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Naturopathy for Covid-19—Research References

VITAMIN A

Timoneda J, Rodríguez-Fernández L, Zaragozá R, et al. Vitamin A Deficiency and the Lung. Nutrients. 2018;10(9):1132. Published 2018 Aug 21.
Vitamin A deficiency has been associated with an increased risk of respiratory infections and other lung diseases such as childhood asthma and COPD.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6164133/

Stephensen CB, Lietz G. Vitamin A in resistance to and recovery from infection: relevance to SARS-CoV2 [published online ahead of print, 2021 Jan 20]. Br J Nutr. 2021;1-10.
Vitamin A was termed 'the anti-infective' vitamin approximately 90 years ago because a deficiency was known to increase the risk of infections, particularly lung infections. Vitamin A also regulates the production of mucin, which is a physical barrier to infection. Vitamin A reserves are quickly depleted by infections. In the respiratory tract, vitamin A deficiency increases the severity of inflammation and tissue damage following viral infection. It impairs the ability of the lung to repair damaged tissues, potentially leading to long-lasting scarring, lung fibrosis and reduced lung capacity.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7884725/

Stephensen CB. Vitamin A, infection, and immune function. Annu Rev Nutr. 2001;21:167-92
Vitamin A deficiency impairs the regeneration of mucosal barriers damaged by infection. It also diminishes antibody responses as well as the function of many white blood cells.
https://pubmed.ncbi.nlm.nih.gov/11375434/

Stephensen C, and Lietz G. (2021). Vitamin A in resistance to and recovery from infection: Relevance to SARS-CoV2. British Journal of Nutrition, 1-10.
https://www.cambridge.org/core/journals/british-journal-of-nutrition/article/vitamin-a-in-resistance-to-and-recovery-from-infection-relevance-to-sarscov2/9E196F75CD83F33075B96703F76CA0C8#

VITAMIN C

William F. Simmons and Robert G. Smith, PhDHigh-Dose Vitamin C Success Story in COVID-19. Townsend Letter: Vitamin C and Coronavirus: Not a Vaccine, Just a Humble Cure
The story of Covid-19 treatment in China, using high doses of vitamin C.
https://www.townsendletter.com/article/online-vitamin-c-coronavirus-humble-cure/

Hemilä H, de Man AME. Vitamin C and COVID-19. Front Med (Lausanne). 2021 Jan 18;7:559811.
In critically ill patients, plasma vitamin C levels are commonly very low. Gram doses of vitamin C are needed to increase the plasma vitamin C levels of critically ill patients to the levels of ordinary healthy people. A meta-analysis of 12 trials with 1,766 patients found that vitamin C reduced the length of ICU stay on average by 8%. Another meta-analysis found that vitamin C treatment shortened the duration of mechanical ventilation in ICU patients.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7848027/

VITAMIN D

Ellen CG Grant. BMJ 2020;371:m4938
Nineteen world-wide studies have demonstrated that low blood levels of Vitamin D are associated with severe or fatal Covid-19. The latest International studies indicate that a blood level of more than 30ng/ml (75nmol/L) is a level that indicates protection against serious or fatal Covid-19 infection. A target level of 40ng/ml (100nmol/L) would appear to be appropriate, and to achieve this vitamin D in a daily supplement of 4,000 units is effective, perfectly safe, and costs about 12 GBP per year.
https://www.bmj.com/content/371/bmj.m4938/rr-0

SELENIUM

Khatiwada, S., Subedi, A. A Mechanistic Link Between Selenium and Coronavirus Disease 2019 (COVID-19). Curr Nutr Rep 10, 125–136 (2021).
In a small study in South Korea, vitamin D and selenium deficiency were seen in 76% and 42% of

COVID-19 patients, with higher deficiency rate in patients with severe disease. Infectious viral diseases such as HIV, influenza and Ebola are more likely to evolve and spread in areas where soils are deficient in selenium. Under selenium-deficient conditions, viruses are found to mutate rapidly to become more virulent. With selenium sufficiency, virus mutation and virulence decrease. So selenium plays a vital role in reducing the rate and severity of viral infections. Preliminary evidence has shown selenium to be very important in critically ill COVID-19 patients.
https://link.springer.com/article/10.1007/s13668-021-00354-4

Zhang J, Taylor EW, Bennett K, Saad R, Rayman MP. Association between regional selenium status and reported outcome of COVID-19 cases in China. Am J Clin Nutr. 2020;111(6):1297-1299.
Experience shows that Covid-19 patients from areas with high selenium levels have a higher cure rate and lower mortality compared to those in low selenium areas. Several studies across the world show the importance of a balanced diet with nutrients and trace elements to build a robust immune system to fight the Covid-19 virus.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7197590/

Guillin OM, Vindry C, Ohlmann T, Chavatte L. Selenium, Selenoproteins and Viral Infection. Nutrients. 2019;11(9):2101. Published 2019 Sep 4.
Oxidative stress is one of the hallmarks of viral infection. In turn, oxidative stress can enhance viral replication leading to a vicious circle. Viral infection simultaneously increases the demand for antioxidant nutrients, and causes their loss, leading to a deficiency that can be compensated by micronutrient supplementation. Among the nutrients implicated in viral infection, selenium has an important role in antioxidant defense. Selenium deficiency has been associated with the pathogenicity of several viruses.
https://pubmed.ncbi.nlm.nih.gov/31487871/#

ZINC

Mossink JP. Zinc as nutritional intervention and prevention measure for COVID–19 disease. BMJ Nutrition, Prevention & Health 2020;bmjnph-2020-000095.
Zinc is critical for antiviral immunity and works with vitamin A to maintain the integrity of the mucosa. It helps to control the release of inflammatory cytokines, and prevent excessive inflammatory reactions. It has also shown direct antiviral activity for a number of RNA viruses. Mild zinc deficiency, commonly seen with ageing, leads to dysregulation of the immune system, decreasing some functions but enhancing the production of inflammatory cytokines. This is known as 'inflammageing'. Under these conditions, intracellular zinc loses bioavailability. However, bioavailable intracellular zinc is needed to inhibit proteins needed for the life cycle of the RNA virus. Various widely used drugs to treat high blood pressure, and also statin drugs, have been reported to negatively influence zinc status.
https://nutrition.bmj.com/content/early/2020/06/11/bmjnph-2020-000095

Inoue K, O'Bryant Z, Xiong ZG. Zinc-permeable ion channels: effects on intracellular zinc dynamics and potential physiological/ pathophysiological significance. Curr Med Chem. 2015;22(10):1248-1257.
23% of the world's population has been estimated to be zinc deficient
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4363167/

ZINC IONOPHORES

Zinc ionophores are substances which target zinc outside the cell, transferring it to compartments inside the cell, where it interferes with virus replication.

Pal A, Squitti R, Picozza M, et al. Zinc and COVID-19: Basis of Current Clinical Trials. Biol Trace Elem Res. 2021;199(8):2882-2892.
Both hydroxychloroquine and chloroquine inhibit some steps of Covid-19 replication by reducing acidity within the cell, and act as Zn ionophores which means that they shuttle zinc past the cell surface membrane, into the inner cell, thus increasing the intracellular concentration of zinc.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7580816/

Derwand R, Scholz M. Does zinc supplementation enhance the clinical efficacy of chloroquine/ hydroxychloroquine to win today's battle against COVID-19? Medical Hypotheses, Volume 142, 2020, 109815, ISSN 0306-9877.
It is well known that zinc is needed for an effective antiviral response. Chloroquine and hydroxychloroquine are ionophores - they specifically target zinc outside the cell, transferring it to compartments inside the cell, where it interferes with coronavirus replication. In order to replicate, coronavirus within the cell requires acidification, and

it is thought that these drugs also inhibit its replication by reducing acidity. The use of these drugs together with effective zinc supplementation may result in increased intracellular zinc levels and therefore a more effective inhibition of Covid-19 replication inside the cell.
https://www.sciencedirect.com/science/article/pii/S0306987720306435

Samad N, Sodunke TE, Abubakar AR, Jahan I, Sharma P, Islam S, Dutta S, Haque M. The Implications of Zinc Therapy in Combating the COVID-19 Global Pandemic. J Inflamm Res. 2021;14:527-550.
A number of published studies that illustrate the efficacy of zinc therapy in managing COVID-19 patients. Several molecules such as the drug hydroxychloroquine, but also the nutrients quercetin (found in onions), luteolin (found in celery) and ECGC (found in green tea) are ionophores - they aid the entry of zinc into the cells, enabling it to block the life cycle of the Covid-19 virus.
https://www.dovepress.com/the-implications-of-zinc-therapy-in-combating-the-covid-19-global-pand-peer-reviewed-fulltext-article-JIR

GLUTATHIONE

Polonikov A. Endogenous Deficiency of Glutathione as the Most Likely Cause of Serious Manifestations and Death in COVID-19 Patients. ACS Infect Dis. 2020;6(7):1558-1562.
Glutathione is known as the 'master antioxidant'. A glutathione deficiency is the most likely cause of the severe form of Covid-19.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7263077/

Guloyan V, Oganesian B, Baghdasaryan N, et al. Glutathione Supplementation as an Adjunctive Therapy in COVID-19. Antioxidants (Basel). 2020;9(10):914. Published 2020 Sep 25.
High levels of the cytokines IL-6 and TNF-α are mainly thought to drive the inflammation of Covid-19. Glutathione has been found to reduce IL-6 in other diseases, and also to inhibit viral replication. Glutathione supplementation needs to be taken in liposomal form to bypass the digestive system.
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/32992775/

Silvagno F, Vernone A, Pescarmona GP. The Role of Glutathione in Protecting against the Severe Inflammatory Response Triggered by COVID-19. Antioxidants (Basel). 2020;9(7):624. Published 2020 Jul 16.
Low levels of glutathione is thought to be one of the major causes of the hyper-inflammation linked to severe Covid-19. N-acetylcysteine is used by the body to make glutathione. It also combats oxidative stress, which plays a major part in inflammatory diseases, including Covid-19.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7402141/

N-ACETYLCYSTEINE

De Flora S, Balansky R, La Maestra S. Rationale for the use of N-acetylcysteine in both prevention and adjuvant therapy of COVID-19. FASEB J. 2020;34(10):13185-13193.
Oxidative stress promotes the entry of viruses into our cells by altering the ACE2 proteins on the cell surface. The virus raises oxidative stress and stimulates inflammatory cytokine production. Its aim is to enhance its own replication. Oxidative stress can be reduced with natural antioxidants, particularly selenium and N-acetylcysteine (NAC). NAC promotes glutathione synthesis and has been successfully used to reduce the risk of flu. Many research studies are currently in progress to test whether it can contribute to treatment for the severe form of Covid-19.
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/32780893/

Ibrahim, Homam et al. "Therapeutic blockade of inflammation in severe COVID-19 infection with intravenous N-acetylcysteine." Clinical immunology (Orlando, Fla.) vol. 219 (2020): 108544.
In a group of ten Covid-19 patients who were treated with NAC, it brought clinical improvement and markedly reduced inflammation in all patients.
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/32707089/

BROMELAIN

Sagar S, Rathinavel AK, Lutz WE, et al. Bromelain inhibits SARS-CoV-2 infection via targeting ACE-2, TMPRSS2, and spike protein. Clin Transl Med. 2021;11(2):e281.
Bromelain pre-treatment significantly inhibits Covid-19 binding and infection, suggesting that it can be used as an antiviral. It also has a profound anti-fibrosis and anti-clotting action.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7811777/

The Study of Quadruple Therapy Zinc, Quercetin, Bromelain and Vitamin C on the Clinical Outcomes of Patients Infected With COVID-19 (clinical trial in progress).
Bromelain decreases the majority of pathways to inflammation and has demonstrated a significant role as an anti-inflammatory agent in various conditions.
https://clinicaltrials.gov/ct2/show/NCT04468139

QUERCETIN

Colunga Biancatelli RML, Berrill M, Catravas JD, Marik PE. Quercetin and Vitamin C: An Experimental, Synergistic Therapy for the Prevention and Treatment of SARS-CoV-2 Related Disease (COVID-19). Front Immunol. 2020;11:1451. Published 2020 Jun 19.
Quercetin has been shown to be effective against a broad range of viruses including human respiratory syncytial virus (hRSV), rhinovirus, echovirus, coxsackievirus, poliovirus, parainfluenza type 3, Herpes Simplex Virus-1, cytomegalovirus, SARS-CoV-1, dengue virus, and Hepatitis C virus. It displays a broad range of antiviral properties which can interfere at multiple steps of pathogen virulence, including virus entry and virus replication. It works best in combination with vitamin C.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7318306/

The Study of Quadruple Therapy Zinc, Quercetin, Bromelain and Vitamin C on the Clinical Outcomes of Patients Infected With COVID-19 (clinical trial in progress).
Quercetin aids the entry of zinc into cells. This improves the acid/alkaline balance inside the cell, helping to prevent the entry of RNA viruses (including Covid-19).
https://clinicaltrials.gov/ct2/show/NCT04468139

Pawar, Anil, and Amit Pal. "Molecular and functional resemblance of dexamethasone and quercetin: A paradigm worth exploring in dexamethasone-nonresponsive COVID-19 patients." Phytotherapy research : PTR vol. 34,12 (2020): 3085-3088.
Quercetin and another related flavonoid, luteolin, can inhibit the entry of SARS virus into the host cell by targeting the ACE2 protein.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7537236/

Di Pierro F, Derosa G, Maffioli P, et al. Possible Therapeutic Effects of Adjuvant Quercetin Supplementation Against Early-Stage COVID-19 Infection: A Prospective, Randomized, Controlled, and Open-Label Study. Int J Gen Med. 2021;14:2359-2366. Published 2021 Jun 8.
A 30-day study on 152 Covid-19 patients, using a daily dose of 1000 mg quercetin phytosome (a more absorbable form) showed a reduction in frequency and length of hospitalization, need of non-invasive oxygen therapy, progression to intensive care units and number of deaths.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8197660/

Agrawal PK, Agrawal C, Blunden G. Quercetin: Antiviral Significance and Possible COVID-19 Integrative Considerations. Natural Product Communications. December 2020.
Quercetin is a naturally occurring dietary flavonoid, well known to ameliorate chronic diseases and ageing processes in humans. Its antiviral properties have been investigated in numerous studies. Studies have demonstrated that quercetin can interfere with various stages of the coronavirus entry and replication cycle.
https://journals.sagepub.com/doi/full/10.1177/1934578X20976293

Saeedi-Boroujeni A, Mahmoudian-Sani MR. Anti-inflammatory potential of Quercetin in COVID-19 treatment. J Inflamm (Lond). 2021 Jan 28;18(1):3.
How quercetin works as anti-inflammatory
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/33509217/

Dabeek WM, Marra MV. Dietary Quercetin and Kaempferol: Bioavailability and Potential Cardiovascular-Related Bioactivity in Humans. Nutrients. 2019;11(10):2288. Published 2019 Sep 25.
Quercetin from onions has the highest rate of intestinal absorption. Co-ingestion of quercetin with dietary fat increases absorption from the small intestine, so fried onions are recommended for consumption.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6835347/

CURCUMIN

How curcumin may prevent a cytokine storm
Peter AE, Sandeep BV, Rao BG, Kalpana VL. Calming the Storm: Natural Immunosuppressants as Adjuvants to Target the Cytokine Storm in COVID-19. Front Pharmacol. 2021;11:583777.
Published 2021 Jan 27. doi:10.3389/

fphar.2020.583777
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/33708109/

Liu Z, Ying Y. The Inhibitory Effect of Curcumin on Virus-Induced Cytokine Storm and Its Potential Use in the Associated Severe Pneumonia. Front Cell Dev Biol. 2020;8:479. Published 2020 Jun 12. doi:10.3389/fcell.2020.00479
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/32596244/

Dhar S, Bhattacharjee P. Promising role of curcumin against viral diseases emphasizing COVID-19 management: A review on the mechanistic insights with reference to host-pathogen interaction and immunomodulation. J Funct Foods. 2021;82:104503.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8057770/

More reviews supporting the use of curcumin

Mrityunjaya M, Pavithra V, Neelam R, Janhavi P, Halami PM, Ravindra PV. Immune-Boosting, Antioxidant and Anti-inflammatory Food Supplements Targeting Pathogenesis of COVID-19. Front Immunol. 2020;11:570122. Published 2020 Oct 7.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7575721/

Keflie TS, Biesalski HK. Micronutrients and bioactive substances: Their potential roles in combating COVID-19. Nutrition. 2021;84:111103. doi:10.1016/j.nut.2020.111103
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/33450678/

Thota SM, Balan V, Sivaramakrishnan V. Natural products as home-based prophylactic and symptom management agents in the setting of COVID-19. Phytother Res. 2020;34(12):3148-3167.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7461159/

HONEY

Abedi F, Ghasemi S, Farkhondeh T, Azimi-Nezhad M, Shakibaei M, Samarghandian S. Possible Potential Effects of Honey and Its Main Components Against Covid-19 Infection. Dose Response. 2021;19(1):1559325820982423. Published 2021 Mar 30.
Numerous studies have found that honey can combat a number of viruses: herpes zoster, rubella, influenza, respiratory syncytial virus, AIDS, viral hepatitis, gingivostomatitis, rabies, rhinoconjunctivitis and Covid-19. It appears to be able to interrupt the proteins necessary for viral attachment and entry into host cells. Honey can also lower levels of inflammatory prostaglandins. Systemic inflammation in Covid-19 patients can be suppressed with honey, and a number of clinical trials are in progress. Honey can also combat coagulation.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8020257/

Hossain KS, Hossain MG, Moni A, Rahman MM, Rahman UH, Alam M, Kundu S, Rahman MM, Hannan MA, Uddin MJ. Prospects of honey in fighting against COVID-19: pharmacological insights and therapeutic promises. Heliyon. 2020 Dec;6(12):e05798.
Several studies have proved its potential healing capability against numerous chronic diseases/ conditions, including pulmonary disorders, cardiac disorders, diabetes, hypertension, autophagy dysfunction, bacterial, and fungal infections. More importantly, honey has proved its virucidal effect on several enveloped viruses such as HIV, influenza virus, herpes simplex, and varicella-zoster virus.
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/33363261/

Clinical trials currently taking place using honey to combat Covid-19
https://clinicaltrials.gov/ct2/results?cond=covid-19&term=honey&cntry=&state=&city=&dist=&Search=Search

FEVERFEW

Bahrami M, Kamalinejad M, Latifi SA, Seif F, Dadmehr M. Cytokine storm in COVID-19 and parthenolide: Preclinical evidence. Phytother Res. 2020 Oct;34(10):2429-2430. doi: 10.1002/ptr.6776. Epub 2020 Jun 27.
According to in vitro and in vivo studies, feverfew could significantly reduce the production of cytokines IL-1, IL-2, IL-6, IL-8, and TNF-α
https://www.ncbi.nlm.nih.gov/pmc/articles/pmid/32472655/