and use thereof Assignee: Laila Nutraceuticals Filing Date: 19/10/2018 Status: Published 24/04/2020 201741013035 Title: Composition for the treatment of diabetes mellitus type 2 Inventor: Madheswaran Filing Date: 11/04/2017 Status: Published: 19/10/2018</p>
Other references	<ul style="list-style-type: none"> • http://cms.herbalgram.org/herbalgram/issue99/hg99-herbprofile.html?ts=1588999095&signature=94fa1f0c0884d7d389e1f9d7c53f6bba (American Botanical Council database)

2. Background information

About TFORD-COVID19

The Principal Scientific Advisor to the GoI, Dr K VijayRaghavan, has constituted a S&T Core Group on COVID19. Under the aegis of the S&T Core Group on COVID19, a Task Force has been constituted focused on Repurposing of Drugs for COVID19 (in short “TFORD-COVID19”). The Task Force is being coordinated by Dr V Premnath, Head, NCL Innovations at CSIR-NCL and Director, Venture Center and Dr Anurag Agarwal, Director, CSIR-IGIB. The Nerve Center for the Coordination is located be at Venture Center, Pune (located in the campus of CSIR-NCL).

Credits

Editors: Dr. Priya Nagaraj & Dr Smita Kale; Contributors: Dr. Priya Nagaraj, Dr. Vidula Walimbe, Dr. Smita Kale, Dr. Kirtee Wani, Dr. Tejas Shah, Dr. Swati Joshi, Dr. Manisha Premnath, Dr. Premnath V; Information also contributed by Dr Gopakumar Nair, GNAS and GnanLex.

About Advisory Group

The Nerve Center at TFORD-COVID19 has constituted an inter-disciplinary Advisory Group. This Advisory Group reviews the information compiled by the Nerve Center, provides suggestions on data, information sources, organization of data etc. while also providing inputs to refine the analysis and create a structured information base to support decision-making. The Advisory Group also provides expert input and opinions on certain selected points where experience-based inputs are needed. The members of the Advisory Group for each Discussion Paper are listed at <https://nclinnovations.org/covid19/teams/>.

Disclaimer

This Medicinal Herbal Brief is a compilation of information available openly with no opinions or judgments or recommendations. This document is meant to compile high-quality information that can form the basis for informed discussion and decision-making. It is not meant to reflect the Government’s position or that of any specific organization or individual. This information should also not be interpreted as guidance for clinical case management.