




Effects of Gene-Eden-VIR and Novirin on SARS-CoV: Implications for COVID-19

Hanan Polansky, PhD¹, and Gillad Lori, BSc¹ 

Abstract

The coronavirus (SARS-CoV-2), which causes COVID-19, is a betacoronavirus closely related to the human severe acute respiratory syndrome (SARS)-coronavirus (SARS-CoV). The recent COVID-19 outbreak created an urgent need for treatment. To expedite the development of such treatment, pharmaceutical companies and government agencies are currently testing several existing drugs for their effect on the virus. Gene-Eden-VIR and Novirin are natural, broad-spectrum, antiviral treatments proven to be safe and effective in several clinical studies. In this article, we present evidence indicating that the 5 Gene-Eden-VIR/Novirin ingredients have anti-betacoronavirus, and specifically, anti-SARS-CoV effects. We consider this evidence as a first indication of the anti-coronavirus effects of Gene-Eden-VIR/Novirin. Next, we are planning to conduct a clinical study with users of the treatments to test the effects of Gene-Eden-VIR/Novirin on individuals at risk and those infected with the virus.

Keywords

COVID-19, coronavirus, SARS-CoV-2

Received March 12, 2020. Received revised May 4, 2020. Accepted for publication May 8, 2020.

A novel coronavirus (SARS-CoV-2), which causes COVID-19, emerged in December 2019 in Wuhan city in China. The virus's most recently estimated reproductive number is 2.24¹ to 4.08² R_0 , and its fatality rate is 3.4%.³ Samples collected from patients revealed that the SARS-CoV-2 is a betacoronavirus, most closely related to a bat CoV (RaTG13) with 96% identity,^{4,5} and 2 other bat-derived Severe Acute Respiratory Syndrome (SARS)-like coronaviruses (SL-CoVZC45 and SL-CoVZXC21), with 88% identity.⁶ In addition, further analysis showed that SARS-CoV-2 is also closely related to the human SARS-CoV, with 79% identity.^{4,6} The later has an almost identical main protease (3CLpro) amino acid sequence to the SARS-CoV-2 with 96% identity and 99% similarity.⁷

To expedite the development of a treatment, pharmaceutical companies and government agencies are currently testing several existing drugs for their effect on the SARS-CoV-2 virus. For instance, a study reported that a combination of lopinavir and ritonavir, 2 HIV protease inhibitors, which were effective against a SARS infection in patients,⁸ reduced the viral load in a single SARS-CoV-2 infected patient.⁹ Another study showed that 2 compounds, remdesivir, a broad-spectrum antiviral drug, which was found to be effective against betacoronaviruses in vitro and in vivo, and chloroquine, an antimalarial drug, blocked a SARS-CoV-2 infection in vitro at low concentrations and high selectivity index (remdesivir, $IC_{50} = 0.77 \mu M$, $SI >$

129; chloroquine, $IC_{50} = 1.13 \mu M$, $SI > 88$). Remdesivir was also effective in one SARS-CoV-2 infected patient, and it is currently tested in Chinese patients as a treatment for COVID-19. Early clinical trials performed in China demonstrated the efficacy of chloroquine in the treatment of COVID-19.¹⁰

Gene-Eden-VIR/Novirin is a natural, broad-spectrum, antiviral treatment. The formula includes 5 ingredients: a 100 mg extract of quercetin, a 150 mg extract of green tea, a 50 mg extract of cinnamon, a 25 mg extract of licorice, and 100 μg of selenium. Clinical studies showed that Gene-Eden-VIR/Novirin is a safe and effective treatment against several viruses, including the human papillomavirus (HPV), herpes simplex virus (HSV), Epstein-Barr virus (EBV), human cytomegalovirus (HCMV), and hepatitis C virus (HCV).¹¹⁻¹⁴ In another study, Polansky et al suggested that the possible broad antiviral effects of Gene-Eden-VIR/Novirin may be mediated through the treatment's effect on the immune system.¹⁵

¹ The Center for the Biology of Chronic Disease, Valley Cottage, NY, USA

Corresponding Author:

Hanan Polansky, The Center for the Biology of Chronic Disease (CBCD), 616 Corporate Way, Suite 2-3665, Valley Cottage, NY 10989, USA.
Email: hpolansky@cbcd.net



In the next section, we review evidence on the effects of the Gene-Eden-VIR/Novirin ingredients on the betacoronaviruses family of viruses, and specifically, the SARS-CoV virus.

Quercetin

Quercetin is a flavonol with a variety of biological effects, including antioxidant, anti-inflammatory, and antiviral.^{16,17} It has anti-infective and anti-replicative effects on a number of viruses, including RNA viruses.¹⁶⁻¹⁹ Studies showed that micromolar doses of quercetin can inhibit betacoronavirus infectious activities in vitro. One study reported that quercetin blocked pseudotype SARS-CoV entry into host cells ($EC_{50} = 83.2 \mu\text{M}$).²⁰ Two other studies observed that quercetin specifically inhibited the 2 SARS-CoV proteases, PLpro ($IC_{50} = 8.6 \mu\text{M}^{21}$) and 3CLpro ($IC_{50} = 52.7 \mu\text{M},^{21} 73 \mu\text{M}^{22}$), and the Middle Eastern Respiratory Syndrome protease 3CLpro ($IC_{50} = 34.8 \mu\text{M}^{21}$). In addition, quercetin's anti-inflammatory properties may have beneficial effects in respiratory viral infections, including CoV.^{23,24} Studies suggested that quercetin can modulate the cytokine release pattern associated with hyperinflammation and cytokine storm,²³ while upregulating the proliferation of regulatory T helper cells.²⁴

Green Tea

Green tea is made of leaves from the plant *Camellia sinensis* in a process that allows the preservation of certain flavonols commonly known as catechins.²⁵ Several papers suggested that catechins have broad antiviral effects against many viruses.²⁶ With regard to betacoronaviruses, one of the main catechins in green tea is epigallocatechin gallate (EGCG). This catechin was found to induce mild inhibitory effects on SARS-CoV 3CLpro ($IC_{50} = 73 \mu\text{M}$) in vitro.²²

Cinnamon

Cinnamon extract is most commonly derived from the species *Cinnamomum cassia*. Studies demonstrated that the plant has inhibitory effects on RNA viral infections in vitro.^{27,28} Zhuang et al also showed that a cinnamon extract inhibited an infection with the wild type SARS-CoV in vitro ($IC_{50} = 43 \mu\text{M}$).²⁹ The proposed possible mechanism was blocking cell entry via endocytosis.

Licorice

Licorice extract, derived from the root of *Glycyrrhiza glabra*, has broad antiviral³⁰ and immunostimulating effects. In vitro³¹ and human studies³² showed that licorice stimulates the proliferation and activation of the human lymphocytes CD4+, CD8+, B cells, and NK cells. Reports from CoV patients indicate the involvement of this type of immune cells prior to the resolution of the disease, while overaccumulation of innate immunity cells, such as macrophages and neutrophils, at the site of infection, was associated with severe cases and death.^{33,34} Thus, licorice may promote early adaptive

immunity-mediated clearance of the virus and prevent hyperinflammation. In addition, studies demonstrated a direct weak anti-infective activity of licorice's main active ingredient, glycyrrhizin, on SARS-CoV in vitro.^{35,36}

Selenium

Selenium is a trace element involved in redox regulation. Its antioxidative effect is exerted through the incorporation as selenocysteine into a group of proteins called selenoproteins.³⁷ Selenium deficiency increases the levels of reactive oxygen species and oxidative stress, which impairs the response of the immune system to viruses^{38,39} and increases the rate of mutation of RNA viruses.³⁷⁻⁴⁰ This impaired response may be manifested in several forms^{38,39}: decreased immune cells function, as a result of oxidative damage; decreased cell-mediated immunity; more severe and persistent inflammation of the lungs, as seen in influenza A virus (IAV) infection; and an imbalance in the proliferation of different T cell types, including T helper cells (Th1/Th2) ratio. The increase in viral rate of mutation coupled with the decrease in the immune response to the viral infection may increase virulence, as it increases the population size of quasispecies, and, as a result, gives rise to new more virulent strains. These new strains can become dominant and increase the pathogenicity of the infection.⁴¹ Hart-hill⁴² suggested that this mechanism, which has been observed with other RNA viruses in selenium-deficient mice models, also occurred in the SARS-CoV outbreak in 2002. It is interesting that the outbreak started in areas of low selenium soil in China, such as Wuhan city. It should be noted that excess selenium is also detrimental to health. Studies showed that supranutritional supplementation of selenium caused an imbalance in the proliferation profile of T cell types, and impaired immune response.^{39,43} Finally, studies showed that adequate levels of selenium supplementation to selenium-deficient patients increased the immune response to viral infections, and decreased the virulence of several viruses, in some cases to the point of complete prevention of the disease.³⁷⁻⁴⁰

Summary

In this article, we describe the effects of Gene-Eden-VIR/Novirin ingredients on the family of betacoronaviruses, and specifically SARS-CoV. We chose SARS-CoV because of its high level of sequence identity to the SARS-CoV-2 virus. We show that Gene-Eden-VIR/Novirin ingredients have anti-coronavirus effects, including inhibition of cell entry and infection, inhibition of replication, inhibition of the viral proteases, and reducing virulent quasispecies formation. In addition, different ingredients of Gene-Eden-VIR/Novirin may have positive effects on the response of the immune system to the SARS-CoV-2 virus by reducing detrimental hyperinflammation and increasing the function of specific immune components crucial for effective clearance of the virus. Importantly, a treatment approach that controls viral loads, while attenuating excessive inflammatory response, has been

suggested as beneficial in CoV infections. We consider this evidence as a first indication of the anti-coronavirus effects of Gene-Eden-VIR/Novirin. Next, we are planning to conduct a clinical study with users of the treatments to test the effects of Gene-Eden-VIR/Novirin on the SARS-CoV-2 virus.

Author Contributions

All authors contributed equally.

Declaration of Conflicting Interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article. Hanan Polansky is the inventor of the Gene-Eden-VIR/Novirin formula. Gillad Lori has no conflict of interest to disclose.

Funding

The authors received no financial support for the research, authorship, and/or publication of this article.

ORCID iD

Gillad Lori  <https://orcid.org/0000-0001-8225-8205>

Ethical Approval

Not applicable.

References

- Zhao S, Lin Q, Ran J, et al. Preliminary estimation of the basic reproduction number of novel coronavirus (2019-nCoV) in China, from 2019 to 2020: a data-driven analysis in the early phase of the outbreak. *Int J Infect Dis.* 2020;92:214-217.
- Cao Z, Zhang Q, Lu X, et al. Estimating the effective reproduction number of the 2019-nCoV in China [published online January 29, 2020]. *MedRxiv.* doi:10.1101/2020.01.27.20018952
- World Health Organization (WHO). *WHO Director-General's opening remarks at the media briefing on COVID-19 - 3 March 2020.* <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19-3-march-2020>
- Zhou P, Yang CL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature.* 2020;579:270-273. doi:10.1038/s41586-020-2012-7
- Ceraolo C, Giorgi FM. Genomic variance of the 2019-nCoV coronavirus. *J Med Virol.* 2020;92:522-528. doi:10.1002/jmv.25700
- Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet.* 2020;395:391-393.
- Stoermer M. Homology models of coronavirus 2019-nCoV 3CLpro protease [published online February 5, 2020]. *ChemRxiv.* doi:10.26434/chemrxiv.11637294.v3
- Chu CM, Cheng VCC, Hung IFN, et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax.* 2004;59:252-256.
- Lim J, Jeon S, Shin HY, et al. Case of the index patient who caused tertiary transmission of coronavirus disease 2019 in Korea: the application of lopinavir/ritonavir for the treatment of COVID-19 pneumonia monitored by quantitative RT-PCR. *J Korean Med Sci.* 2020;35:e79.
- Gao J, Tian Z, Yang X. Breakthrough: chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends.* 2020;14:72-73. doi:10.5582/bst.2020.01047
- Polansky H, Itzkovitz E. Gene-Eden-VIR is antiviral: results of a post marketing clinical study. *Pharmacol Pharm.* 2013;4:1-8. doi:10.4236/pp.2013.46A001
- Polansky H, Javaherian A, Itzkovitz E. Clinical trial of herbal treatment Gene-Eden-VIR/Novirin in oral herpes. *J Evid Based Integr Med.* 2018;23:2515690X18806269.
- Polansky H, Javaherian A, Itzkovitz E. Clinical study of Gene-Eden-VIR/Novirin in genital herpes: suppressive treatment safely decreases the duration of outbreaks in both severe and mild cases. *Clin Trans Med.* 2016;5:40.
- Polansky H, Itzkovitz E, Javaherian A. Human papillomavirus (HPV): systemic treatment with Gene-Eden-VIR/Novirin safely and effectively clears virus. *Drug Des Dev Theory.* 2017;11:575-583.
- Polansky H, Dafni I. Gene-Eden, a broad range, natural antiviral supplement, may shrink tumors and strengthen the immune system. *Acta Oncol.* 2010;49:397-399.
- Maalik A, Khan F, Mumtaz A, et al. Pharmacological applications of quercetin and its derivatives: a short review. *Trop J Pharma Res.* 2014;13:1561-1566.
- David AVA, Arulmoli R, Parasuraman S. Overviews of biological importance of quercetin: a bioactive flavonoid. *Pharmacogn Rev.* 2016;10:84-89.
- Kinker B, Comstock AT, Sajjan US. Quercetin: a promising treatment for the common cold. *J Anc Dis Prev Rem.* 2014;2:111.
- Wu W, Li R, Li X, et al. Quercetin as an antiviral agent inhibits influenza A virus (IAV) entry. *Viruses.* 2016;8:6.
- Yi L, Li Z, Yuan K, et al. Small molecules blocking the entry of severe acute respiratory syndrome coronavirus into host cells. *J Virol.* 2004;78:11334-11339.
- Park JY, Yuk HJ, Ryu HW, et al. Evaluation of polyphenols from *Broussonetia papyrifera* as coronavirus protease inhibitors. *J Enzyme Inhib Med Chem.* 2017;32:504-512.
- Nguyen TYH, Woo HJ, Kang HK, et al. Flavonoid-mediated inhibition of SARS coronavirus 3C-like protease expressed in *Pichia pastoris*. *Biotechnol Lett.* 2012;34:831-838.
- Kim YJ, Park W. Anti-inflammatory effect of quercetin on RAW 264.7 mouse macrophages induced with polyinosinic-polycytidylic acid. *Molecules.* 2016;21:450.
- Hosseinzade A, Sadeghi O, Biregani AN, Soukhtehzari S, Brandt GS, Esmailzadeh A. Immunomodulatory effects of flavonoids: possible induction of T CD4+ regulatory cells through suppression of mTOR pathway signaling activity. *Front Immunol.* 2019;10:1664-3224.
- Chacko SM, Thambi PT, Kuttan R, Nishigaki I. Beneficial effects of green tea: a literature review. *Chin Med.* 2010;5:13.
- Xu J, Xu Z, Zheng W. A review of the antiviral role of green tea catechins. *Molecules.* 2017;22:1337.
- Yeh CF, Chang JS, Wang KC, Shieh DE, Chiang LC. Water extract of *Cinnamomum cassia* Blume inhibited human respiratory

- syncytial virus by preventing viral attachment, internalization, and syncytium formation. *J Ethnopharmacol.* 2013;147:321-326.
28. Fatima M, Zaidi NU, Amraiz D, Afzal F. In vitro antiviral activity of *Cinnamomum cassia* and its nanoparticles against H7N3 influenza A virus. *J Microbiol Biotechnol.* 2016;26:151-159.
29. Zhuang M, Jiang H, Suzuki Y, et al. Procyanidins and butanol extract of *Cinnamomi cortex* inhibit SARS-CoV infection. 2009; 82:73-81.
30. Wang L, Yang R, Yuan B, Liu Y, Liu C. The antiviral and antimicrobial activities of licorice, a widely-used Chinese herb. *Acta Pharm Sin B.* 2015;5:310-315.
31. Cheel J, Onofre G, Vokurkova D, Tumova L, Neugebauerová J. Licorice infusion: chemical profile and effects on the activation and the cell cycle progression of human lymphocytes. *Pharmacogn Mag.* 2010;6:26-33.
32. Brush J, Mendenhall E, Guggenheim A, et al. The effect of *Echinacea purpurea*, *Astragalus membranaceus* and *Glycyrrhiza glabra* on CD69 expression and immune cell activation in humans. *Phytother Res.* 2006;20:687-695.
33. Thevarajan I, Nguyen THO, Koutsakos M, et al. Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19. *Nat Med.* 2020;26:453-455.
34. Channappanavar R, Perlman S. Pathogenic human coronavirus infections: causes and consequences of cytokine storm and immunopathology. *Semin Immunopathol.* 2017;39:529-539.
35. Cinatl J, Morgenstern B, Bauer G, Chandra P, Rabenau H, Doerr HW. Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus. *Lancet.* 2003;361:2045-2046.
36. Hoever G, Baltina L, Michaelis M, et al. Antiviral activity of glycyrrhizic acid derivatives against SARS-coronavirus. *J Med Chem.* 2005;48:1256-1259.
37. Guillin OM, Vindry C, Ohlmann T, Chavatte L. Selenium, selenoproteins and viral infection. *Nutrients.* 2019;11:2101.
38. Hoffmann PR, Berry MJ. The influence of selenium on immune responses. *Mol Nutr Food Res.* 2008;52:1273-1280.
39. Steinbrenner H, Al-Quraishy S, Dkhil MA, Wunderlich F, Sies H. Dietary selenium in adjuvant therapy of viral and bacterial infections. *Adv Nutr.* 2015;6:73-82.
40. Beck M, Levander O, Handy J. Selenium deficiency and viral infection. *J Nutr.* 2003;133(5 suppl 1):1463S-1467S.
41. Domingo E. Rapid evolution of viral RNA genomes. *J Nutr.* 1997; 127(5 suppl):958S-961S.
42. Harthill M. Review: micronutrient selenium deficiency influences evolution of some viral infectious diseases. *Biol Trace Elem Res.* 2011;143:1325-1336.
43. Ivory K, Prietoa E, Spinks C, Armah C, Goldson A, Dainty J, Nicoletti C. Selenium supplementation has beneficial and detrimental effects on immunity to influenza vaccine in older adults. *Clin Nutr.* 2017;36:407-415.