



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: *Artemisia annua*

**Ref:** TFORD/MHB/006 **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.

**Circulation restrictions:** Non-confidential. Open Access. If you use this information in any other document or communication, please credit is as "Medicinal Herbal Brief: *Artemisia annua*, Task Force on Repurposing of Drugs for COVID19, India, April 2020".

### 1. Summary Information on *Artemisia annua*

Information About the Herb for Reported Indication(s)	
Common Name	Qinhao, Sweet wormwood
Botanical Name (Family)	<i>Artemisia annua</i> (Asteraceae)
Type of Plant/Source of Herbal Ingredients	Annual Plant Source – Aerial parts and leaves (dried) <a href="https://www.who.int/medicines/publications/traditional/ArtemisiaMonograph.pdf">https://www.who.int/medicines/publications/traditional/ArtemisiaMonograph.pdf</a>
TKDL Information	No mentions for this Herb in TKDL
Indian Pharmacopeia Information	Herbal Drug Monograph available in Indian Pharmacopeia 2018
Reported Pharmacological Effects	Anti-malarial, Anti-pyretic, Anti-inflammatory, Anti-bacterial <a href="https://www.who.int/medicines/publications/traditional/ArtemisiaMonograph.pdf">https://www.who.int/medicines/publications/traditional/ArtemisiaMonograph.pdf</a>
Reported Therapeutic Target(s)	Targets reported for Bioactive (for details please see Bioactive Section)
Reported Mode of Action	Key literature for <i>A.annua</i> are Chinese publications which could not be retrieved. Mode of action is described for the Bioactive Artemisinin.
Herb is reported to be beneficial for which conditions?	Malaria with chills and fever <a href="https://www.who.int/medicines/publications/traditional/ArtemisiaMonograph.pdf">Pharmacopoeia of The People's Republic of China: Volume I</a> <a href="https://www.who.int/medicines/publications/traditional/ArtemisiaMonograph.pdf">https://www.who.int/medicines/publications/traditional/ArtemisiaMonograph.pdf</a>
Is the herb or its extract form used for clinical purposes?	Yes – Both
Prescribed Dose	<ul style="list-style-type: none"> <li>Remove summer-heat, relieve consumptive fever, and treat malarial attacks.: 6–12 g, added to the decoction when it is nearly done</li> <li>Analgesic–antipyretic: 25–30 g dried herb boiled for less than 30 minutes to make a decoction: once per day, for 7 days</li> <li>Lupus erythematosus: use honey and the fine-ground powder of <i>A. annua</i> to make a pill: 36–54 g per day, for 2–3 months. <a href="https://www.who.int/medicines/publications/traditional/ArtemisiaMonograph.pdf">https://www.who.int/medicines/publications/traditional/ArtemisiaMonograph.pdf</a></li> </ul>
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	Abdominal pain and diarrhea, bradycardia,, flu-like symptoms and fever, low reticulocyte count, seizures, skin rash, nausea, vomiting, loss of appetite and hepatotoxicity <a href="https://www.medsafe.govt.nz/profs/class/Agendas/Agenda63/MCC63_72e_artemisiaannua.pdf">https://www.medsafe.govt.nz/profs/class/Agendas/Agenda63/MCC63_72e_artemisiaannua.pdf</a>
Reported Drug-Herb interactions	Data not available
Link to Datasheet	Data not available
Regions where Herb is found	Local Distribution: Kashmir, Uttar Pradesh, Himachal Pradesh, Uttarakhand Global Distribution: China, Kenya, Tanzania, Vietnam <a href="https://www.researchgate.net/publication/304353516_Cultivation_of_Artemisia_Artemisia_annua_Linn">https://www.researchgate.net/publication/304353516_Cultivation_of_Artemisia_Artemisia_annua_Linn</a>
Is the Herb or Extract being sold in India?	Yes – Both
Indian Manufacturer(s)	CSIR-CIMAP, IPCA <a href="http://thescitech.com/admin/includes/abstractpdf/2014-20-0152dccb2820050.pdf">http://thescitech.com/admin/includes/abstractpdf/2014-20-0152dccb2820050.pdf</a>
International Manufacturer(s)	Shaanxi Yi An Biological Technology, ArtemiLife, Several in China
Cost of the Herb and Extract products in India	Herb- Rs.25/kg for leaves but cost varies depending on the quality Extract- Data not available
<b>Information About the Major Bioactive for Reported Indication(s)</b> <b>NOTE – THIS INFORMATION IS ONLY FOR THE MAJOR BIOACTIVE IN THE HERB</b>	
What is the Major Bioactive in the Herb?	Artemisinin
Is the Major Bioactive, in isolated form used for clinical purposes?	Yes. But, due to poor solubility of Artemisinin, its semi-synthetic derivatives like Arthemether, Arteether (oil soluble) and Artesunate (water soluble) are most commonly used in formulations.
Drug Bank ID	DB13132 <a href="https://www.drugbank.ca/drugs/DB13132">https://www.drugbank.ca/drugs/DB13132</a>
Reported Pharmacological effects	Antimalarial, antibacterial, anticancer, antiviral <a href="https://www.drugbank.ca/drugs/DB13132">https://www.drugbank.ca/drugs/DB13132</a>
Reported Therapeutic Target	P-type ATPases <a href="https://www.ncbi.nlm.nih.gov/pubmed/12931192">https://www.ncbi.nlm.nih.gov/pubmed/12931192</a>
Reported Mode of Action	Anti-malarial activity: Artemisinin derivatives are compounds containing endoperoxide bridges which are essential for antimalarial activity. Artemisinin is believed to act via a two-step mechanism. It is first activated by intra-parasitic heme-iron which catalyzes the cleavage of this endoperoxide. A resulting free radical intermediate may then kill the parasite by alkylating one or more essential malarial protein(s). <a href="https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2778258/">https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2778258/</a>
Bioactive is reported to be beneficial for which conditions?	WHO recommends artemisinin-based combination therapies (ACTs) for the treatment of Uncomplicated Malaria <a href="https://www.who.int/malaria/areas/treatment/overview/en/">https://www.who.int/malaria/areas/treatment/overview/en/</a> Food and Drug Administration (FDA) approval was given for use of artemether-lumefantrine for treating uncomplicated malaria in the United States in April 2009. <a href="https://www.aappublications.org/content/30/6/30">https://www.aappublications.org/content/30/6/30</a>
Prescribed Dose	For Malaria - WHO recently approved riamet (Coartem), lumefantrine 120 mg combined with artemether 20 mg. Treatment includes administering 4 tablets initially, repeating dosage in 8 hours, and then taking twice daily for the next 2 days. The combination has proven to be effective, with reported cure rates up to 98%.

	For Arthritis: 150 mg twice daily of <i>Artemisia annua</i> extract has been evaluated for 12 weeks in osteoarthritis. <a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022268s019lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022268s019lbl.pdf</a>
Route of Administration	Oral
Safety Profile (dose range in which it has been tested to be safe in humans)	No adverse effects reported for dose upto 100mg/kg <a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022268s019lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022268s019lbl.pdf</a>
Adverse events/Side effects reported at the current prescribed dose	Nausea, vomiting, loss of appetite, and dizziness. Mild blood abnormalities have also been noted. Cardiac- QTc prolongation, bradycardia, hepatotoxicity <a href="https://www.ncbi.nlm.nih.gov/pubmed/10796551">https://www.ncbi.nlm.nih.gov/pubmed/10796551</a> <a href="https://www.ncbi.nlm.nih.gov/pubmed/25043597">https://www.ncbi.nlm.nih.gov/pubmed/25043597</a>
Reported Drug-Bioactive interactions	Concurrent administration of artemisinins with drugs prolonging Q-T like astemizole, antiarrhythmics, tricyclic antidepressants and phenothiazines may increase the risk of cardiac conduction. Artemisinin is metabolized in vitro by CYP2B6, CYP3A4, and CYP2A6. Since artemisinin induces CYP2C19 <a href="https://www.sciencedirect.com/topics/neuroscience/artemisinin">https://www.sciencedirect.com/topics/neuroscience/artemisinin</a>
Link to Datasheet for Bioactive	<a href="https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022268s019lbl.pdf">https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/022268s019lbl.pdf</a>
Is the Bioactive being sold in India?	Yes
Indian Manufacturer(s)	Cipla
International Manufacturer(s)	Sanofi, Wuhan Monad Medicine Tech Co.,LTD, Xieli pharmaceuticals Ltd, ArtemiLife™
Cost of the Bioactive in India	Artemisinin powder (Rs. 15000/kg), Artemisinin tablets- Rs.7000/90 tablets pack
<b>Information About the Candidate for COVID-19</b>	
Repurposing Claim	Data not available
Rationale for Repurposing for COVID19/MoA? –	<p><i>A.annua</i>:</p> <ul style="list-style-type: none"> <li>• Anti-viral activity: Reported for extract of <i>A.annua</i>. Extract inhibits replication of SARS-CoV (2 strains) in VeroE6 cells with EC50= 34.5 (Strain –BJ-001) and 39.2 (Strain-BJ-006). <a href="http://www.hdbiosciences.com/Download/Identification%20of%20natural%20compounds%20with%20antiviral%20activities%20against%20SARS-associated%20coronavirus.pdf">http://www.hdbiosciences.com/Download/Identification%20of%20natural%20compounds%20with%20antiviral%20activities%20against%20SARS-associated%20coronavirus.pdf</a></li> <li>• On April 9<sup>th</sup> 2020, Max Planck Institute of Colloids and Interfaces, Potsdam (Germany) announced a collaboration with ArtemiLife., a US based company and medical researchers in Denmark and Germany to test <i>Artemisia annua</i> plant extract and Artemisinin derivatives in laboratory cell studies against SARS-CoV-2 <a href="https://www.mpg.de/14663263/artemisia-annua-to-be-tested-against-covid-19">https://www.mpg.de/14663263/artemisia-annua-to-be-tested-against-covid-19</a></li> </ul> <p>Artemisinin:</p> <ul style="list-style-type: none"> <li>• Anti-viral activity: Artemisinin and its derivatives reported to induce inhibition of Human Cytomegalovirus and other members of the <i>Herpesviridae</i> family (e.g., Herpes Simplex Virus Type 1 and Epstein-Barr virus), Hepatitis B, Hepatitis C, and Bovine Viral Diarrhea virus in in-vitro studies. <a href="https://academic.oup.com/cid/article-abstract/47/6/804/325924">https://academic.oup.com/cid/article-abstract/47/6/804/325924</a> <a href="https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0081783">https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0081783</a> <a href="https://www.mdpi.com/2076-2607/8/1/85/pdf">https://www.mdpi.com/2076-2607/8/1/85/pdf</a></li> <li>• Anti-inflammatory: Artemisinin is reported to alleviate pathological lung injury in a septic rat model. It also reduces the levels of pro-inflammatory cytokines TNFa, IL-6, in lung tissue. <a href="https://europepmc.org/article/cba/637350">https://europepmc.org/article/cba/637350</a></li> </ul>

Proposed use as Primary or Adjuvant?	Primary	
Pre-Clinical Data available for COVID-19	Data not available	
Status of Clinical Trials	<p>No ongoing trials</p> <p>A news article reported that “A Curcumin and Artemisinin-based oral spray has been proposed as a treatment for COVID-19 patients and a clinical trial will be conducted, ASX-listed phytocannabinoid firm MGC Pharmaceuticals has revealed.</p> <p><a href="https://www.nutraingredients-asia.com/Article/2020/04/23/COVID-19-natural-product-trial-New-curcumin-artemisinin-supplement-to-be-tested-on-patients">https://www.nutraingredients-asia.com/Article/2020/04/23/COVID-19-natural-product-trial-New-curcumin-artemisinin-supplement-to-be-tested-on-patients</a></p>	
Trial Details	Data not available	
Key Data from Clinical Trials	Data not available	
IP Status	Status/ Molecule	<i>Artemisia annua</i>
	Approved and Active applications	<p><a href="#">232569</a>            Title: A process for isolating artemisinin from <i>Artemisia annua</i>            Assignee: Council Of Scientific &amp; Industrial Research (Central Institute Of Medicinal And Aromatic Plants, Lucknow)            Priority date: 27/03/2002            Granted date: 24/03/2009            Expected expiry date: 27/03/2023</p>
	Pending applications	<p><a href="#">201611006947</a>            Title: A novel herbal composition effective against HummaEijamiyah (malaria) and a process for its preparation thereof            Assignee: Central Council For Research In Unani Medicine (CCRUM)            Filing date: 29/02/2016            Status: Published: 01/09/2017  <a href="#">26/MUM/2015</a>            Title: Process for purification of artemisinin and other constituents from <i>Artemisia annua</i> in high yield and high purity            Inventor: Ashish Omprakash Mantri            Filing date: 05/0/2015            Status: Published: 08/07/2016  <a href="#">853/MUMNP/2011</a>            Title: Hydrolysates made of plant extracts and antibacterial agent containing the same            Assignee: Bionorica SE            Priority date: 31/10/2008            Status: Published: 10/02/2012  <a href="#">201717047338</a>            Title: Compositions methods and medical compositions for treatment of and maintaining the health of the liver            Applicant: Unigen INC.            Filing date: 29/12/2017            Status: Published 16/03/2018</p>
	Expired or Lapsed applications	<p><a href="#">652/DEL/1997</a>            Title: An improved process for the simultaneous production of artemisinin and essential oil from the plant <i>Artemisia annua</i>            Assignee: Council of Scientific and Industrial Research (Central Institute Of Medicinal And Aromatic Plants, Lucknow)            Filing date: 17/03/1997            Publication date: 12/09/2008            Status: Published, Request for examination not filed  <a href="#">3033/CHE/2007</a>            Title: Microbial bioconversion of Arteannuin B to</p>
© Venture Center, 2020		Page 4 of 1

	<p>Artemisinin by <i>Streptomyces Pactum</i> Applicant: Centre For Biotechnology Priority date: 20/12/2002 Date of Publication 11/09/2009 Status: Deemed to be abandoned U/S 21(1)</p>
Other references	<ul style="list-style-type: none"><li>• <a href="https://pubchem.ncbi.nlm.nih.gov/compound/Artemisinin">https://pubchem.ncbi.nlm.nih.gov/compound/Artemisinin</a></li><li>• <a href="https://newdrugapprovals.org/tag/artemisinin/">https://newdrugapprovals.org/tag/artemisinin/</a></li><li>• <a href="https://news.mongabay.com/2020/04/madagascars-president-promotes-unproven-herbal-cure-for-covid-19/">https://news.mongabay.com/2020/04/madagascars-president-promotes-unproven-herbal-cure-for-covid-19/</a></li><li>• <a href="https://www.ncbi.nlm.nih.gov/pubmed/25609991">https://www.ncbi.nlm.nih.gov/pubmed/25609991</a></li></ul>

## 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.*