



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: *Andrographis paniculata*

Ref: TFORD/MHB/005 **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 *Andrographis paniculata*

Information About the Herb for Reported Indication(s)	
Common Name	Green Chireta, Kalmegh
Botanical Name (Family)	<i>Andrographis paniculata</i> , (Fabaceae)
Type of Plant/Source of Herbal Ingredients	Annual Herbaceous Plant Source – Aerial parts (dried) https://apps.who.int/iris/bitstream/handle/10665/42052/9241545372.pdf?sequence=2
TKDL Information	No mention for this Herb in TKDL. 7 mentions for its Bioactive - Andrographolide
Indian Pharmacopeia Information	Herbal Drug Monograph available in Indian Pharmacopeia 2018
Reported Pharmacological Effects	Anti-bacterial, Anti-HIV, immunostimulatory, Anti-pyretic, Anti-diarrhoeal, Anti-inflammatory, Anti-malarial, Anti-venom, Anti-hepatotoxic WHO medicinal plants: Volume 2
Reported Therapeutic Target(s)	Targets reported for Bioactive (for details please see Bioactive Section)
Reported Mode of Action	<ul style="list-style-type: none"> Anti-HIV activity: Interferes with viral adsorption, and inhibits viral replication Immunostimulatory activity: Increases proliferation of lymphocytes and production of IL-2 Anti-inflammatory activity: Inhibits LPS-stimulated NO production in a concentration-dependent manner https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3619690/#B75
Herb is reported to be beneficial for which conditions?	Prophylaxis and symptomatic treatment of Upper Respiratory Infections, such as the Common Cold and Uncomplicated Sinusitis, Bronchitis and Pharyngotonsillitis, Lower Urinary Tract Infections, Acute Diarrhoea, Bacillary Dysentery, Carbuncles, Colitis, Dyspepsia, Fevers, Hepatitis, Malaria, Mouth Ulcers, Sores, Tuberculosis and Venomous snake bites WHO medicinal plants: Volume 2
Is the herb or its extract form used for	Yes- Both

clinical purposes?	
Prescribed Dose	<ul style="list-style-type: none"> • Pyrexia: a decoction from 3 g crude drug, twice daily • Common cold: 1.5–3.0 g powdered crude drug three times daily, after meals and at bedtime • Diarrhea: a decoction from 3–9 g crude drug as a single dose as needed or two tablets of 500 mg four times daily, after meals and at bedtime WHO medicinal plants: Volume 2
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	Large oral doses of the <i>Andrographis</i> may cause gastric discomfort, vomiting and loss of appetite (due to bitter taste of Andrographolide). Anaphylactic reactions may occur if the crude drug extract is injected. Two cases of urticaria have been reported. WHO medicinal plants: Volume 2
Reported Drug-Herb interactions	Extracts of <i>Andrographis</i> may have a synergistic effect with isoniazid
Link to Datasheet	https://www.tga.gov.au/sites/default/files/safety-review-andrographis.pdf
Is the Herb or Extract being sold in India?	Yes - Both
Indian Manufacturer(s)	All-Seasons Herbs, Himalayan Herbaria, Herbal world and others
International Manufacturer(s)	Data not available
Cost of the Herb and Extract products in India	High quality extract - Rs. 1200-1600/kg
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?	Andrographolide
Is the Major Bioactive, in isolated form used for clinical purposes?	Yes
Drug Bank ID	DB05767 https://www.drugbank.ca/drugs/DB05767
Reported Pharmacological effects	Neuroprotective, Immunostimulatory, Anti-oxidant, Anti-cancer, Anti-inflammatory, Anti-microbial, Anti-hepatotoxic https://doi.org/10.15406/ijcam.2018.11.00425
Reported Therapeutic Target	Tumor necrosis factor , Interleukin-1 beta , Interleukin-6 , Nuclear factor NF-kappa-B p100 subunit , Nuclear factor NF-kappa-B p105 subunit
Reported Mode of Action	Andrographolide acts on multiple cellular targets in inflammatory signal transduction pathways, suppressing expression of pro-inflammatory cytokines such as TNF- α , IL-1 β and IL-6. It also inhibits NF-kB activation https://www.drugbank.ca/drugs/DB05767
Bioactive is reported to be beneficial for which conditions?	<ul style="list-style-type: none"> • Viral Infections - Used in the treatment of dengue, chikungunya, swine flu, influenza, or any other suspected viral fever • Upper Respiratory Tract Infections – Used in the treatment of various upper respiratory tract infections such as sinusitis, tonsillitis, etc. https://www.ncbi.nlm.nih.gov/pubmed/14750201 https://www.ncbi.nlm.nih.gov/pubmed/12809357
Prescribed Dose	<ul style="list-style-type: none"> • Usual daily dose of Andrographolides for common cold, sinusitis, and tonsillitis is 60 mg, but doses up to 1,200 mg have been reported

	<ul style="list-style-type: none"> Familial Mediterranean Fever- 48 mg daily A clinical trial in children with upper respiratory tract infection reported use of andrographolide 30 mg daily for 10 days https://www.ncbi.nlm.nih.gov/pubmed/14750201 https://www.ncbi.nlm.nih.gov/pubmed/12809357 https://www.ncbi.nlm.nih.gov/pubmed/1797953
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	Large oral doses may cause gastric discomfort, vomiting and loss of appetite. Urticaria in few cases reported https://apps.who.int/iris/bitstream/handle/10665/42052/9241545372.pdf?sequence=2&hx0026;ua=1 https://www.sciencedirect.com/science/article/pii/S0944711397800025?via%3Dihub
Reported Drug-Bioactive interactions	Over 400 drug interactions listed on DrugBank CYP3A4 inhibition https://www.drugbank.ca/drugs/DB05767
Link to Datasheet for Bioactive	Data not available
Regions where Herb is found	Local Distribution: Assam, Andhra Pradesh, Bihar, West Bengal, Jharkand, Gujarat, Goa, Delhi, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Orissa, Rajasthan, Tamil Nadu, Uttar Pradesh http://www.biodiversityofindia.org/index.php?title=Andrographis_paniculata#tab=Habitat_and_Geographical_Spread
Is the Bioactive being sold in India?	Yes
Indian Manufacturer(s)	More than 20 manufactures
International Manufacturer(s)	Jiangxi Qingfeng Pharmaceutical Company (Xiyanping injection)
Cost of the Bioactive in India	Rs. 200/gm (Andrographolide powder)
Information About the Candidate for COVID-19	
Repurposing Claim	Data not available
Rationale for Repurposing for COVID19/MoA? –	<p><i>A.paniculata</i>:</p> <ul style="list-style-type: none"> Anti-viral activity against Epstein-Barr-Virus, Simian- Retro-Virus, Dengue in pre-clinical studies (in-vitro and in-vivo) https://www.sciencedirect.com/science/article/pii/S1978301916300766#bbib3 https://www.jstage.jst.go.jp/article/bpb/31/11/31_11_2018/article http://www.ayujournal.org/article.asp?issn=0974-8520;year=2018;volume=39;issue=2;spage=87;epage=91;aulast=Ramalingam A review article by an Ayurvedic research group suggest <i>A.paniculata</i> could be considered for evaluation as a prophylactic therapy for COVID-19 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7177084/ <p>Andrographolide:</p> <ul style="list-style-type: none"> Anti-viral activity against Herpes Simplex Virus-1, H1N1 and HIV in pre-clinical studies (in-vitro and in-vivo) https://www.jstage.jst.go.jp/article/bpb/32/8/32_8_1385/article https://www.jstage.jst.go.jp/article/bpb/31/11/31_11_2018/article https://www.sciencedirect.com/science/article/pii/S0223523412004564?via%3Dihub https://onlinelibrary.wiley.com/doi/abs/10.1002/ptr.1765 Immunostimulatory activity reported in animal models of cancer and autoimmune diseases. Andrographolide enhances Natural Killer activity,

	<p>increases secretion of IL-2 and IFN-g by T cells and inhibits tumor growth in cancer models and interferes with maturation of dendritic cells, induces antigen specific tolerance and prevents detrimental autoimmune responses in autoimmune disease models.</p> <ul style="list-style-type: none"> • https://www.nature.com/articles/aps2009205
Proposed use as Primary or Adjuvant?	Data not available
Pre-Clinical Data available for COVID-19	<p>Docking studies - Andrographolide docks against the inhibitor region of the main protease of SARS-CoV-2 (Mpro) with a docking score of - 3.094357 Kcal/mol. Studies were done using crystal structure of SARS-CoV-2 main protease.</p> <p>https://www.tandfonline.com/doi/full/10.1080/07391102.2020.1760136</p>
Status of Clinical Trials	No ongoing trials
Trial Details	Data not available
Key Data from Clinical Trials	Data not available
IP Status	<p>Status/ Molecule <i>Andrographis paniculata</i></p> <p>Approved and Active applications</p> <p>309835 Title: Compositions comprising Andrographis Paniculata and Ginkgo Biloba extracts complexed with phospholipids Assignee: Indena S.P.A. Priority Date: 12/01/2010 Grant date: 25/03/2019 Expected Expiry Date: 03/01/2031</p> <p>239346 Title: A synergistic antipyretic composition and a process for the preparation thereof Assignee: Council of Scientific & Industrial Research (National Botanical Research Institute, Lucknow) Filing date: 05/06/2006 Grant date: 16/03/2010 Expected Expiry Date: 21/12/2024</p> <p>Pending applications</p> <p>201741015402 Title: Synergistic herbal extract formulation for the management of diabetes mellitus and detoxification Assignee: ArulsamyelphinePrabakar Filing date: 02/05/2017 Status: Published: 09/11/2018</p> <p>201711006973 Title: Devolvement of microencapsulated formulation based on andrographolide and method of preparation thereof Assignee: Indian Council Of Agricultural Research Filing date: 28/02/2017 Status: Published: 31/08/2018</p> <p>201711005894 Title: An antipyretic herbal composition Assignee: Jitendra Awasthi Filing date: 20/02/2017 Status: Published: 24/08/2018</p> <p>201641016724 Title: Design and characterization of nanoparticles containing Andrographis Paniculata for colorectal cancer Assignee: TimmakonduNarasimman , Arumugam Sumathi, Lourdu Mary Filing date: 13/05/2016 Status: Published: 17/11/2017</p> <p>201641009857 Title: A composition comprising andrographispaniculata, and theobroma cocoa and uses thereof Assignee: ITC Limited</p>

	<p>Filing date:21/03/2016 Status: Published: 22/09/2017 201641004921 Title: Composition comprising Andrographis Paniculata extract, and VitisVinifera L, extract, and uses thereof Assignee: ITC Life Sciences & Technology Centre Filing date: 11/02/2016 Status: Publication date: 18/08/2017 411/MUM/2014 Title: Novel capsule formulation for vishmajvara Assignee:Dr. Maria Carina Cordeiro Filing date: 06/02/2014 Status: Published: 27/11/2015 1252/MUMNP/2006 Title: Crude extracts from Andrographis Paniculata Assignee: Hutchison Medipharma Enterprises Limited Priority date: 28/04/2004 Status: Published 07/09/2007 2687/CHE/2011 Title: Method of inducing the production of andrographolide from andrographispaniculata and composite media compositions thereof Assignee: S.D College Filing date: 04/08/2011 Status: Published: 21/06/2013 208/KOL/2013 Title: A herbal composition for treatment of malaria Inventor: Pandey, Rajmangal Filing date: 25/02/2013 Status: Published: 27/02/2015 808/MUM/2013 Title: Herbal composition for the treatment of herpes Inventor:Mehra, Apurve Filing date: 15/03/2013 Status: Published: 20/01/2015 978/DEL/1999 Title: Unani composition Jigrina for the treatment of viral hepatitis and jaundice Assignee: Hakim Abdul Hameed Filing date: 15/07/1999 Status: Published: 31/08/2016 1772/CHE/2011 Title: Compositions and methods for the cure of HIV/AIDS Inventor: Rajesh Radhakrishnan Filing date: 25/05/2011 Status: Published: 30/11/2012 1517/MUM/2012 Title: Novel anti-HIV Herbal composition, method of preparation of the same and use thereof Inventor: Dr. Manish A. Rachchh Filing date: 18/05/2012 Status: Published: 16/05/2014 2645/DEL/2005 Title: Herbo-mineral compound formulation for the management of maturity onset diabetes mellitus Inventor:ShubhashChander Sehgal Filing date: 04/10/2005 Publication date: 02/10/2009 Status: In Order of Grant (NBA Approval Received) 3/DEL/2010 (No link on WIPO site) Title: A herbal composition as hepatoprotective and treatment for liver disorders Assignee: Himalaya Global Holdings Ltd. Date of Filing: 01/01/2010 Status: Published: 08/07/2011</p>
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	<p>Expired or Lapsed application or status not known</p> <p>1717/KOLNP/2010 Title: Andrographis paniculata extract Assignee: Hutchison Medipharma Enterprises Limited Priority Date: 02/11/2007 Publication date: 27/08/2010 Status: Abandoned</p> <p>243944 Title: A medicinal composition useful in treatment of HIV/AIDS Inventor: Banarsi Lal Dua Filing date: 22/03/2004 Grant date: 11/11/2010 Status: Patent has Ceased on: 11/02/2011</p> <p>400/CHE/2004 Title: Novel plant extracts having anti hepatitis b activity and a process for their preparation Assignee: University of Madras Filing date: 30/04/2004 Publication date: 09/03/2007 Status: Abandoned</p> <p>1515/MUM/2012 Title: Novel cardioprotective herbal composition, method of preparation of the same and use thereof Inventor: Dr. Manish A. Rachchh Filing date: 18/05/2012 Publication date: 16/05/2014 Status: Abandoned</p> <p>237192 Title: Herbal composition for treatment of diabetes Inventor: Babulal Bhawarlal Jain Filing date: 13/06/2006 Grant date: 09/12/2009 Status: Patent has Ceased on 13/06/2014</p> <p>237191 Title: Herbal composition for treatment of psoriasis</p>
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	<p>Inventor: Babulal Bhawarlal Jain Filing date: 13/06/2006 Grant date: 09/12/2009 Status: Patent has Ceased on 13/06/2014 220806 Title: A herbal preparation and a process for the prevention of liver cirrhosis of varying etiology Inventor: Ravi Patodia Filing date: 18/06/2002 Grant date: 05/06/2008 Status: Patent Ceased as of 11.10.2008 1565/DEL/2004 Title: A novel herbal composition useful for treatment of hepatitis & as dietary supplement of hepatitis patient Inventor: Narendra Kumar Awasthy Filing date: 23/08/2004 Publication date: 02/02/2007 Status: Abandoned</p>
Other references	<ul style="list-style-type: none"> ▪ https://medcraveonline.com/JLPRR/JLPRR-07-00224.pdf ▪ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7177084/

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

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