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 GoI

Medicinal Herb Briefs: *Zingiber officinale*

Ref: TFORD/MHB/004	**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 *Zingiber officinale*

Information About the Herb for Reported Indication(s)	
Common Name	Ginger
Botanical Name (Family)	*Zingiber officinale* Roscoe (Zingiberaceae)
Type of Plant/Source of Herbal Ingredients	Perineal Herb Source – Rhiozomes (fresh and dried) https://apps.who.int/iris/bitstream/handle/10665/42052/9241545178.pdf?sequence=1
TKDL Information	245 mentions for this Herb in TKDL
Indian Pharmacopeia Information	Herbal Drug Monograph available in Indian Pharmacopeia 2018
Reported Pharmacological Effects	Immuno-modulatory, Anti-tumorigenic, Anti-inflammatory, Anti-apoptotic, Anti-hyperglycemic, Anti-lipidemic and Anti-emetic actions https://doi.org/10.1016/j.fct.2007.09.085
Reported Therapeutic Target(s)	Targets NFκB, MAPK, JNK, ERK1/2 mediated signalling pathways leading to pro-inflammatory cytokine release (PGE-2, TNF-alpha, and IL-1beta) https://www.ncbi.nlm.nih.gov/pubmed/19233241 https://www.ncbi.nlm.nih.gov/pubmed/19061005
Reported Mode of Action	Anti-inflammatory activity: *Z.officinale* suppresses prostaglandin synthesis through inhibition of COX -1 and COX-2. It also suppresses leukotriene biosynthesis by inhibiting 5-lipoxygenase. It inhibits the induction of several genes involved in the inflammatory response including genes encoding cytokines, chemokines, and the inducible enzyme COX-2. Also reported that it inhibits macrophage and neutrophils activation as well as negatively affecting monocyte and leukocyte migration. https://www.liebertpub.com/doi/abs/10.1089/jmf.2005.8.125 https://www.ncbi.nlm.nih.gov/pubmed/29253614 https://www.ncbi.nlm.nih.gov/pubmed/11553371
Herb is reported to be beneficial for which conditions?	• Prophylaxis of nausea and vomiting associated with motion sickness, postoperative nausea, pernicious vomiting in pregnancy, and sea sickness. • Treatment of Dyspepsia, Flatulence, Colic, Vomiting, Diarrhea, Spasms, and

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	other stomach complaints. Powdered ginger is further employed in the treatment of colds and flu, to stimulate the appetite, as a narcotic antagonist, and as an anti-inflammatory agent in the treatment of migraine headache and rheumatic and muscular disorders World Health Organization. 1999. 'Rhizoma Zingiberis.' *WHO Monographs on Selected Medicinal Plants,* Vol. 1.
Is the herb or its extract form used for clinical purposes?	Yes – Both
Prescribed Dose	• 2-3 ml of the drug in juice form with honey • For motion sickness in adults and children more than 6 years: 0.5 g, 2–4 times daily. Dyspepsia, 2–4g daily, as powdered plant material or extracts http://www.ayurveda.hu/api/API-Vol-2.pdf World Health Organization. 1999. 'Rhizoma Zingiberis.' *WHO Monographs on Selected Medicinal Plants,* Vol. 1.
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	Ginger is listed on the U. S. FDA's GRAS (generally recognized as safe) list The British Herbal Compendium documents no adverse effects of ginger https://www.fda.gov/food/food-additives-petitions/food-additive-status-list https://bhma.info/british-herbal-compendium-vol-1/
Reported Drug-Herb interactions	Few ginger–drug interactions have been reported in the literature • Ginger does not interact with the anti-coagulant drug Warfarin • Ginger and Nifedipine have a synergistic effect on anti-platelet aggregation https://www.ncbi.nlm.nih.gov/pubmed/11091007 https://www.ncbi.nlm.nih.gov/pubmed/16883626
Link to Datasheet	Data not available
Regions where Herb is found	Local Distribution: Andhra Pradesh, Andaman & Nicobar, Arunachal Pradesh, Assam, Bihar, Chhattisgarh, Gujarat, Himachal Pradesh, Jammu & Kashmir, Karnataka, Kerala, Madhya Pradesh, Maharashtra, Manipur, Meghalaya, Mizoram, Nagaland, Orrisa Global Distribution: China, Nigeria, Indonesia, Bangladesh, Thailand, Philippines, Jamaica http://agritech.tnau.ac.in/banking/PDF/Ginger.pdf
Is the Herb or Extract being sold in India?	Yes – Both
Indian Manufacturer(s)	Herb- Fresh rhizomes available in local markets. Extract- Synthite Industries, Kancor, Alchem International, Arjuna Naturals
International Manufacturer(s)	Ransom Naturals (UK) https://www.pharmacompass.com/manufacturers-suppliers-exporters/zingiber-officinale-rhizoma
Cost of the Herb and Extract products in India	High quality extract – Rs.850 and above for 1kg
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 Bioactive reported Constituents reported - Fresh Ginger volatile oil contains Cineole Zingiberol, and Sesquiterpene like Zingiberene, Bisobolene and Sesqui phellandrene, Gingerosol in the oleo-resin http://www.ayurveda.hu/api/API-Vol-2.pdf
Is the Major	Not Applicable

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Bioactive, in isolated form used for clinical purposes?	
Drug Bank ID	Not Applicable
Reported Pharmacological effects	Not Applicable
Reported Therapeutic Target	Not Applicable
Reported Mode of Action	Not Applicable
Bioactive is reported to be beneficial for which conditions?	Not Applicable
Prescribed Dose	Not Applicable
Route of Administration	Not Applicable
Safety Profile (dose range in which it has been tested to be safe in humans)	Not Applicable
Adverse events/Side effects reported at the current prescribed dose	Not Applicable
Reported Drug-Bioactive interactions	Not Applicable
Link to Datasheet for Bioactive	Not Applicable
Is the Bioactive being sold in India?	Not Applicable
Indian Manufacturer(s)	Not Applicable
International Manufacturer(s)	Not Applicable
Cost of the Bioactive in India	Not Applicable
Information About the Candidate for COVID-19	
Repurposing Claim	Treatment; New Indication + New dose (not confirmed)
Rationale for Repurposing for COVID19/MoA? –	• Anti-inflammatory activity: Z.officinale inhibits various signaling pathways including NF-kB mediated pro-inflammatory cytokine expression as demonstrated in-vitro and in-vivo studies. It is also reported to be a natural immune booster. https://www.tandfonline.com/doi/full/10.1080/10408398.2011.633249?needAccess=true https://www.ncbi.nlm.nih.gov/pubmed/19061005 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2664283/ • Anti-viral activity: Reported for extracts against Feline Calcivirus, Chikungnya, Human Respiratory Syncytial Virus, Avian influenza virus H9N2 in in-vitro studies. https://www.sciencedirect.com/science/article/abs/pii/S0378874112007404 https://www.ncbi.nlm.nih.gov/pubmed/17296159 https://doi.org/10.4315/0362-028X.JFP-15-593 https://link.springer.com/article/10.1007/s13337-020-00584-0 https://www.ncbi.nlm.nih.gov/pubmed/29039335
Proposed use as Primary or Adjuvant?	Primary and Adjuvant
Pre-Clinical Data	2 docking studies (1 published, 1 in review) shows that 6-Gingerol (bioactive

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available for COVID-19	phenolic phytocompound found in fresh ginger rhizome) binds to several SARS-CoV-2 targets –Main protease (Study 1: -15.7591 KJ/mol; Study 2: Binding energy ΔG -5.38) viral RNA binding protein and Spike glycoprotein which are essential for viral entry and replication. https://www.researchgate.net/publication/340790291 https://www.preprints.org/manuscript/202003.0450/v1
Status of Clinical Trials	2 trials ongoing in India (with formulations containing *Z.officinale* extract)
Trial Details	See the table 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/2020/04/024883 (Treatment)	Interventional,Randomised controlled, Single blinded multicentre , comparative study	Herb Extract	112	ZingiVir-H tablet Dose: 500 mg each consumed once in 3 hours ±1 hour between 6 AM and 9 PM in a given day for a minimum duration of 10 days to Maximum 15 days as per the clinical conditions and disease outcome Stage: Data not available	Primary: The Odds of Ratio for Improvement on a 7-point Ordinal Scale on Day 15 [Time Frame: Day 15 from the day of study inclusion] Secondary: To find out the anti pyretic activity of ZingiVir H	No
CTRI/2020/05/024967 (Treatment)	Interventional, Single arm trial	Herb Extract	30	MyVir tablet Dose: Twice daily after meal for 21days Stage: Data not available	Primary: Improvement in Immunity and anti viral properties in patients who are assessed daily for symptoms which include cough, fever with or without chills and difficulty in breathing for the period they are in quarantine. Secondary: Improvement in the clinical variables including total Leukocyte Count Absolute Leukocyte Count, IL-6 and Hs CRP baseline to end of the quarantine period i.e. 21 days	No

Key Data from Clinical Trials	Data not available	
IP Status	Status/ Molecule	*Zingiber officinale*
	Approved and Active applications	227674 (No link on WIPO site) Title: Herbal compositions for treatment of aids and preparation thereof Inventor: Ayare Shambabu Devappa Filing Date: 14/07/2003 Grant date: 13/02/2009 Expected Expiry Date: 14/07/2023 225350

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Expired or Lapsed application	234888 Title: A herbal composition having anti allergic properties and a process for the preparation thereof Assignee: Natural Remedies Private Ltd Filing Date: 28/02/2000 Grant date: 17/07/2009 Status: Patent Ceased on 02/03/2015 194805 (No link on WIPO site) Title: A process for the preparation of a synergistic pharmaceutical formulation with boosted immunosuppression Assignee: Council of Scientific & Industrial Research

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(Regional Research Laboratory, Jammu)
Filing Date: 06/10/2000
Grant date: 22/03/2006
Status: Patent Ceased on 07/10/2019
242831
Title: An anti-microbial composition
Assignee: The Quigley Corporation
Priority Date: 06/02/2002
Grant date: 17/09/2010
Status: Patent Ceased on 20/12/2010
188/DEL/2004
Title: A herbo mineral preparation for general immunity and strengthening the body of children
Assignee: Central Council for Research in Ayurveda and Siddha
Filing Date: 11/02/2004
Publication date: 29/12/2006
Status: Patent application refused for grant
1249/MUM/2006
Title: Synergistic herbal anthelmintic composition
Assignee: Advanced Enzyme Technologies Limited
Filing Date: 07/08/2006
Published: 31/10/2008
Status: Patent Application Withdrawn u/s 11(B)(4)(i)
2736/DEL/2009
Title: A herbal composition for inflammatory disorders
Assignee: Himalaya Global Holdings Limited
Filing Date: 30/12/2009
Publication date: 08/07/2011
Status: Withdrawn/ Abandoned
2863/DELNP/2009
Title: Compositions and methods for treating infectious bronchits
Assignee: The Quigley Corporation
Priority Date: 14/12/2006
Publication date: 19/06/2009
Status: Withdrawn/ Abandoned
1568/MUM/2010
Title: A composition for treatment of osteoarthritis and other painful, inflammatory musculoskeletal disorders
Assignee: Enovate Biolife Private Limited
Filing Date: 18/05/2010
Publication date: 17/08/2012
Status: No updates on Indian patent site
22/DEL/2010 (No link on WIPO site)
Title: Herbal composition for diarrhoea
Assignee: Himalaya Global Holdings Ltd
Filing Date: 05/01/2010
Publication date: 08/07/2011
Status: No update on Indian patent site
2716/DEL/2011
Title: A novel ayurvedic formulation for the treatment of cough and other associated symptoms
Assignee: Akums Drugs & Pharmaceuticals Limited
Filing Date: 20/09/2011
Publication date: 22/03/2013
Status: Abandoned u/s section 21(1)
823/DEL/2011
Title: Ayurvedic formulation for the management of gout and related symptoms
Assignee: Akums Drugs & Pharmaceuticals Limited
Filing Date: 24/03/2011
Publication date: 19/10/2012
Status: Abandoned u/s section 21(1)
607/CHE/2012
Title: A nano-herbomineral composition and process of preparation thereof for treatment of allergic and bronchial

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	disorders Inventor: Dwibhashyam Venkata Sreeramamurty Filing Date: 20/02/2012 Published: 30/03/2012 Status: Abandoned 608/CHE/2012 Title: A herbal formulation and method of preparation thereof for treatment of thyroid and neurological disorders Inventor: Dwibhashyam Venkata Sreeramamurty Filing Date: 20/02/2012 Publication date: 30/03/2012 Status: Abandoned 1514/MUM/2012 Title: Novel immunostimulant herbal composition; method of preparation of the same and use thereof Assignee: Dr. Manish A. Rach Filing Date: 18/05/2012 Publication date: 03/01/2014 Status: Abandoned 4444/CHE/2015 Title: A novel formulation for anti inflammation containing curcumin and ginger Assignee: Plant Lipids Private Limited Filing Date: 25/08/2015 Publication date: 03/03/2017 Status: No Request for Examination Filed. Appears Abandoned 201611031146 Title: Production of ayurvedic preparations from hers for treatment of liver cancer Inventor: Arun Kumar Filing Date: 13/09/2016 Publication date: 03/03/2017 Status: No request for examination filed, appears Abandoned 201841012153 Title: A herbal composition, and implementations thereof Assignee: ITC Limited Filing Date: 30/03/2018 Publication Date: 04/10/2019 Status: Appears Abandoned
Other references	• https://www.ema.europa.eu/en/documents/herbal-monograph/draft-community-herbal-monograph-zingiberis-rhizoma_en.pdf • http://cms.herbalgram.org/expandedE/Gingerroot.html?ts=1589043328&signature=c32c758bd493d8dcf2a9827671207031

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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/ .

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