

Licorice Inhibits Replication of Coronavirus

Analysis by [Dr. Joseph Mercola](#)

✓ Fact Checked

STORY AT-A-GLANCE

- › Glycyrrhizin, the major ingredient in licorice root, has shown effectiveness against SARS virus in scientific studies
- › It has been effective in treating viruses such as herpes, HIV, hepatitis, influenza, encephalitis and pneumonia
- › Glycyrrhizin outperformed conventional antiviral medications against SARS in research published in the journal The Lancet
- › The substance seems to work earlier in the virus replication cycle, compared to other medications, inhibiting absorption and penetration of the virus

During the COVID-19 pandemic, social distancing and hygiene seem to be having some effect on "flattening the curve" and slowing the spread of the virus. The use of ultraviolet (UV) light to decontaminate medical facilities, [proper hand-washing](#) and [disinfectants](#), equipment and even [protective facemasks](#) also seems to be useful.

But people will still contract COVID-19, and effective treatments are lacking and needed. That's why some scientific studies are looking at a natural product that has long been known to have antiviral effects¹ – glycyrrhizin, the major active constituent in [licorice root](#).

[Glycyrrhizin](#) was valued in ancient Arabia and Greece for treating coughs and in China for relieving irritation of the mucous membranes. In modern times, glycyrrhizin has been shown to be a formidable antiviral, fighting herpes, HIV, hepatitis, influenza, encephalitis

and pneumonia as well as less known viruses like respiratory syncytial virus, arboviruses, vaccinia virus and vesicular stomatitis virus.²

Still, it's glycyrrhizin's effectiveness against **SARS** (severe acute respiratory syndrome) that has scientists hoping this important natural substance may be a tool against COVID-19.

Glycyrrhizin Has Medicinal Properties

You may think of licorice as an extract, a sweetener or even a candy, like Good and Plenty, but it's actually complex biochemically and offers important medical benefits. According to PubChem, a database of chemical molecules maintained by the National Center for Biotechnology Information,³

"Glycyrrhizic acid is extracted from the root of the licorice plant; Glycyrrhiza glabra. It is a triterpene glycoside with glycyrrhetic acid that possesses a wide range of pharmacological and biological activities ... potential immunomodulating, anti-inflammatory, hepato- and neuro-protective, and antineoplastic activities.

Glycyrrhizin modulates certain enzymes involved in inflammation and oxidative stress, and downregulates certain pro-inflammatory mediators, thereby protecting against inflammation- and reactive oxygen species (ROS)-induced damage. Glycyrrhizin may also suppress the growth of susceptible tumor cells."

According to Botanical Medicine, the anti-inflammatory actions of glycyrrhizin (GL) may stem from suppression of cytokines:⁴

"As testimony to its anti-inflammatory properties, glycyrrhizin alleviated allergic asthma in an experimental mouse model, increased the IL-4 and IL-5 levels, decreased eosinophil counts and IgE levels, and upregulated total IgG2a in serum.

These results indicated that glycyrrhizin interfered with the production of IgE by decreasing the IgE-stimulating cytokines. It also attenuated lung inflammation and mucus production in mice."

Glycyrrhizin Works Against SARS, a COVID-19-Like Virus

SARS-CoV-2,⁵ the virus that causes COVID-19, is similar to SARS-CoV-1, the coronavirus that surfaced in 2003. Its genome shares 79.5% of the SARS-CoV-1 genome's information and both enter human alveolar epithelial cells through binding with ACE2 receptors.⁶

Early SARS-CoV-1 patients were given the viral compound ribavirin, but it showed little benefit.⁷ Corticosteroids were also tried in SARS-CoV-1 patients and patients with MERS (Middle East Respiratory Syndrome), which occurred 10 years later, but there was "no evidence showing that the mortality of SARS-CoV-1 and MERS patients was reduced," as reported in the International Journal of Biological Sciences.⁸

Soon after the SARS-CoV-1 outbreak, the medical journal The Lancet published a research letter suggesting that glycyrrhizin might fight SARS:⁹

"The outbreak of SARS warrants the search for antiviral compounds to treat the disease. At present, no specific treatment has been identified for SARS-associated coronavirus infection. We assessed the antiviral potential of ribavirin, 6-azauridine, pyrazofurin, mycophenolic acid, and glycyrrhizin against two clinical isolates of coronavirus from patients with SARS ...

Of all the compounds, glycyrrhizin was the most active in inhibiting replication of the SARS-associated virus. Our findings suggest that glycyrrhizin should be assessed for treatment of SARS."

Glycyrrhizin had several positive actions, wrote the researchers:¹⁰

"In addition to inhibition of virus replication, glycyrrhizin inhibits adsorption and penetration of the virus — early steps of the replicative cycle ... Glycyrrhizin was

most effective when given both during and after the adsorption period ...

... glycyrrhizin and its aglycone metabolite 18 β glycyrrhetinic acid upregulate expression of inducible nitrous oxide synthase and production of nitrous oxide in macrophages.

Nitrous oxide inhibits replication of several viruses – eg, Japanese encephalitis virus, which can also be inhibited by glycyrrhizin. Our preliminary results show that glycyrrhizin induces nitrous oxide synthase in Vero cells [cells used in cultures] and that virus replication is inhibited when the nitrous oxide donor is added to the culture medium."

Glycyrrhizin May Act Differently From Other Substances

According to the Journal of General Virology, glycyrrhizin's method of stopping the replication of SARS viruses may differ from other treatments that have been tried:¹¹

"Unlike IFN- α and ribavirin, there are few clues to the antiviral mechanism of glycyrrhizin. Our data indicate that, as for ribavirin, glycyrrhizin only moderately affects coronavirus replicase functions.

*However, in contrast to ribavirin, glycyrrhizin has been shown to inhibit SARS-CoV replication in tissue culture. This indicates that glycyrrhizin may not target the coronavirus replication machinery and that antiviral effects may be exerted, for example, during virus adsorption or release."*¹²

Stopping replication is especially challenging because of the peculiarities of the SARS virus. According to General Cell Biology & Physiology:¹³

"These analyses revealed that SARS-CoV-2 reshapes central cellular pathways, such as translation, splicing, carbon metabolism and nucleic acid metabolism. Small molecule inhibitors targeting these pathways were tested in cellular infection assays and prevented viral replication."

Glycyrrhizin's upregulation of nitric oxide and nitric oxide synthase in macrophages, which was noted in the International Journal of Infectious Diseases, may explain its ability to stop replication of SARS and hopefully other coronaviruses like SARS-CoV-2.¹⁴

Glycyrrhizin May Be Effective Against COVID-19

The failure of Western pharmaceutical treatments for SARS has put the spotlight on Traditional Chinese Medicine (TCM), a practice in which glycyrrhizin is a staple.

According to the International Journal of Biological Sciences:¹⁵

"Ranging from case reports, case series, controlled observational studies and randomized clinical trials, clinical studies aiming to examine the effect of TCM on SARS have been carried out and reported. There are quite compelling evidences support the notion that TCM has beneficial effect in the treatment or prevention of SARS ...

For example, the rate of fatality in Hong Kong and Singapore was approximately 18%, while the rate for Beijing was initially more than 52% ... The dramatic reduced fatality from late May in Beijing was believed to be associated with the use of TCM as a supplement to the conventional therapy."

As COVID-19 reportedly first surfaced in China, The Globe and Mail reported that many nationals were turning to traditional treatments, while health leaders reported "'significant' benefits from mixing Chinese and Western medicine."¹⁶

"For authorities in Wuhan to counsel use of traditional Chinese medicine 'makes sense,' so long as it is in conjunction with Western drugs, said Jindrich Cinatl, a virologist who co-authored the 2003 [Lancet] study. 'In Western medicine, we have drugs that attack just a concrete target,' he said in an interview. 'With traditional medicine, you can prevent virus absorption to cells, virus replication and so on.'"

Jakkapong Watcharachaijunta, a medical researcher, told Thailand Medical News he thinks glycyrrhizin is a promising COVID-19 treatment:¹⁷

"Though the new 2019-nCov virus [since renamed SARS-CoV-2] is a different strain, it is very close to the SARS coronavirus genetically wise and maybe this should be an interesting starting point."

In a Pandemic, New Drugs or Vaccines Won't Be the Answer

With COVID-19 now present on every continent except Antarctica, it is clear that treatments are needed immediately, but rushing new drugs to the market could cause adverse side effects to be missed. Further, a commentary written by Derek Lowe, who holds a Ph.D. in organic chemistry and has worked for several major pharmaceutical companies, expresses little hope for the existing medications being tested or for the development of entirely new ones:¹⁸

"A drug discovery program from scratch against a new pathogen is ... not a trivial exercise ... Many such efforts in the past have come to grief because by the time they had anything to deliver the epidemic itself had passed. Indeed, Gilead's remdesivir had already been dropped as a potential Ebola therapy.

You will either need to have a target in mind up front or go phenotypic. For the former, what you'd see are better characterizations of the viral protease and more extensive screens against it. Two other big target areas are viral entry (which involves the "spike" proteins on the virus surface and the ACE2 protein on human cells) and viral replication."

There are many challenges to developing a new **antiviral drug** and the process is extremely complex and slow, which means even if they end up being effective, they may be too late to be of use. According to Lowe:¹⁹

"Phenotypic screens are perfectly reasonable against viral pathogens as well, but you'll need to put time and effort into that assay up front, just as with any phenotypic effort, because as anyone who does that sort of work will tell you, a bad phenotypic screen is a complete waste of everyone's time."

It has recently been determined by Nextstrain.org, which tracks viral genomes across the planet, that SARS-CoV-2 is mutating 1,000 times faster than influenza viruses and 36,000 times faster than influenza virus. This strongly suggests that vaccines' efforts will fail 1,000 times worse than the miserable [flu vaccine](#).

The Benefits of Glycyrrhizin Are Already Available

One of glycyrrhizin's advantages is that it has a long history of medicinal use and could potentially help those in need much sooner than an experimental drug just entering testing, but the fact remains that infectious disease that emerges in any country or continent has the potential to spread swiftly and cause a pandemic. According to Antiviral Research, the SARS outbreak produced greater world cooperation and reporting:²⁰

"One legacy of the outbreak was the formulation of the international Health Regulations (IHR) in 2005 and their acceptance by the World Health Assembly in 2007. The IHR require countries to report unusual and unexplained outbreaks of infectious disease and to develop the public health capacity to detect and respond to such diseases ...

SARS and other contemporary zoonotic threats, such as H5N1 avian influenza, have highlighted the need for collaboration among those responsible for human and animal health, and the environment.

This led to the formalization of the concept of "One Health," which fosters collaborative effects of multiple disciplines to attain optimal health for people, animals, and the environment."

The relevant international organizations now have formal working agreements and a framework within which they can coordinate activities to assess risks at the animal/human/ecosystem interface, according to the review. There is also an improved understanding of inter-species transmission and zoonotic pathogens that are behind many pandemics.

As the COVID-19 pandemic continues, a natural product like glycyrrhizin, with known medical benefits and few of the risks associated with harsh medications, is good news.