

Supporting Information

6-Shogaol exhibits anti-viral and anti-inflammatory activity in COVID-19 associated inflammation by regulating NLRP3 inflammasome

Jyoti Kode^{1,2,#,*}, Jitendra Maharana^{3,#,γ}, Asif Amin Dar^{4,#}, Shayanti Mukherjee^{5,6}, Nikhil Gadewal⁷, Dilep Kumar Sigalapalli⁸, Satyanshu Kumar⁹, Debashis Panda¹⁰, Soumyajit Ghosh^{11,12}, Supriya Suman Keshry^{11,13}, Prabhudutta Mamidi¹¹, Soma Chattopadhyay¹¹, Trupti Pradhan¹, Vaishali Kailaje¹⁴, Sunil Inamdar^{15,16}, Vidula Gujjarwar¹⁷

Box S1

ITAMs holds great promise as a complementary therapy for patients with COVID-19. Qamar et al¹ have screened a medicinal plant database containing 32,297 potential anti-viral phytochemicals and shortlisted nine best hits (that may be further optimized and explored) as inhibitory agents for SARS-CoV2 3CLpro activity, which encodes virus replication. They further reported that preclinical and clinical studies are warranted to develop these potential inhibitors into novel clinically useful drugs. In addition, several textual formulations contain herbs such as **Guduchi, Shunthi, Marich, Tvak, Ela, Ashwagandha, Madhuyashthi, Vasa, Pimpali, Tulsi, Bhumyamalaki, Vacha, Aconitum**, and others. These are frequently used, commonly available, botanically identified, and undisputed herbs which might play an important role in treatment of SARS-CoV2.

Bṛhat-Trayī, “The Great Text Triad” elaborates diseases into the following categories: **Jwar** (fever), **Raktapitta** (bleeding disorder), **Swasa** (breathing difficulty), **Kapha** (cough), **Vatarakta** (autoimmune skin and joint disease) and others. It explains that rather than changing the pattern of medicines according to the disease, strengthening the immune system might be a more effective and preventive method. Hence, for life-threatening diseases, especially fast-spreading respiratory diseases, drugs which quickly boost the immunity are to be used immediately. Ginger enhances the immune response and are known to be two of the few best drugs among these medicines.

Supporting Figures

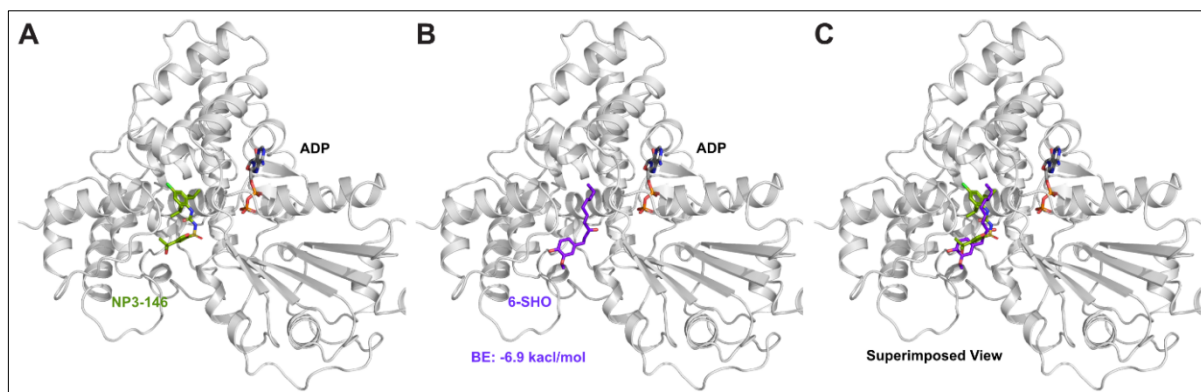


Figure S1. Molecular docking of 6-SHO in the NP3-146 binding site of NLRP3-NACHT. (A) crystal structure of NLRP3^{NACHT} domain (PDBID: 7ALV) with ADP and NP3-146 compound. (B) Docked 6-SHO in the NP3-146 binding cavity, displayed in violet stick model with AutoDock Vina binding energy value. (C) Superimposed view of ADP/NP3-146 and ADP/6-SHO-bound NLRP3-NACHT.

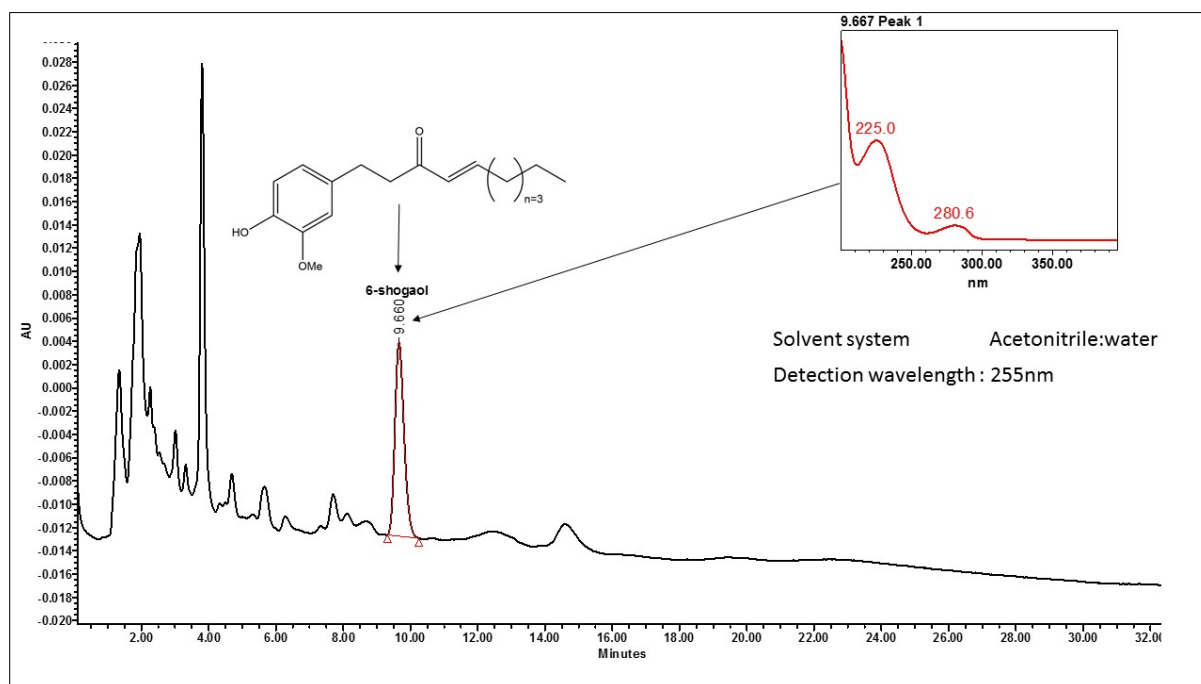


Figure S2. 6-SHO in ginger extract; confirmed by matching the spectra in HPLC-PDA chromatogram.

Data on treatment outcome of COVID-19 patients enrolled at CBPACS

1. CBPACS designated as CHC on 16.04.2020
2. First patient admitted on 18.04.2020
3. Total number of patients admitted in this facility till today- 2208
4. Total number of patients discharged – 1970
5. Total number of patients admitted as on today - 01
6. Total number of patients referred higher center- 237
7. Total number of casualty-NIL
8. Total number of RT-PCR test done – 2540
9. Total number of Rapid Antigen Test (RAT) test done-5410
10. Total number of clinical trials related to COVID-04
11. Management protocol adopted by Sansthan-

First Protocol(adopted from 18.04.2020)

Nagaradi kwath- 30 ml, Amalki powder - 3gm, Sanshamni vati- 2-2-2

Second Protocol(adopted from 28.09.2020)

Nagaradi kwath-30 ml, Agasty Haritaki-5 gm TSF, Sitopladi powder-3 gm bd,
Sanshamni vati- 2-2-2, Yavani ark- 2 tsf BD

Figure S3. Clinical trial whose treatment included ginger containing formulation for treatment of COVID-19. Trial demonstrated the successful outcome (funded by Ministry of AYUSH, GoI).

Supporting Table

Table S1 | Clinical Trials for COVID-19 using Traditional Medicine or Alternative Medicine

| Sl. No. | Clinical Trial Title | Trial ID |
|---------|---|--|
| 1 | The efficacy and safety of high dose intravenous vitamin C in the treatment of novel coronavirus pneumonia (COVID-19): a prospective, randomize, controlled trial | ChiCTR2000032400 |
| 2 | START (Siddha Treatment Accelerating Recovery from SARS-CoV2 Test) trial of Siddha treatment for patients with novel coronavirus infectious disease (COVID-19) | ISRCTN13311119 |
| 3 | Effect of herbal medicine containing Saatar, Hofarigon and Fennel on COVID-19 patients | IRCT20200404046935N1 |
| 4 | DangguiShaoyao Powder in the synergistic treatment of novel coronavirus pneumonia (COVID-19) | ChiCTR2000032098 |
| 5 | The effect of herbal drugs (Echinacea and Ginger) on Improvement of clinical symptoms and hospitalizations in suspected COVID-19 outpatient cases | IRCT20200415047089N1 |
| 6 | The effect of MCT Oil on COVID-19 | IRCT20160313027033N2 |
| 7 | Efficacy of Chinese Herbal Tea in the Prevention of Novel Coronavirus Pneumonia (COVID-19): a Randomized Controlled Trial | ChiCTR2000031944 |
| 8 | Evaluation the effect of asafoetida in the treatment of coronavirus infection | IRCT20200413047053N1 |
| 9 | Effect of Intravenous vitamin c in Patients with COVID-19 | IRCT20200411047025N1 |
| 10 | Evaluating the effect of Phyllanthus emblica on COVID 19 patients | IRCT20200404046937N2 |
| 11 | Evaluation the effect of licorice for treatment of coronavirus | IRCT20200404046933N1 |
| 12 | The effect of elderberry syrup against COVID-19 symptoms | IRCT20200406046965N1 |
| 13 | The effect of SOVODAK in the treatment of COVID-19 patients | IRCT20200403046926N1 |
| 14 | Effect of crocetin on COVID-19 | IRCT20081019001369N3 |
| 15 | Evaluation of the efficacy of oral 25-hydroxyvitamin D3 on COVID-19 | IRCT20200401046909N1 IRCT20200401046909N2 |
| 16 | Effect of herbal capsule, Viroherb, and herbal syrup, Fenugreek in treatment of COVID-19 | IRCT20200402046923N1 |
| 17 | Effect of Algomed, Menta longifolia, Chamomile, Althaea rosea, Malva sylvestris, Lepidium sativum supplements on the Severity and Consequences of Coronavirus 19 disease (COVID-19) | IRCT20151228025732N51 |
| 18 | Effect of IMFLUNA herbal compound on covid-19 pneumonia symptoms | IRCT20080901001157N16 |
| 19 | Study of the effect of vitamin C in patients with Covid-19 | IRCT20200324046850N5 |

| | | |
|----|---|----------------------|
| 20 | Evaluation of the effect of traditional Iranian medicine product on improvement of clinical manifestation of COVID-19 | IRCT20101219005416N2 |
| 21 | The effect of Tanacetum parthenium (L) Sch syrup on clinical manifestations of patients with COVID-19 | IRCT20180610040049N4 |
| 22 | Effect of oral multi-herbal preparation on COVID-19 | IRCT20180712040449N2 |
| 23 | The effect of Trachyspermumcopticum syrup on clinical manifestations of patients with COVID-19 | IRCT20180610040049N3 |
| 24 | Effect of vitamin A in patients with COVID19 | IRCT20170117032004N3 |

Supporting Reference

(1) Tahir Ul Qamar, M.; Alqahtani, S. M.; Alamri, M. A.; Chen, L. L. Structural basis of SARS-CoV-2 3CL(pro) and anti-COVID-19 drug discovery from medicinal plants. *J Pharm Anal* 2020, 10 (4), 313-319. DOI: 10.1016/j.jpha.2020.03.009 From NLM PubMed-not-MEDLINE.