Andrographolide & Covid-19 / Sars-Cov-2

Article Table – Natural Products: Peer-Reviewed Published Evidence-Base Citations

PubMed Evidence-base Citations with Abstracts of Journal reference with PMID links to articles supporting consideration of natural product Andrographolide in Covid-19 / Sars-Cov-2
(Andrographolide is in plant Andrographis paniculata, commonly known as green chiretta)

1.	NHP: Andrographolide	NHP #01
2.	1. **Leveraging knowledge of Asian herbal medicine and its active compounds as COVID-19 treatment and prevention**. ABSTRACT: The outbreak of COVID-19 disease has led to a search for effective vaccines or drugs. However, insufficient vaccine supplies to meet global demand and no effective approved prescribed drugs for COVID-19 have led some people to consider the use of alternative or complementary medicines, such as traditional herbal medicine. Medicinal plants have various therapeutic properties that depend on the active compounds they contain. Obviously, herbal medicine has had an essential role in treatment and prevention during COVID-19 outbreak, especially in Asian cultures. Hence, we reviewed the uses of herbal medicine in Asian cultures and described the prominent families and species that are sources of antiviral agents against COVID-19 on the basis of case reports, community surveys, and guidelines available in the literature databases. Antiviral efficacy as determined in laboratory testing was assessed, and several promising active compounds with their molecular targets in cell models against SARS-CoV-2 viral infection will be discussed. Our review findings revealed the highly frequent use of Lamiaceae family members, Zingiber officinale, and Glycyrrhiza spp. as medicinal sources for treatment of COVID-19. In addition, several plant bioactive compounds derived from traditional herbal medicine, including andrographolide, panduratin A, baicalein, digoxin, and digitoxin, have shown potent SARS-CoV-2 antiviral activity as compared with some repurposed FDA-approved drugs. These commonly used plants and promising compounds are recommended for further exploration of their safety and efficacy against COVID-19. • Diagnosis: Covid-19, Sars-Cov-106. • Citation: Desy Liana, Anuchit Phanumartwiwath. Leveraging knowledge of Asian herbal medicine and its active compounds as COVID-19 treatment and prevention. Journal of natural medicines (09 Oct 2021) PMID:34623617 doi:10.1007/s11418-021-01575-1.	PMID: 34623617
3.	2. **Artemether, Artesunate, Arteannuin B, Echinatin, Licochalcone B and Andrographolide Effectively Inhibit SARS-CoV-2 and Related Viruses In Vitro.** ABSTRACT: Since the first reported case caused by the novel coronavirus SARS-CoV-2 infection in Wuhan, COVID-19 has caused serious deaths and an ongoing global pandemic, and it is still raging in more than 200 countries and regions around the world and many new variants have appeared in the process of continuous transmission. In the early stage of the epidemic prevention and control and clinical treatment, traditional Chinese medicine played a huge role in China. Here, we screened out six monomer compounds, including artemether, artesunate, arteannuin B, echinatin, licochalcone B and andrographolide, with excellent anti-SARS-CoV-2 and anti-GX_P2V activity from Anti-COVID-19 Traditional Chinese Medicine Compound Library containing 389 monomer compounds extracted from traditional Chinese medicine prescriptions "three formulas and three drugs". Our discovery preliminary proved the stage of action of those compounds against SARS-CoV-2 and provided inspiration for further research and clinical applications. • Diagnosis: Covid-19, Sars-Cov-103. • Citation: Yunjia Hu, Meiqin Liu, Hongbo Qin, Haofeng Lin, Xiaoping An, Zhengli Shi, Lihua Song, Xinglou Yang, Huahao Fan, Yigang Tong. Artemether, Artesunate, Arteannuin B, Echinatin, Licochalcone B and Andrographolide Effectively Inhibit SARS-CoV-2 and Related Viruses In Vitro. Frontiers in cellular and infection microbiology (17 Sep 2021) PMID:34527599 PMC8435859 doi:10.3389/fcimb.2021.680127.	PMID: 34527599

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4.	3. **The dual role of phytochemicals on SARS-CoV-2 inhibition by targeting host and viral proteins**. ABSTRACT: The severe acute respiratory syndrome-2019 has affected more than 190 million people around the world and caused severe crises throughout the globe. Due to rapid mutation in the viral genome, it became important to simultaneously improvise the host immunity while targeting the viral protein to reduce the severity of the infection. The current computational work focuses on multi-level rigorous screening of 47 medicinal plant-based phytochemicals for discovering effective phytochemical inhibitors against the host and viral targets. A total of 586 phytochemicals were analyzed in detail based on their drug-likeness, pharmacological properties, and structure-based activity against the viral proteins (Spike glycoprotein, Papain-like protease, and Main protease) and host proteins (ACE2, Importin-subunit α-5, and β-1). Phytochemicals showing higher binding affinity with the dual capacity to target both the categories of proteins were further analyzed by profiling their chemical reactivity using Density-functional theory (DFT) based quantum chemical methods. Finally, detailed molecular dynamics simulations were performed to analyze the interactions of the complexes. The results revealed that the selected phytochemicals from Andrographis paniculata , Aconitum heterophyllum , Costus speciosus and Inula racemosa may have the capacity to act with prominent affinity towards the host and viral proteins. Therefore, The Combination of active phytochemicals of these plants may prove to be more beneficial and can be used for developing the potential phytotherapeutic intervention. • Diagnosis: Covid-19, Sars-Cov-100. • Citation: Prakrity Singh, Shweta Singh Chauhan, Shraddha Pandit, Meetali Sinha, Shristee Gupta, Anshika Gupta, Ramakrishnan Parthasarathi. The dual role of phytochemicals on SARS-CoV-2 inhibition by targeting host and viral proteins. Journal of traditional and complementary medicine (14 Sep 2021) PMID:34513611 PMC8424525 doi:10.1016/j.jtcme.2021.09.001.	PMID: 34513611
5.	**4. Which East Asian herbal medicines can decrease viral infections?** ABSTRACT: Whilst Western research for the COVID-19 crisis focuses on vaccination, in East Asia traditional herbal prescriptions are studied for SARS-CoV2 therapy. In Japan, Maoto (Ephedrae herba 4 g, Armeniacae semen 4 g, Cinnamomi cortex 3 g, and Glycyrrhizae radix 2 g, JPXVII) is used based on clinical evidence for its effect on early phase influenza (also caused by RNA viruses) comparable to that of oseltamivir. The Health Ministry of Thailand has approved Andrographis paniculata (Jap. Senshinren) extracts for treatment of COVID-19. Its combination (4 g) with Maoto, Maoto-ka-senshinren, seems most promising for the treatment of viral pandemics. In China, the official guideline for COVID-19 treatment contains TCM medications with antiviral, as well as immunmodulatory and anti-inflammatory effects such as: Qing-Fei-Pai-Du-Tang (Jap. Seihai-haidokuto) contains 21 drugs; Shufeng Jiedu Jiaonang (Bupleuri radix 8 g, Forsythiae fructus 8 g, Glycyrrhizae radix 4 g, Isatidis radix 8 g, Patriniae herba 8 g, Phragmitis rhizoma 6 g, Polygoni cuspidati rhizoma 10 g, Verbenae herba 8 g); Fufang Yuxingcao Heiji (Forsythiae fructus 0.6 g, Houttuyniae herba 6 g, Isatidis radix 1.5 g, Lonicerae flos 0.6 g, Scutellariae radix 1.5 g) first gained prominence during the 2002 SARS epidemic. With no Western medicine available, the following overview discusses efficacy and mechanisms in view of viral entry and replication of different East Asian herbal remedies for COVID-19 treatment. • Diagnosis: Covid-19, Sars-Cov-98. • Citation: Kenny Kuchta, Silke Cameron, Minwon Lee, Shao-Qing Cai, Yukihiro Shoyama. Which East Asian herbal medicines can decrease viral infections? Phytochemistry reviews : proceedings of the Phytochemical Society of Europe (02 Sep 2021) PMID:34466134 PMC8391007 doi:10.1007/s11101-021-09756-2.	PMID: 34466134
6.	**5. Potential of diterpene compounds as antivirals, a review.** ABSTRACT: Viruses cause widely transmitted diseases resulting in pandemic conditions. Currently, the world is being hit by the Covid-19 pandemic caused by the SAR-CoV-2 infection. Countries in the world are competing to develop antivirals to overcome this problem. Diterpene compounds derived from natural ingredients (plants, corals, algae, fungi, sponges) and synthesized products have potential as antivirals. This article summarizes the different types of diterpenes such as daphnane, tiglilane, kaurane, abietane, pimarane, labdane, dollabelane, jatrophane, dolastane, prenylated guaiane, tonantzitlolone, casbane, have antivirals activity such as targeting HIV, Coxsackie virus, herpes virus, hepatitis virus, influenza virus, Chikungunya virus, Zika virus, dengue virus, and SARS-CoV. Some compounds such as andrographolide and its derivatives show promising activity in inhibiting the influenza virus. Additionally, compounds such as pineolidic acid, forskolin, sugiol, and many other diterpene compounds showed anti-SAR-CoV	PMID: 34405122

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	activity. The diterpene compound class's high antivirals potential does not rule out the possibility that these compounds can also act as anti-SAR-CoV-2 drugs in the future. • Diagnosis: Covid-19, Sars-Cov-95. • Citation: Andika Pramudya Wardana, Nanik Siti Aminah, Mila Rosyda, Muhammad Ikhlas Abdjan, Alfinda Novi Kristanti, Khun Nay Win Tun, Muhammad Iqbal Choudhary, Yoshiaki Takaya. Potential of diterpene compounds as antivirals, a review. Heliyon (19 Aug 2021) PMID:34405122 PMC8359577 doi:10.1016/j.heliyon.2021.e07777.	
7.	**6. Molecular encapsulation of andrographolide in 2-hydroxypropyl-β-cyclodextrin cavity: synthesis, characterization, pharmacokinetic and in vitro antiviral activity analysis against SARS-CoV-2.** ABSTRACT: In present investigation, AND-2-HyP- β -CYD (Andrographolide-2-Hydroxypropyl- β -cyclodextrin) complex was synthesized and characterized for antiviral and pharmacokinetic profile. The linear host-guest relation suggested synthesis of a 1:1 complex of AND with 2-HyP- β -CYD by inclusion mode. The Kc, stability constant of the two phase system of AND with 2-HyP- β -CYD computed to be 38.60 x 10 -3 M. 1 H NMR spectrum of AND indicated the presence of triplet at 6.63-ppm which was up-fielded in AND-2-HyP- β -CYD complex at 6.60-ppm (doublet) confirmed the insertion of AND in cavity of 2-HyP- β -CYD through lactone ring. AND-2-HyP-β-CYD complex exhibited the IC 50 of 0.1- µ g.mL -1 (E gene) and 0.29- µ g.mL -1 (N gene) against SARS-CoV-2 infected Vero6 cells. Moreover, a 1.5-fold increment in extent of absorption of AND was noticed post complexation. The bioavailability was estimated to be 15.87 ± 3.84% and 23.84 ± 5.46%, respectively for AND and AND-2-HyP- β -CYD complex. AND-2-HyP- β -CYD complex may be a prospective candidate for further studies to evolve as a clinically viable formulation against SARS-CoV-2. • Diagnosis: Covid-19, Sars-Cov-92. • Citation: Shashi Chandrama Singh, Dharmendra Kumar Khatri, Kulbhaskar Singh, Vinay Kumar Kanchupalli, Jitender Madan, Shashi Bala Singh, Harshpal Singh. Molecular encapsulation of andrographolide in 2-hydroxypropyl-β-cyclodextrin cavity: synthesis, characterization, pharmacokinetic and in vitro antiviral activity analysis against SARS-CoV-2. Heliyon (17 Aug 2021) PMID:34395929 PMC8351079 doi:10.1016/j.heliyon.2021.e07741.	PMID: 34395929
8.	**7. Andrographolide binds to spike glycoprotein and RNA-dependent RNA polymerase (NSP12) of SARS-CoV-2 by in silico approach: a probable molecule in the development of anti-coronaviral drug.** ABSTRACT: The SARS-CoV-2 belongs to Coronaviridae family infects host cells by the interaction of its spike glycoprotein and angiotensin-converting enzyme 2 (ACE 2) of host cells. Upon entry, the virus uses its RNA dependent RNA polymerase (NSP12) for transcribing its genome to survive in the cell and spread its infection. The protein sequences of receptor-binding domain (RBD) of spike glycoprotein, and NSP12 exhibits high homology in the family of Coronoviridae and are ideal candidates for the development of anti-coronaviral drugs. In the quest to identify inhibitory molecules against these proteins, we searched several molecules that are present in naturally occurring medicinal plants database. Andrographolide which is largely present in the leaf extracts of Andrographis paniculata (AP) and is known to exhibit antiviral, antibacterial, and stabilizes Th1/Th2/Th17 responses; taking this clue, we used in silico approaches to see the binding of andrographolide to RBD and NSP12 molecules. Our docking results showed very strong affinity of andrographolide to RBD and NSP12 of the SARS-CoV-2 virus with dock scores of -10.3460 for RBD and -10.7313 for NSP12 indicating andrographolide acts as an inhibitor of RBD and NSP12. These unique properties of andrographolide, AP extract, can be tested as anti-coronaviral drug. • Diagnosis: Covid-19, Sars-Cov-89. • Citation: Lokanathan Srikanth, Potukuchi Venkata Gurunadha Krishna Sarma. Andrographolide binds to spike glycoprotein and RNA-dependent RNA polymerase (NSP12) of SARS-CoV-2 by in silico approach: a probable molecule in the development of anti-coronaviral drug. Journal, genetic engineering & biotechnology (14 Jul 2021) PMID:34255214 PMC8276218 doi:10.1186/s43141-021-00201-7.	PMID: 34255214
9.	**8. A Computational Approach Identified Andrographolide as a Potential Drug for Suppressing COVID-19-Induced Cytokine Storm.** ABSTRACT: The newly identified betacoronavirus SARS-CoV-2 is the causative pathogen of the coronavirus disease of 2019 (COVID-19) that killed more than 3.5 million people till now. The cytokine storm induced in severe COVID-19 patients causes hyper-inflammation, is the primary reason for respiratory and multi-organ failure and fatality. This work uses a rational computational strategy to identify the existing drug molecules to target host pathways to	PMID: 34248936

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	reduce the cytokine storm. We used a " host response signature network " consist of 36 genes induced by SARS-CoV-2 infection and associated with cytokine storm. In order to attenuate the cytokine storm, potential drug molecules were searched against "host response signature network" . Our study identified that drug molecule andrographolide, naturally present in a medicinal plant Andrographis paniculata , has the potential to bind with crucial proteins to block the TNF-induced NFkB1 signaling pathway responsible for cytokine storm in COVID-19 patients. The molecular docking method showed the binding of andrographolide with TNF and covalent binding with NFkB1 proteins of the TNF signaling pathway. We used a rational computational approach to repurpose existing drugs targeting host immunomodulating pathways. Our study suggests that andrographolide could bind with TNF and NFkB1 proteins, block TNF-induced cytokine storm in COVID-19 patients, and warrant further experimental validation. • Diagnosis: Covid-19, Sars-Cov-86. • Citation: Mohd Rehan, Firoz Ahmed, Saad M Howladar, Mohammed Y Refai, Hanadi M Baeissa, Torki A Zughaibi, Khalid Mohammed Kedwa, Mohammad Sarwar Jamal. A Computational Approach Identified Andrographolide as a Potential Drug for Suppressing COVID-19-Induced Cytokine Storm. Frontiers in immunology (13 Jul 2021) PMID:34248936 PMC8264290 doi:10.3389/fimmu.2021.648250.	
10.	9. **A Computational-Based Drug Repurposing Method Targeting SARS-CoV-2 and its Neurological Manifestations Genes and Signaling Pathways**. ABSTRACT: Coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) as a global concern involves infections in multiple organs. Much of the research up to now has been descriptive on neurological manifestations followed by SARS-CoV-2 infection. Despite considerable efforts on effective SARS-CoV-2 vaccine, novel therapeutic options for COVID-19 comorbidities are warranted. One of the fast ways to introduce possible effective drugs for clinical trials is bioinformatics methods. We have conducted a comprehensive enrichment analysis of genes involved in SARS-CoV-2 and neurological disorders associated with COVID-19. For this purpose, gene sets were extracted from the GeneWeaver database. To find out some significant enriched findings for common genes between SARS-CoV-2 and its neurological disorders, several practical databases were used. Finally, to repurpose an efficient drug, DrugBank databases were used. Overall, we detected 139 common genes concerning SARS-CoV-2 and their neurological disorders. Interestingly, our study predicted around 6 existing drugs (ie, carvedilol, andrographolide, 2-methoxyestradiol, etanercept, polaprezinc, and arsenic trioxide) that can be used for repurposing. We found that polaprezinc (zinc l-carnosine) drug is not investigated in the context of COVID-19 till now and it could be used for the treatment of COVID-19 and its neurological manifestations. To summarize, enrichment and network data get us a coherent picture to predict drug repurposing to speed up clinical trials. • Diagnosis: Covid-19, Sars-Cov-83. • Citation: Ali Sepehrinezhad, Fariborz Rezaeitalab, Ali Shahbazi, Sajad Sahab-Negah. A Computational-Based Drug Repurposing Method Targeting SARS-CoV-2 and its Neurological Manifestations Genes and Signaling Pathways. Bioinformatics and biology insights (03 Jul 2021) PMID:34211268 PMC8216348 doi:10.1177/11779322211026728.	PMID: 34211268
11.	**10. Inhibitory Potential of Phytochemicals on Interleukin-6-Mediated T-Cell Reduction in COVID-19 Patients: A Computational Approach.** ABSTRACT: A recent COVID-19 pandemic has resulted in a large death toll rate globally and even no cure or vaccine has been successfully employed to combat this disease. Patients have been reported with multi-organ dysfunction along with acute respiratory distress syndrome which implies a critical situation for patients and made them difficult to breathe and survive. Moreover, pathology of COVID-19 is also related to cytokine storm which indicates the elevated levels of interleukin (IL)-1, IL-6, IL-12, and IL-18 along with tumor necrosis factor (TNF)-α. Among them, the proinflammatory cytokine IL-6 has been reported to be induced via binding of severe acute respiratory syndrome coronavirus 2 (SARS)-CoV-2 to the host receptors. Interleukin-6 blockade has been proposed to constitute novel therapeutics against COVID-19. Thus, in this study, 15 phytocompounds with known antiviral activity have been subjected to test for their inhibitory effect on IL-6. Based on the affinity prediction, top 3 compounds (isoorientin, lupeol, and andrographolide) with best scores were selected for 50 ns molecular dynamics simulation and MMGB/PBSA binding free energy analysis. Three phytocompounds including isoorientin, lupeol, and andrographolide have shown strong interactions with the targeted protein IL-6 with least binding energies (-7.1 to -7.7 kcal/mol). Drug-likeness and ADMET profiles of prioritized phytocompounds are also very prominsing and can be further tested to be potential IL-6 blockers and thus benficial for COVID-19 treatment. The moelcular dynamics simulation couple with MMGB/PBSA binding free energy estimation validated conformational stability of the ligands and stronger intermolecular binding. The mean RMSD of the complexes is as: IL6-isoorientin complex	PMID: 34163151

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	(3.97 Å ± 0.77), IL6-lupeol (3.97 Å ± 0.76), and IL6-andrographolide complex (3.96 Å ± 0.77). In addition, the stability observation was affirmed by compounds mean RMSD: isoorientin (0.72 Å ± 0.32), lupeol (mean 0.38 Å ± 0.08), and andrographolide (1.09 Å ± 0.49). A similar strong agreement on systems stability was unraveled by MMGB/PBSA that found net binding net ~ -20 kcal/mol for the complexes dominated by van der Waal interaction energy. It has been predicted that proposing potential IL-6 inhibitors with less side effects can help critical COVID-19 patients because it may control the cytokine storm, a major responsible factor of its pathogenesis. In this study, 3 potential phytocompounds have been proposed to have inhibitory effect on IL-6 that can be tested as potential therapeutic options against SARS-CoV-2. • Diagnosis: Covid-19, Sars-Cov-80. • Citation: Arif Malik, Anam Naz, Sajjad Ahmad, Mansoor Hafeez, Faryal Mehwish Awan, Tassadaq Hussain Jafar, Ayesha Zahid, Aqsa Ikram, Bisma Rauff, Mubashir Hassan. Inhibitory Potential of Phytochemicals on Interleukin-6-Mediated T-Cell Reduction in COVID-19 Patients: A Computational Approach. Bioinformatics and biology insights (25 Jun 2021) PMID:34163151 PMC8191067 doi:10.1177/11779322211021430.	
12.	**11. A molecular dynamics simulation study of the ACE2 receptor with screened natural inhibitors to identify novel drug candidate against COVID-19.** ABSTRACT: The massive outbreak of Novel Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV-2) has turned out to be a serious global health issue worldwide. Currently, no drugs or vaccines are available for the treatment of COVID-19. The current computational study was attempted to identify a novel therapeutic inhibitor against novel SARS-CoV-2 using in silico drug discovery pipeline. In the present study, the human angiotensin-converting enzyme 2 (ACE2) receptor was the target for the designing of drugs against the deadly virus. The 3D structure of the receptor was modeled & validated using a Swiss-model, Procheck & Errat server. A molecular docking study was performed between a group of natural & synthetic compounds having proven anti-viral activity with ACE2 receptor using Autodock tool 1.5.6. The molecular dynamics simulation study was performed using Desmond v 12 to evaluate the stability and interaction of the ACE2 receptor with a ligand. Based on the lowest binding energy, confirmation, and H-bond interaction, cinnamic acid (-5.20 kcal/mol), thymoquinone (-4.71 kcal/mol), and andrographolide (Kalmegh) (-4.00 kcal/mol) were screened out showing strong binding affinity to the active site of ACE2 receptor. MD simulations suggest that cinnamic acid, thymoquinone, and andrographolide (Kalmegh) could efficiently activate the biological pathway without changing the conformation in the binding site of the ACE2 receptor. The bioactivity and drug-likeness properties of compounds show their better pharmacological property and safer to use. The study concludes the high potential of cinnamic acid, thymoquinone, and andrographolide against the SARS-CoV-2 ACE2 receptor protein. Thus, the molecular docking and MD simulation study will aid in understanding the molecular interaction between ligand and receptor binding site, thereby leading to novel therapeutic intervention. • Diagnosis: Covid-19, Sars-Cov-77. • Citation: Neha Srivastava, Prekshi Garg, Prachi Srivastava, Prahlad Kishore Seth. A molecular dynamics simulation study of the ACE2 receptor with screened natural inhibitors to identify novel drug candidate against COVID-19. PeerJ (14 May 2021) PMID:33981493 PMC8074842 doi:10.7717/peerj.11171.	PMID: 33981493
13.	**12. Efficacy and safety of Xiyanping injection in the treatment of COVID-19: A multicenter, prospective, open-label and randomized controlled trial.** ABSTRACT: Xiyanping (XYP) is a Chinese herbal medicine used in the clinic to treat respiratory infection and pneumonia. Recent evidence identified XYP as a potential inhibitor of severe acute respiratory syndrome coronavirus 2, implying XYP as a possible treatment for the coronavirus disease 2019 (COVID-19). Here, we conducted a prospective, multicenter, open-label and randomized controlled trial to evaluate the safety and effectiveness of XYP injection in patients with mild to moderate COVID-19. We consecutively recruited 130 COVID-19 patients with mild to moderate symptoms from five study sites, and randomized them in 1:1 ratio to receive XYP injection in combination with standard therapy or receive standard supportive therapy alone. We found that XYP injection significantly reduced the time to cough relief, fever resolution and virus clearance. Less patients receiving XYP injection experienced disease progression to the severe stage during the treatment process. No severe adverse events were reported during the study. Taken together, XYP injection is safe and effective in improving the recovery of patients with mild to moderate COVID-19. However, further studies are warranted to evaluate the efficacy of XYP in an expanded cohort comprising COVID-19 patients at different disease stages. • Diagnosis: Covid-19, Sars-Cov-74.	PMID: 33979464

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	• Citation: Xin-Yi Zhang, Lang Lv, Yu-Long Zhou, Liang-Dong Xie, Qin Xu, Xiao-Fan Zou, Yan Ding, Jie Tian, Jia-Liang Fan, Hai-Wei Fan, Yi-Xi Yang, Xiao-Qun Ye. Efficacy and safety of Xiyanping injection in the treatment of COVID-19: A multicenter, prospective, open-label and randomized controlled trial. Phytotherapy research : PTR (13 May 2021) PMID:33979464 PMC8242486 doi:10.1002/ptr.7141.	
14.	**13. Andrographis paniculata (Burm. F) Wall ex Nees: Antiviral properties.** ABSTRACT: Andrographis paniculata is home to a rich variety of molecules especially andrographolide and its derivatives. Clinical properties of the andrographolide are multifarious and include: analgesic, antipyretic, antiretroviral, antiproliferative, antimalarial, antithrombotic, antihyperglycemic, antiurolethial, antilesihmaniasis, hepatoprotective, immune-modulatory, protective against alcohol induced toxicity and cardioproetcive activity and anticancer activity. Andrographolide, neoandrographolide, dehydroandrographolide and several natural and synthetic derivatives of it: 14-deoxy-11,12-didehydroandrographolide and 14-deoxyandrographolide, dehydroandrographolide succinic acid monoester (DAMS), 14-ά-lipoyl andrographolide (AL-1), 14-acetyl-3,9-isopropyl-ideneandrographolide, 14-acetylandrographolide, 3,14,19-triacetylandrographolide, and 3,9-isopropyl-idene andrographolide, are shown to possess significant antiviral activity against HIV, influenza A, HBV, HCV, HPP and HSV. Studies on SARS CoV 2 is restricted to in silico molecular docking studies on viral targets and selected host target proteins. The main targets of andrographolide and its derivatives are fusion and adsorption of virus to the host cell, binding to viral receptor and co-receptor, enzymes involved in DNA/RNA/Genome replication by the virus, translation, post-translation and reverse transcription. Andrographolide as a drug is yet to reach its full therapeutic potential since this molecule shows low bioavailability. Andrographolide therapy is in need of an appropriate delivery system that may increase its bioavailability. Further high-quality studies are needed to firmly establish the clinical efficacy of the plant. • Diagnosis: Covid-19, Sars-Cov-71. • Citation: Ashwini Khanderao Jadhav, Sankunny Mohan Karuppayil. Andrographis paniculata (Burm. F) Wall ex Nees: Antiviral properties. Phytotherapy research : PTR (01 May 2021) PMID:33929758 doi:10.1002/ptr.7145.	PMID: 33929758
15.	14. **Anti-SARS-CoV-2 Activity of Andrographis paniculata Extract and Its Major Component Andrographolide in Human Lung Epithelial Cells and Cytotoxicity Evaluation in Major Organ Cell Representatives**. ABSTRACT: The coronaviruses disease 2019 (COVID-19) caused by a novel coronavirus (SARS-CoV-2) has become a major health problem, affecting more than 50 million people with over one million deaths globally. Effective antivirals are still lacking. Here, we optimized a high-content imaging platform and the plaque assay for viral output study using the legitimate model of human lung epithelial cells, Calu-3, to determine the anti-SARS-CoV-2 activity of Andrographis paniculata extract and its major component, andrographolide. SARS-CoV-2 at 25TCID 50 was able to reach the maximal infectivity of 95% in Calu-3 cells. Postinfection treatment of A. paniculata and andrographolide in SARS-CoV-2-infected Calu-3 cells significantly inhibited the production of infectious virions with an IC 50 of 0.036 µg/mL and 0.034 µM, respectively, as determined by the plaque assay. The cytotoxicity profile developed over the cell line representatives of major organs, including liver (HepG2 and imHC), kidney (HK-2), intestine (Caco-2), lung (Calu-3), and brain (SH-SY5Y), showed a CC 50 of >100 µg/mL for A. paniculata extract and 13.2-81.5 µM for andrographolide, respectively, corresponding to a selectivity index of over 380. In conclusion, this study provided experimental evidence in favor of A. paniculata and andrographolide for further development as a monotherapy or in combination with other effective drugs against SARS-CoV-2 infection. • Diagnosis: Covid-19, Sars-Cov-68. • Citation: Khanit Sa-Ngiamsuntorn, Ampa Suksatu, Yongyut Pewkliang, Piyanoot Thongsri, Phongthon Kanjanasirirat, Suwimon Manopwisedjaroen, Sitthivut Charoensutthivarakul, Patompon Wongtrakoongate, Supaporn Pitiporn, Jarinya Chaopreecha, Supasek Kongsomros, Kedchin J. Anti-SARS-CoV-2 Activity of Andrographis paniculata Extract and Its Major Component Andrographolide in Human Lung Epithelial Cells and Cytotoxicity Evaluation in Major Organ Cell Representatives. Journal of natural products (13 Apr 2021) PMID:33844528 PMC8056600 doi:10.1021/acs.jnatprod.0c01324.	PMID: 33844528
16.	15. **Network bioinformatics analysis provides insight into drug repurposing for COVID-19**. ABSTRACT: The COVID-19 disease caused by the SARS-CoV-2 virus is a health crisis worldwide. While developing novel drugs and vaccines is long, repurposing existing drugs against COVID-19 can yield treatments with known preclinical, pharmacokinetic, pharmacodynamic, and toxicity profiles, which can rapidly enter clinical trials. In this study, we present a novel network-based drug repurposing platform to identify candidates for the treatment of COVID-19. At	PMID: 33817623

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	the time of the initial outbreak, knowledge about SARS-CoV-2 was lacking, but based on its similarity with other viruses, we sought to identify repurposing candidates to be tested rapidly at the clinical or preclinical levels. We first analyzed the genome sequence of SARS-CoV-2 and confirmed SARS as the closest virus by genome similarity, followed by MERS and other human coronaviruses. Using text mining and database searches, we obtained 34 COVID-19-related genes to seed the construction of a molecular network where our module detection and drug prioritization algorithms identified 24 disease-related human pathways, five modules, and 78 drugs to repurpose. Based on clinical knowledge, we re-prioritized 30 potentially repurposable drugs against COVID-19 (including pseudoephedrine, andrographolide, chloroquine, abacavir, and thalidomide). Our work shows how in silico repurposing analyses can yield testable candidates to accelerate the response to novel disease outbreaks. • Diagnosis: Covid-19, Sars-Cov-65. • Citation: Xu Li, Jinchao Yu, Zhiming Zhang, Jing Ren, Alex E Peluffo, Wen Zhang, Yujie Zhao, Jiawei Wu, Kaijing Yan, Daniel Cohen, Wenjia Wang. Network bioinformatics analysis provides insight into drug repurposing for COVID-19. Medicine in drug discovery (06 Apr 2021) PMID:33817623 PMC8008783 doi:10.1016/j.medidd.2021.100090.	
17.	**16. Herbal Medicine in Fighting Against COVID-19: New Battle with an Old Weapon.** ABSTRACT: World population has been suffering due to the outbreak of present pandemic situation of COVID-19. The disease has become life-threatening in a very short time with touching on most of the citizenry and economic systems globally. The novel virus, SARS-CoV-2 has been known as the causative agent of COVID-19. The SARS-CoV-2 is single stranded RNA virus having ~30 kb genomic components which are 70% identical to SARS-CoV. The main process of pathophysiology of COVID-19 has been associated with the interaction of a novel coronavirus with host cell receptor, angiotensin-converting enzyme-2 (ACE 2) by fusion. Therapeutic agents having serine protease inhibitors and ACE-2 blockers may be explored for the treatment by inhibiting the viral target such as Mpro, RdRp, PLpro and helicase. Herbal medicine has a wide array chemical entity with potential health benefits including antiviral activity which may be explored as alternative treatment of COVID-19. The herbal bioactives like catechins, andrographolide, hesperidin, biorobin, scutellarein, silvestrol, shikonin, tryptanthrin, vitexin quercetin, myricetin, caffeic acid, psoralidin, luteolin etc have showed potential inhibitory effect against SARS-CoV-2. Recent research reports indicate that the various plant secondary metabolites have shown the potential antiviral activities. The present review article highlights on the recent information on the mechanism of actions and applications of herbal medicine in the treatment of COVID-19. • Diagnosis: Covid-19, Sars-Cov-62. • Citation: Ranjit K Harwansh, Shiv Bahadur. Herbal Medicine in Fighting Against COVID-19: New Battle with an Old Weapon. Current pharmaceutical biotechnology (23 Mar 2021) PMID:33749558 doi:10.2174/1389201022666210322124348.	PMID: 33749558
18.	**17. Ethnobotany, Pharmacological activities and Bioavailability studies of "King of Bitter" (Kalmegh): A Review (2010-2020).** ABSTRACT: Andrographis paniculata, commonly known as "Kalmegh", is an annual herbaceous plant from family Acanthaceae. The whole plant of A. paniculata has explored for multiple pharmacological activities and is scientifically recognized by in-vivo and in-vitro studies. Various biotechnologically engineered techniques have been explored to enhance the bioavailability of this plant. In this review, we aim to present comprehensive recent advances in the ethnopharmacology, phytochemistry, specific pharmacology, safety and toxicology and bioavailability of A. paniculata and its pure compounds. Possible directions for future research are also outlined in brief, which will encourage advance investigations on this plant. Information on the recent updates of the present review is collected from different electronic scientific databases such as Science Direct, PubMed, Scopus, and Google Scholar. All the composed information is classified into different sections according to the objective of the paper. More than hundred research and review papers have been studied and incorporated in the present manuscript. After vast literature search of A. paniculata, we present a noteworthy report of various phytoconstituents present in plant, which are accountable for potential therapeutic properties of the plant. Forty-five of studied articles give general information about introduction, ethnobotany and traditional uses of the plant. Twenty-two papers enclosed information about the phytoconstituents present in different parts of A. paniculata and seventy-two papers briefly outlined the pharmacological activities like antioxidant, anti-dengue, anti-ulcerogenic, antifungal, some miscellaneous activities like activity against SARS-CoV-2, antidiarrhoeal. Nineteen studies highlighted the research work conducted by various researchers to increased bioavailability of A. paniculata and two studies reported the safety and toxicology of the plant. This review incorporated the scientifically validated research work	PMID: 33745423

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	encompassing the ethnobotanical description of the subjected plant, phytochemical profile, various pharmacological activities, and recent approaches to enhance the bioavailability of active metabolites. • Diagnosis: Covid-19, Sars-Cov-59. • Citation: Sharuti Mehta, Anil Kumar Sharma, Rajesh Kumar Singh. Ethnobotany, Pharmacological activities and Bioavailability studies of "King of Bitter" (Kalmegh): A Review (2010-2020). Combinatorial chemistry & high throughput screening (23 Mar 2021) PMID:33745423 doi:10.2174/1386207324666210310140611.	
19.	18. **An in-silico approach to identify the potential hot spots in SARS-CoV-2 spike RBD to block the interaction with ACE2 receptor**. ABSTRACT: A novel acute viral pneumonia induced by SARS-CoV-2 exploded at the end of 2019, causing a severe medical and economic crisis. For developing specific pharmacotherapy against SARS-CoV-2, an in silico virtual screening was developed for the available in-house molecules. The conserved domain analysis was performed to identify the highly conserved and exposed amino acid regions in the SARS-CoV-2-S RBD sites. The Protein-Protein interaction analyses demonstrated the higher affinity between the SARS-CoV-2-S and ACE2 due to varieties of significant interactions between them. The computational alanine scanning mutation study has recognized the highly stabilized amino acids in the SARS-CoV-2-S RBD/ACE2 complex. The cumulative sequence investigations have inferred that Lys417, Phe486, Asn487, Tyr489, and Gln493 are perhaps the iconic target amino acids to develop a drug molecule or vaccine against SARS-CoV-2 infection. Most of the selected compounds include luteolin, zhebeirine, 3-dehydroverticine, embelin, andrographolide, ophiopogonin D, crocin-1, sprengerinin A, B, C, peimine, etc. were exhibited distinguish drug actions through the strong hydrogen bonding with the hot spots of the RBD. Besides, the 100 ns molecular dynamics simulation and free energy binding analysis showed the significant efficacy of luteolin to inhibit the infection of SARS-CoV-2.Communicated by Ramaswamy H. Sarma. • Diagnosis: Covid-19, Sars-Cov-56. • Citation: Antony Stalin, Ding Lin, Balakrishnan Senthamarai Kannan, Yue Feng, Yanjing Wang, Wei Zhao, Savarimuthu Ignacimuthu, Dong-Qing Wei, Yuan Chen. An in-silico approach to identify the potential hot spots in SARS-CoV-2 spike RBD to block the interaction with ACE2 receptor. Journal of biomolecular structure & dynamics (10 Mar 2021) PMID:33685364 doi:10.1080/07391102.2021.1897682.	PMID: 33685364
20.	19. **Estimation of drug-likeness properties of GC-MS separated bioactive compounds in rare medicinal Pleione maculata using molecular docking technique and SwissADME in silico tools**. ABSTRACT: The main aim of the paper was to determine bioactive compounds in Pleione maculata extracts using gas chromatographic technique and to investigate their drug-likeness potential using molecular docking algorithm and ADME studies on the recent intractable disease, for example, SARS-CoV-2. Pleione maculata sample was prepared for GC-MS analysis. The peak components were identified based on the NIST Library. Molecular docking was performed using PatchDock, and energy refinement was carried out using the FireDock algorithm followed by drug-likeness analysis using the SwissADME tool. The mass spectrum revealed various pharmacologically important compounds and novel compounds 8-oxatetracyclo{5.2.1.1(2,6). 1(4,10)}dodecane, 7-tert-butyl-1,9,9-trimeth, docosane, 2,4-dimethyl, kryptogenin 2,4-dinitrophenyl hydrazine, and N -decyl-alpha, D -2-deoxyglycoside which are reported for the first time. Molecular docking using PatchDock illustrates GC-MS compounds Nor-diazepam,3-{ N -hydroxymethyl}aminocarbonyloxy a good docking and high binding affinity with atomic contact energy -10.95 kcal/mol against SARS-CoV-2 spike protein S2 subunit. ADME analysis predicts Nor-diazepam,3-{N-hydroxymethyl}aminocarbonyloxy and andrographolide showed very high drug-likeness parameters with no metabolism disturbances. The random control antiviral drug arabidiol revealed a lower binding affinity and lower solubility compared to bioactive compounds of P. maculata . The study depicts the first and novel report on various pharmaceutical important GC-MS bioactive compounds and molecular docking study on Pleione maculata having potential against various intractable diseases. The online version contains supplementary material available at 10.1007/s13721-020-00276-1. • Diagnosis: Covid-19, Sars-Cov-53. • Citation: Hakani D Sympli. Estimation of drug-likeness properties of GC-MS separated bioactive compounds in rare medicinal Pleione maculata using molecular docking technique and SwissADME in silico tools. Network modeling and analysis in health informatics and bioinformatics (02 Mar 2021) PMID:33643765 PMC7903411 doi:10.1007/s13721-020-00276-1.	PMID: 33643765
21.	**20. Natural Agents Modulating ACE-2: A Review of Compounds with Potential against SARS-CoV-2 Infections.**	PMID: 33459225

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	ABSTRACT: One of the biggest challenges of public health worldwide is reducing the number of events and deaths related to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections. The angiotensinconverting enzyme 2 (ACE-2), a carboxypeptidase that degrades angiotensin II into angiotensin 1-7, has been identified as a potent receptor for SARS-CoV-2. In the last decades, ACE inhibition has assumed a central role in reducing cardiovascular and renal events. However, with the advent of COVID-19, attention has been turned to ACE-2 as a possible target to reduce virus binding to different human cells. This review aims to discuss recent developments related to the medicinal properties of natural compounds as ACE/ACE-2 inhibitors, which should be highlighted in the future development of studies looking for modulators in SARS-CoV-2 infection. Data show that bioactive compounds isolated from several natural products act by inhibiting ACE/ACE-2, which changes the entire axis of this system. Of the compounds addressed in this review, 7 phenolic compounds, including quercetin, curcumin, naringenin, luteolin, hesperidin, mangiferin, and gallic acid showed binding affinity with molecular ACE-2 target in silico, and 1, esculetin, decreased ACE-2 expression in vivo. Regarding terpenoids and alkaloids, nimbin, withaferin A, andrographolide, zingiberene and, berberine, piperine and thebaine, respectively, showed a binding affinity with molecular ACE-2 target in silico. These findings reinforce the need for future preclinical and clinical studies on these compounds and specific inhibitory effects on ACE-2 of all the other compounds described herein only as nonspecific ACE inhibitors. It is important to mention that some natural compounds such as magnolol, resveratrol, rosmarinic acid, tanshinone IIA, and nicotine have also demonstrated the potential to increase the activity or expression of ACE-2, and could therefore aggravate SARS-CoV-2 infection. • Diagnosis: Covid-19, Sars-Cov-50. • Citation: Arquimedes Gasparotto Junior, Sara Emília Lima Tolouei, Francislaine Aparecida Dos Reis Lívero, Francielli Gasparotto, Thaise Boeing, Priscila de Souza. Natural Agents Modulating ACE-2: A Review of Compounds with Potential against SARS-CoV-2 Infections. Current pharmaceutical design (19 Jan 2021) PMID:33459225 doi:10.2174/1381612827666210114150607.	
22.	21. **In silico docking analysis revealed the potential of phytochemicals present in Phyllanthus amarus and Andrographis paniculata, used in Ayurveda medicine in inhibiting SARS-CoV-2**. ABSTRACT: The Severe acute respiratory syndrome coronavirus- 2 (SARS-CoV-2) has resulted in outbreak of global pandemic, fatal pneumonia in human referred as Coronavirus Disease-2019 (Covid-19). Ayurveda, the age old practice of treating human ailments in India, can be considered against SARS-CoV-2. Attempt was made to provide preliminary evidences for interaction of 35 phytochemicals from two plants (Phyllanthus amarus and Andrographis paniculata used in Ayurveda) with SARS-CoV-2 proteins (open & closed state S protein, 3CLpro, PLpro and RdRp) through in silico docking analysis. The nucleotide analogue remdesivir, being used in treatment of SARS-CoV-2, was used as a positive control. The results revealed that 18 phytochemicals from P. amarus and 14 phytochemicals from A. paniculata shown binding energy affinity/dock score < - 6.0 kcal/mol, which is considered as minimum threshold for any compound to be used for drug development. Phytochemicals used for docking studies in the current study from P. amarus and A. paniculata showed binding affinity up to - 9.10 kcal/mol and - 10.60 kcal/mol, respectively. There was no significant difference in the binding affinities of these compounds with closed and open state S protein. Further, flavonoids (astragalin, kaempferol, quercetin, quercetin-3- O -glucoside and quercetin) and tannins (corilagin, furosin and geraniin) present in P. amarus have shown more binding affinity (up to - 10.60 kcal/mol) than remdesivir (up to - 9.50 kcal/mol). The pharmacokinetic predictions suggest that compounds from the two plants species studied in the current study are found to be non-carcinogenic, water soluble and biologically safe. The phytochemicals present in the extracts of P. amarus and A. paniculata might have synergistic effect with action on multiple target sites of SARS-CoV-2. The information generated here might serve as preliminary evidence for anti SARS-CoV-2 activity of phytochemicals present from P. amarus and A. paniculata and the potential of Ayurveda medicine in combating the virus. The online version contains supplementary material available at 10.1007/s13205-020-02578-7. • Diagnosis: Covid-19, Sars-Cov-47. • Citation: Shridhar Hiremath, H D Vinay Kumar, M Nandan, M Mantesh, K S Shankarappa, V Venkataravanappa, C R Jahir Basha, C N Lakshminarayana Reddy. In silico docking analysis revealed the potential of phytochemicals present in Phyllanthus amarus and Andrographis paniculata, used in Ayurveda medicine in inhibiting SARS-CoV-2. 3 Biotech (19 Jan 2021) PMID:33457171 PMC7799430 doi:10.1007/s13205-020-02578-7.	PMID: 33457171
23.	**22. The coronavirus disease 2019 main protease inhibitor from Andrographis paniculata (Burm. f) Ness.** ABSTRACT:	PMID: 33425697

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	The coronavirus disease 2019 (COVID-19) pandemic has attracted worldwide attention. Andrographis paniculata (Burm. f) Ness (AP) is naturally used to treat various diseases, including infectious diseases. Its Andrographolide has been clinically observed for anti-HIV and has also in silico tested for COVID-19 main protease inhibitors. Meanwhile, the AP phytochemicals content also provides insight into the molecular structures diversity for the bioactive discovery. This study aims to find COVID-19 main protease inhibitor from AP by the molecular docking method and determine the toxicity profile of the compounds. The results obtained two compounds consisting of flavonoid glycosides 5,4'-dihydroxy-7-O- β -D-pyran-glycuronate butyl ester and andrographolide glycoside 3-O-β-D -glucopyranosyl-andrographolide have lower free binding energy and highest similarity in types of interaction with amino acid residues compared to its co-crystal ligands (6LU7) and Indinavir or Remdesivir. The toxicity prediction of the compounds also reveals their safety. These results confirm the probability of using AP phytochemical compounds as COVID-19 main protease inhibitors, although further research must be carried out. • Diagnosis: Covid-19, Sars-Cov-45. • Citation: Sukardiman, Martha Ervina, Mohammad Rizki Fadhil Pratama, Hadi Poerwono, Siswandono Siswodihardjo. The coronavirus disease 2019 main protease inhibitor from Andrographis paniculata (Burm. f) Ness. Journal of advanced pharmaceutical technology & research (12 Jan 2021) PMID:33425697 PMC7784943 doi:10.4103/japtr.JAPTR_84_20.	
24.	**23. Activity of phytochemical constituents of Curcuma longa (turmeric) and Andrographis paniculata against coronavirus (COVID-19): an in silico approach.** ABSTRACT: In early 2020, many scientists are rushing to discover novel drugs and vaccines against the coronavirus, and treatments for COVID-19, because coronavirus disease 2019 (COVID-19), a life-threatening viral disease, affected first in China and quickly spread throughout the world. In this article, in silico studies have been performed to explore the binding modes of chemical constituents for natural remedies like Curcuma longa (turmeric) and Andrographis paniculata against COVID-19 (PDB ID 5R82) targeting coronavirus using Schrodinger suit 2019-4. The molecular docking studies are performed by the Glide module, in silico ADMET screening was performed by the QikProp module, and binding energy of ligands was calculated using the Prime MM-GB/SA module. The chemical constituents from turmeric like cyclocurcumin and curcumin and from Andrographis paniculata like andrographolide and dihydroxy dimethoxy flavone are significantly binding with the active site of SARS CoV-2 main protease with Glide score more than - 6 when compared to the currently used drugs hydroxychloroquine (- 5.47) and nelfinavir (- 5.93). When compared to remdesivir (- 6.38), cyclocurcumin from turmeric is significantly more active. The docking results of the compounds exhibited similar mode of interactions with SARS CoV-2. Main protease and the residues THR24, THR25, THR26, LEU27, SER46, MET49, HIE41, GLN189, ARG188, ASP187, MET165, HIE164, PHE181, and THR54 play a crucial role in binding with ligands. Based on in silico investigations, the chemical constituents from turmeric like cyclocurcumin and curcumin and from Andrographis paniculata like andrographolide and dihydroxy dimethoxy flavone, significantly binding with the active site of SARS CoV-2 main protease, may produce significant activity and be useful for further development. • Diagnosis: Covid-19, Sars-Cov-42. • Citation: Kalirajan Rajagopal, Potlapati Varakumar, Aparma Baliwada, Gowramma Byran. Activity of phytochemical constituents of Curcuma longa (turmeric) and Andrographis paniculata against coronavirus (COVID-19): an in silico approach. Future journal of pharmaceutical sciences (21 Nov 2020) PMID:33215042 PMC7562761 doi:10.1186/s43094-020-00126-x.	PMID: 33215042
25.	**24. Molecular basis for drug repurposing to study the interface of the S protein in SARS-CoV-2 and human ACE2 through docking, characterization, and molecular dynamics for natural drug candidates.** ABSTRACT: A novel coronavirus (SARS-CoV-2) identified in Wuhan state of China in 2019 is the causative agent of deadly disease COVID-19. It has spread across the globe (more than 210 countries) within a short period. Coronaviruses pose serious health threats to both humans and animals. A recent publication reported an experimental 3D complex structure of the S protein of SARS-CoV-2 showed that the ectodomain of the SARS-CoV-2 S protein binds to the peptidase domain (PD) of human ACE2 with a dissociation constant (Kd) of ~ 15 nM. In this study, we focused on inhibitors for ACE2: S protein complex using virtual screening and inhibition studies through molecular docking for over 200,000 natural compounds. Toxicity analysis was also performed for the best hits, and the final complex structures for four complexes were subjected to 400 ns molecular dynamics simulations for stability testing. We found two natural origin inhibitors for the S protein: human ACE2 complex (Andrographolide and Pterostilbene) which displayed better inhibition potential for ACE2 receptor and its binding with the S protein of SARS-CoV-2. Comparative studies were also performed to test and verify that these two drug candidates are also	PMID: 33175236

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	better than hydroxychloroquine which is known to inhibit this complex. However, we needed better potential drug candidates to overcome the side effects of hydroxychloroquine. Supplementary experimental studies need to be carried forward to corroborate the viability of these two new inhibitors for ACE2: S protein complex so as to curb down COVID-19. • Diagnosis: Covid-19, Sars-Cov-39. • Citation: Meshari Alazmi, Olaa Motwalli. Molecular basis for drug repurposing to study the interface of the S protein in SARS-CoV-2 and human ACE2 through docking, characterization, and molecular dynamics for natural drug candidates. Journal of molecular modeling (12 Nov 2020) PMID:33175236 PMC7657070 doi:10.1007/s00894-020-04599-8.	
26.	**25. Immunoprotective potential of Ayurvedic herb Kalmegh (Andrographis paniculata) against respiratory viral infections - LC-MS/MS and network pharmacology analysis.** ABSTRACT: Immunity boosting has emerged as a global strategy to fight the SARS-CoV-2 pandemic situation. In India, AYUSH systems of medicine have been promoted as an immune-protection strategy. Andrographis paniculata (Burm. F) Nees (AP) mentioned in Ayurveda has been widely used for treating sore throat, flu, and upper respiratory tract infections which may provide possible novel therapeutic approaches, exclusively targeting SARS-CoV-2 and its pathways. The present work uses liquid chromatography-tandem mass spectrometry (LC-MS/MS) metabolomics and combination synergy analysis based on network pharmacology to mine multimode evidence to understand the possible mechanism of action, diseases association, protein-protein interaction and major pathways involved therein. Metabolite profiling was performed by Agilent QTOF LC-MS/MS system. Network pharmacology analysis was performed by using functional annotation analysis based on databases like Binding DB, STRING, DAVID and KEGG for further data mining. Further combination synergy was evaluated using "neighbourhood approach" and networks were constructed through Cytoscape 3.2.1. The molecules from kalmegh provides immune-protection and anti-viral response via involving different pathways, like toll-like receptor pathway, PI3/AKT pathway and MAP kinase pathways against COVID-19 infection. The KEGG analysis showed that in a vast majority of the most enriched pathways, AP were associated with viral infections and upper respiratory tract infections. The results suggest a synergy between andrographolide and other molecules identified as safe and efficacious anti-inflammatory agent having effects on upper respiratory tract infections and can significantly decrease the production of cytokines and pro-inflammatory factors in viral infections. • Diagnosis: Covid-19, Sars-Cov-36. • Citation: Subhadip Banerjee, Amit Kar, Pulok K Mukherjee, Pallab K Haldar, Nanaocha Sharma, Chandra Kant Katiyar. Immunoprotective potential of Ayurvedic herb Kalmegh (Andrographis paniculata) against respiratory viral infections - LC-MS/MS and network pharmacology analysis. Phytochemical analysis : PCA (10 Nov 2020) PMID:33167083 doi:10.1002/pca.3011.	PMID: 33167083
27.	**26. A pharmacology-based comprehensive review on medicinal plants and phytoactive constituents possibly effective in the management of COVID-19.** ABSTRACT: Arisen in China, COVID-19 (SARS-CoV-II) is a novel coronavirus that has been expanding fast worldwide. Till now, no definite remedial drug or vaccine has been identified for COVID-19 treatment. Still, for a majority of infected patients, supportive therapy is the cornerstone of the management plan. To the importance of managing the COVID-19 pandemic, this article proposed to collecting capable medicinal plants and bioactive components in both treat and supportive therapy of this novel viral infection. Clinical points in the pathogenesis, symptoms, and complications of COVID-19 were considered. The effective plants and bioactives that may play a role in supportive therapy/management of COVID-19 were searched, collected through the "Scopus" database and listed in three sections. Numerous medicinal plants such as Citrus Spp., Camellia sinensis, and Glycyrrhiza glabra can interference with COVID-19 pathogenesis via inhibition of virus replication and entry to its host cells. Also, some anti-inflammatory herbal medicine such as Andrographis paniculata, Citrus spp., and Cuminum cyminum can relieve fever and cough in COVID-19 patients. Medicinal plants such as G. glabra, Thymus vulgaris, Allium sativum, Althea officinalis, and Panax ginseng may modulate the immune system and possess prevention and supportive therapy. However, more clinical data are required to confirm these hypotheses. • Diagnosis: Covid-19, Sars-Cov-34. • Citation: Atefeh Jalali, Farid Dabaghian, Hossein Akbrialiabad, Farzaneh Foroughinia, Mohammad M Zarshenas. A pharmacology-based comprehensive review on medicinal plants and phytoactive constituents possibly effective in the management of COVID-19. Phytotherapy research : PTR (08 Nov 2020) PMID:33159391 doi:10.1002/ptr.6936.	PMID: 33159391

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28.	**27. COVID-19: Is There Evidence for the Use of Herbal Medicines as Adjuvant Symptomatic Therapy?** ABSTRACT: Current recommendations for the self-management of SARS-Cov-2 disease (COVID-19) include self-isolation, rest, hydration, and the use of NSAID in case of high fever only. It is expected that many patients will add other symptomatic/adjuvant treatments, such as herbal medicines. To provide a benefits/risks assessment of selected herbal medicines traditionally indicated for "respiratory diseases" within the current frame of the COVID-19 pandemic as an adjuvant treatment. The plant selection was primarily based on species listed by the WHO and EMA, but some other herbal remedies were considered due to their widespread use in respiratory conditions. Preclinical and clinical data on their efficacy and safety were collected from authoritative sources. The target population were adults with early and mild flu symptoms without underlying conditions. These were evaluated according to a modified PrOACT-URL method with paracetamol, ibuprofen, and codeine as reference drugs. The benefits/risks balance of the treatments was classified as positive , promising , negative , and unknown . A total of 39 herbal medicines were identified as very likely to appeal to the COVID-19 patient. According to our method, the benefits/risks assessment of the herbal medicines was found to be positive in 5 cases (Althaea officinalis, Commiphora molmol, Glycyrrhiza glabra, Hedera helix , and Sambucus nigra), promising in 12 cases (Allium sativum , Andrographis paniculata , Echinacea angustifolia, Echinacea purpurea, Eucalyptus globulus essential oil , Justicia pectoralis, Magnolia officinalis , Mikania glomerata , Pelargonium sidoides , Pimpinella anisum , Salix sp, Zingiber officinale), and unknown for the rest. On the same grounds, only ibuprofen resulted promising, but we could not find compelling evidence to endorse the use of paracetamol and/or codeine. Our work suggests that several herbal medicines have safety margins superior to those of reference drugs and enough levels of evidence to start a clinical discussion about their potential use as adjuvants in the treatment of early/mild common flu in otherwise healthy adults within the context of COVID-19. While these herbal medicines will not cure or prevent the flu, they may both improve general patient well-being and offer them an opportunity to personalize the therapeutic approaches. • Diagnosis: Covid-19, Sars-Cov-31. • Citation: Dâmaris Silveira, Jose Maria Prieto-Garcia, Fabio Boylan, Omar Estrada, Yris Maria Fonseca-Bazzo, Claudia Masrouah Jamal, Pérola Oliveira Magalhães, Edson Oliveira Pereira, Michal Tomczyk, Michael Heinrich. COVID-19: Is There Evidence for the Use of Herbal Medicines as Adjuvant Symptomatic Therapy? Frontiers in pharmacology (20 Oct 2020) PMID:33071794 PMC7542597 doi:10.3389/fphar.2020.581840.	PMID: 33071794
29.	28. **Andrographolide and its fluorescent derivative inhibit the main proteases of 2019-nCoV and SARS-CoV through covalent linkage**. ABSTRACT: The coronavirus disease 2019 (COVID-19) pandemic caused by 2019 novel coronavirus (2019-nCoV) has been a crisis of global health, whereas the effective vaccines against 2019-nCoV are still under development. Alternatively, utilization of old drugs or available medicine that can suppress the viral activity or replication may provide an urgent solution to suppress the rapid spread of 2019-nCoV. Andrographolide is a highly abundant natural product of the medicinal plant, Andrographis paniculata, which has been clinically used for inflammatory diseases and anti-viral therapy. We herein demonstrate that both andrographolide and its fluorescent derivative, the nitrobenzoxadiazole-conjugated andrographolide (Andro- NBD), suppressed the main protease (M pro) activities of 2019-nCoV and severe acute respiratory syndrome coronavirus (SARS-CoV). Moreover, Andro-NBD was shown to covalently link its fluorescence to these proteases. Further mass spectrometry (MS) analysis suggests that andrographolide formed a covalent bond with the active site Cys 145 of either 2019-nCoV M pro or SARS-CoV M pro . Consistently, molecular modeling analysis supported the docking of andrographolide within the catalytic pockets of both viral M pro s. Considering that andrographolide is used in clinical practice with acceptable safety and its diverse pharmacological activities that could be beneficial for attenuating COVID-19 symptoms, extensive investigation of andrographolide on the suppression of 2019-nCoV as well as its application in COVID-19 therapy is suggested. • Diagnosis: Covid-19, Sars-Cov-28. • Citation: Tzu-Hau Shi, Yi-Long Huang, Chiao-Che Chen, Wen-Chieh Pi, Yu-Ling Hsu, Lee-Chiang Lo, Wei-Yi Chen, Shu-Ling Fu, Chao-Hsiung Lin. Andrographolide and its fluorescent derivative inhibit the main proteases of 2019-nCoV and SARS-CoV through covalent linkage. Biochemical and biophysical research communications (27 Sep 2020) PMID:32977949 PMC7447262 doi:10.1016/j.bbrc.2020.08.086.	PMID: 32977949
30.	29. Molecular modelling investigation for drugs and nutraceuticals against protease of SARS-CoV-2. ABSTRACT:	PMID: 32861974

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	The widespread problem of a 2019-novel coronavirus (SARS-CoV-2) strain outbreak in Wuhan, China has prompted a search for new drugs to protect against and treat this disease. It is necessary to immediately investigate this due to the mutation of the viral genome and there being no current protective vaccines or therapeutic drugs. Molecular modelling and molecular docking based on in silico screening strategies were employed to determine the potential activities of seven HIV protease (HIV-PR) inhibitors, two flu drugs, and eight natural compounds. The computational approach was carried out to discover the structural modes with a high binding affinity for these drugs on the homology structure of the Wuhan coronavirus protease (SARS-CoV-2 PR). From the theoretical calculations, all the drugs and natural compounds demonstrated various favorable binding affinities. An interesting finding was that the natural compounds tested had a higher potential binding activity with the pocket sites of SARS-CoV-2 PR compared to the groups of HIV-PR inhibitors. The binding modes of each complex illustrated between the drugs and compounds interacted with the functional group of amino acids in the binding pocket via hydrophilic, hydrophobic, and hydrogen bond interactions using the molecular dynamics simulation technique. This result supports the idea that existing protease inhibitors and natural compounds could be used to treat the new coronavirus. This report sought to provide fundamental knowledge as preliminary experimental data to propose an existing nutraceutical material against viral infection. Collectively, it is suggested that molecular modelling and molecular docking are suitable tools to search and screen for new drugs and natural compounds that can be used as future treatments for viral diseases. • Diagnosis: Covid-19, Sars-Cov-25. • Citation: Kanchanok Kodchakorn, Yong Poovorawan, Kamol Suwannakarn, Prachya Kongtawelert. Molecular modelling investigation for drugs and nutraceuticals against protease of SARS-CoV-2. Journal of molecular graphics & modelling (31 Aug 2020) PMID:32861974 PMC7434411 doi:10.1016/j.jmgm.2020.107717.	
31.	**30. Molecular docking analysis of Withaferin A from Withania somnifera with the Glucose regulated protein 78 (GRP78) receptor and the SARS-CoV-2 main protease.** ABSTRACT: Design and development of an effective compound to combat COVID-19 is clearly critical in the current circumstances. Therefore, it is of interest to document the molecular docking analysis data of the cellular receptor Glucose regulated protein 78 (GRP78) with Withaferin A from Withania somnifera in the context of COVID-19 pandemic for further consideration. Here, we report the optimal interaction features of withaferin A, artemisinin, curcumin and andrographolide with the GRP78 receptor having low binding energies (-8.7, -7.89, -6.21 and -6.17 kcal/mol respectively) in this report. In order to gain additional insights, the interaction pattern of compounds with SARS-CoV-2 main protease (Mpro) was studied. • Diagnosis: Covid-19, Sars-Cov-22. • Citation: H V Sudeep, K Gouthamchandra, K Shyamprasad. Molecular docking analysis of Withaferin A from Withania somnifera with the Glucose regulated protein 78 (GRP78) receptor and the SARS-CoV-2 main protease. Bioinformation (25 Aug 2020) PMID:32831523 PMC7434955 doi:10.6026/97320630016411.	PMID: 32831523
32.	**31. Establishment and validation of a drug-target microarray for SARS-CoV-2.** ABSTRACT: COVID-19 has become one of the worst epidemic in the world, currently already more than four million people have been infected, which probably co-exist with human beings, and has a significant impact on the global economy and political order. In the process of fighting against the epidemic in China, the clinical value of a variety of herbal medicines has been recognized and written into the clinical application guide. However, their effective molecular mechanism and potential targets are still not clear. Pathology and pharmacology research will gradually attract attention in the post-epidemic outbreak term. Here, we constructed a COVID-19 protein microarray of potential therapy targets, which contains the main drug targets to the SARS-CoV-2 virus and the anti-virus, anti-inflammatory cellar targets of the host. Series of quality controls test has been carried out, which showed that it could be applied for drug target screening of bio-active natural products. The establishment of this microarray will provide a useful tool for the study of the molecular pharmacology of natural products. • Diagnosis: Covid-19, Sars-Cov-19. • Citation: Peng Chen, Zehua Zeng, Hongwu Du. Establishment and validation of a drug-target microarray for SARS-CoV-2. Biochemical and biophysical research communications (24 Aug 2020) PMID:32828312 PMC7373225 doi:10.1016/j.bbrc.2020.05.217.	PMID: 32828312
33.	**32. Structure-based drug designing for potential antiviral activity of selected natural products from Ayurveda against SARS-CoV-2 spike glycoprotein and its cellular receptor.**	PMID: 32656311

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	ABSTRACT: The recent outbreak of COVID-19 caused by SARS-CoV-2 brought a great global public health and economic concern. SARS-CoV-2 is an enveloped RNA virus, from the genus Betacoronavirus. Although few molecules have been tested and shown some efficacy against SARS-CoV-2 in humans but a safe and cost-effective attachment inhibitors are still required for the treatment of COVID-19. Natural products are gaining attention because of the large therapeutic window and potent antiviral, immunomodulatory, anti-inflammatory, and antioxidant properties. Therefore, this study was planned to screen natural products from Ayurveda that have the potential to modulate host immune system as well as block the virus entry in host cells by interfering its interaction with cellular receptor and may be used to develop an effective and broad-spectrum strategy for the management of COVID-19 as well as other coronavirus infections in coming future. To decipher the antiviral activity of the selected natural products, molecular docking was performed. Further, the drug-likeness, pharmacokinetics and toxicity parameters of the selected natural products were determined. Docking results suggest that curcumin and nimbin exhibits highest interaction with spike glycoprotein (MolDock score - 141.36 and - 148.621 kcal/mole) and ACE2 receptor (MolDock score - 142.647 and - 140.108 kcal/mole) as compared with other selected natural products/drugs and controls. Also, the pharmacokinetics data illustrated that all selected natural products have better pharmacological properties (low molecular weight; no violation of Lipinski rule of five, good absorption profiles, oral bioavailability, good blood-brain barrier penetration, and low toxicity risk). Our study exhibited that curcumin, nimbin, withaferin A, piperine, mangiferin, thebaine, berberine, and andrographolide have significant binding affinity towards spike glycoprotein of SARS-CoV-2 and ACE2 receptor and may be useful as a therapeutic and/or prophylactic agent for restricting viral attachment to the host cells. However, few other natural products like resveratrol, quercetin, luteolin, naringenin, zingiberene, and gallic acid has the significant binding affinity towards ACE2 receptor only and therefore may be used for ACE2-mediated attachment inhibition of SARS-CoV-2. • Diagnosis: Covid-19, Sars-Cov-16. • Citation: Vimal K Maurya, Swatantra Kumar, Anil K Prasad, Madan L B Bhatt, Shailendra K Saxena. Structure-based drug designing for potential antiviral activity of selected natural products from Ayurveda against SARS-CoV-2 spike glycoprotein and its cellular receptor. Virusdisease (14 Jul 2020) PMID:32656311 PMC7245990 doi:10.1007/s13337-020-00598-8.	
	33. Ethnomedicines of Indian origin for combating COVID-19 infection by hampering the viral replication: using structure-based drug discovery approach. ABSTRACT: In the present study, we have explored the interaction of the active components from 10 different medicinal plants of Indian origin that are commonly used for treating cold and respiratory-related disorders, through molecular docking analysis. In the current scenario, COVID-19 patients experience severe respiratory syndromes, hence it is envisaged from our study that these traditional medicines are very likely to provide a favourable effect on COVID-19 infections. The active ingredients identified from these natural products are previously reported for antiviral activities against large group of viruses. Totally 47 bioactives identified from the medicinal plants were investigated against the structural targets of SARS-CoV-2 (Mpro and spike protein) and human ACE2 receptor. The top leads were identified based on interaction energies, number of hydrogen bond and other parameters that explain their potency to inhibit SARS-CoV-2. The bioactive ligands such as Cucurbitacin E, Orientin, Bis-andrographolide,
34.	Cucurbitacin B, Isocucurbitacin B, Vitexin, Berberine, Bryonolic acid, Piperine and Magnoflorine targeted the hotspot residues of SARS-CoV-2 main protease. In fact, this protease enzyme has an essential role in mediating the viral replication and therefore compounds targeting this key enzyme are expected to block the viral replication and transcription. The top scoring conformations identified through docking analysis were further demonstrated with molecular dynamics simulation. Besides, the stability of the conformation was studied in detail by investigating the binding free energy using MM-PBSA method. Overall, the study emphasized that the proposed hit Cucurbitacin E and orientin could serve as a promising scaffold for developing anti-COVID-19 drug.Communicated by Ramaswamy H. Sarma. • Diagnosis: Covid-19, Sars-Cov-13. • Citation: Selvaraj Alagu Lakshmi, Raja Mohamed Beema Shafreen, Arumugam Priya, Karutha Pandian Shunmugiah. Ethnomedicines of Indian origin for combating COVID-19 infection by hampering the viral replication: using structure-based drug discovery approach. Journal of biomolecular structure & dynamics (24 Jun 2020) PMID:32573351 PMC7332876 doi:10.1080/07391102.2020.1778537.	PMID: 32573351
	34. Computational investigation on Andrographis paniculata phytochemicals to evaluate their potency against SARS-CoV-2 in comparison to known antiviral compounds in drug trials.	
35.	ABSTRACT:	PMID: 32543978

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	The outbreak due to SARS-CoV-2 (or Covid-19) is spreading alarmingly and number of deaths due to infection is aggressively increasing every day. Due to the rapid human to human transmission of Covid-19, we are in need to find a potent drug at the earliest by ruling-out the traditional time-consuming approach of drug development. This is only possible if we use reliable computational approaches for screening compounds from chemical space or by drug repurposing or by finding the phytochemicals and nutraceuticals from plants as they can be immediately used without the need for carrying out drug-trials to test safety and efficacy. A number of plant products were routinely suggested as drugs in traditional Indian and Chinese medicine. Here using molecular docking approach, and combined molecular dynamics and MM-GBSA based free energy calculations approach, we study the potency of the four selected phytochemicals namely andrographolide (AGP1), 14-deoxy 11,12-didehydro andrographolide (AGP2), neoandrographolide (AGP3) and 14-deoxy andrographolide (AGP4) from A. paniculata plant against the four key targets including three non-structural proteins (3 L main protease (3CLpro), Papain-like proteinase (PLpro) and RNA-directed RNA polymerase (RdRp)) and a structural protein (spike protein (S)) of the virus which are responsible for replication, transcription and host cell recognition. The therapeutic potential of the selected phytochemicals against Covid-19 were also evaluated in comparison with a few commercially available drugs. The binding free energy data suggest that AGP3 could be used as a cost-effective drug-analog for treating covid-19 infection in developing countries.Communicated by Ramaswamy H. Sarma. • Diagnosis: Covid-19, Sars-Cov-7. • Citation: Natarajan Arul Murugan, Chitra Jeyaraj Pandian, Jeyaraman Jeyakanthan. Computational investigation on Andrographis paniculata phytochemicals to evaluate their potency against SARS-CoV-2 in comparison to known antiviral compounds in drug trials. Journal of biomolecular structure & dynamics (17 Jun 2020) PMID:32543978 PMC7309306 doi:10.1080/07391102.2020.1777901.	
36.	**35. Crosstalk between endoplasmic reticulum stress and anti-viral activities: A novel therapeutic target for COVID-19.** ABSTRACT: The outbreak of COVID-19 caused by 2019-nCov/SARS-CoV-2 has become a pandemic with an urgent need for understanding the mechanisms and identifying a treatment. Viral infections including SARS-CoV are associated with increased levels of reactive oxygen species, disturbances of Ca ++ caused by unfolded protein response (UPR) mediated by endoplasmic reticulum (ER) stress and is due to the exploitation of virus's own protein i.e., viroporins into the host cells. Several clinical trials are on-going including testing Remdesivir (anti-viral), Chloroquine and Hydroxychloroquine derivatives (anti-malarial drugs) etc. Unfortunately, each drug has specific limitations. Herein, we review the viral protein involvement to activate ER stress transducers (IRE-1, PERK, ATF-6) and their downstream signals; and evaluate combination therapies for COVID-19 mediated ER stress alterations. Melatonin is an immunoregulator, anti-pyretic, antioxidant, anti-inflammatory and ER stress modulator during viral infections. It enhances protective mechanisms for respiratory tract disorders. Andrographolide, isolated from Andrographis paniculata, has versatile biological activities including immunomodulation and determining SARS-CoV-2 binding site. Considering the properties of both compounds in terms of anti-inflammatory, antioxidant, anti-pyrogenic, anti-viral and ER stress modulation and computational approaches revealing andrographolide docks with the SARS-CoV2 binding site, we predict that this combination therapy may have potential utility against COVID-19. • Diagnosis: Covid-19, Sars-Cov-4. • Citation: Aditi Banerjee, Steven J Czinn, Russel J Reiter, Thomas G Blanchard. Crosstalk between endoplasmic reticulum stress and anti-viral activities: A novel therapeutic target for COVID-19. Life sciences (27 May 2020) PMID:32454157 PMC7245231 doi:10.1016/j.lfs.2020.117842.	PMID: 32454157
37.	**36. Andrographolide as a potential inhibitor of SARS-CoV-2 main protease: an in silico approach.** ABSTRACT: SARS-CoV-2 virus which caused the global pandemic the Coronavirus Disease- 2019 (COVID-2019) has infected about 1,203,959 patients and brought forth death rate about 64,788 among 206 countries as mentioned by WHO in the month of April 2020. The clinical trials are underway for Remdesivir, an investigational anti-viral drug from Gilead Sciences. Antimalarial drugs such as Chloroquine and Hydroxychloroquine derivatives are being used in emergency cases; however, they are not suitable for patients with conditions like diabetes, hypertension and cardiac issues. The lack of availability of approved treatment for this disease calls forth the scientific community to find novel compounds with the ability to treat it. This paper evaluates the compound Andrographolide from Andrographis paniculata as a potential inhibitor of the main protease of SARS-COV-2 (Mpro) through in silico studies such as molecular docking, target analysis, toxicity prediction and ADME prediction. Andrographolide was docked successfully in the binding site of SARS-CoV-2 Mpro. Computational approaches also predicts this molecule to have good solubility, pharmacodynamics property and target accuracy. This molecule also obeys Lipinski's rule,	PMID: 32329419

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	which makes it a promising compound to pursue further biochemical and cell based assays to explore its potential for use against COVID-19.Communicated by Ramaswamy H. Sarma. • Diagnosis: Covid-19, Sars-Cov-1. • Citation: Sukanth Kumar Enmozhi, Kavitha Raja, Irudhayasamy Sebastine, Jerrine Joseph. Andrographolide as a potential inhibitor of SARS-CoV-2 main protease: an in silico approach. Journal of biomolecular structure & dynamics (25 Apr 2020) PMID:32329419 PMC7212536 doi:10.1080/07391102.2020.1760136.	

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