



Nasal spray that reduces COVID-19 severity

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A pharmaceutical company in Vancouver, Canada called SaNOtize, has been developing topical antimicrobial products to help fight drug resistant infections, and recently, to fight SARS-CoV-2, the cause of COVID-19.¹

In March 2021, robust results from a small, randomized, placebo-controlled phase 2 human trial carried out at Ashford and St. Peter's Hospitals in the UK using the SaNOtize-developed nitric oxide (NO) nose spray, were announced. The study evaluated 80 participants (40 in the treated group and 40 in the control group) with confirmed symptomatic cases of COVID-19. Participants self-administered in their nose 120-140 microliters of a spray containing nitric oxide, 5-6 times per day for 9 days. Participants in the treatment group showed a 95% decline in viral load within 24 hours and 99% reduction within 72 hours, and there were no adverse reactions.² This was very significant considering that current vaccines show an absolute risk reduction of only 1%.³

Vaccinated people still get sick from COVID-19, and they can still transmit it,⁴ so the use of other medications may be a very beneficial aspect of controlling SARS-CoV-2 infection.

Lowering the viral load in symptomatic people not only helps to reduce the severity and duration of infection for that person, but also helps to reduce transmission,⁵ potentially reducing the risk to vulnerable people.³

Nitric oxide is a molecule produced naturally in our own body and is a free radical, meaning it will oxidize other molecules including pathogens, and it is used as a signaling molecule in many physiological processes. Our immune cells make NO from the amino acid arginine and oxygen, along with enzymes called nitric oxide synthases. Healthy people make more NO when infected with a pathogen (virus, bacterium, fungus or parasite). In our body, NO signals smooth muscles, such as those in our blood vessels, to relax, which leads to vasodilation and vascular regulation. NO is a prominent molecule used by our immune system to control infections.⁶

Nitric oxide can cause oxidative damage and tissue damage at high concentrations. Therefore, the concentration that is used is very important and must be studied in various populations. It has been shown that at doses of 100-200 ppm, NO has potent anti-microbial activities *in vitro*, and doses of 80 ppm have been safely used in infants as a vasodilator, but further dosage studies need to be completed for use as a treatment for COVID-19 in various populations.⁷

NO inhibits viral replication and also regulates inflammatory reactions that contribute to acute respiratory distress syndrome (ARDS), which is a life-threatening situation seen to occur in patients with severe respiratory infections, such as COVID-19 in vulnerable people. NO supplementation has been shown to prevent cytokine storms, and to improve arterial oxygenation.⁸ It may be that the elderly population that are more susceptible to cytokine storms



with COVID-19 infection, because they produce less endogenous NO than normal and that is contributing to the severity of their disease.

An *in vitro* study showed that NO killed 100% of pneumococcal bacteria in culture.⁹ Gaseous NO was found to have antiviral effects on influenza,¹⁰ and NO has been demonstrated to suppress the replication of wild-type dengue viruses *in vitro*.¹¹ SaNOTize's *in-vitro* data from the Institute of Viral Research, located at Utah State University, showed a complete eradication (to below level of detection) within 2 min. This was tested on the Alpha, Beta and Gamma variants as well as on other respiratory viruses with similar results.

It has also been shown that in our nasal epithelial cells, we normally produce NO, which we then inhale into our lungs that impacts oxygenation. People on ventilators do not breathe through their nose and therefore, have less NO making it to the lungs compared to healthy people breathing through their nose. This study found that 6 out of 6 long term intubated patients had an 18% increase in oxygenation when nasal air containing NO was added to their inhaled air.¹²

In March 2021, in Israel and Bahrain, interim approvals were given to study SaNOTize's nose spray for treatment of COVID-19 infection.¹³ "Manufacturing of (nitric oxide nose spray) NONS, under the brand name Enovid, has begun in Israel with SaNOTize's partner Nextar Chempharma Solutions Ltd., and it is expected to be on sale there this summer." Emergency use submission has been submitted to other regulatory authorities around the world, including Canada and India.

This treatment is another very possible way to reduce severity, shorten the course of SARS-CoV-2 infection, and reduce transmission of COVID-19. It should be considered as a possibly safer alternative to vaccination for some people, considering that the vaccine has been shown to have a significantly higher rate of adverse reactions compared to all other previous vaccines.¹⁴

We have not yet seen the end results of the latest NO clinical trials that are currently ongoing, but the early data looks very promising.

References

1. Website, "SaNotize - The Company - Sanotize." <https://sanotize.com/> (accessed Jul. 05, 2021).
2. S. Winchester, S. John, K. Jabbar, and I. John, "Clinical efficacy of nitric oxide nasal spray (NONS) for the treatment of mild COVID-19 Infection," *Journal of Infection*, May 2021, doi: 10.1016/j.jinf.2021.05.009.
3. P. Olliaro, "What does 95% COVID-19 vaccine efficacy really mean?," *The Lancet Infectious Diseases*, vol. 21, no. 6, p. 769, Jun. 2021, doi: 10.1016/s1473-3099(21)00075-x.
4. "Vaccines protect people from diseases, but don't always prevent disease transmission; research ongoing to determine if COVID-19 vaccines stop transmission - Health Feedback." <https://healthfeedback.org/claimreview/vaccines-protect-people-from-diseases-but-dont-always->

[prevent-disease-transmission-research-ongoing-to-determine-if-covid-19-vaccines-stop-transmission/](#) (accessed Jul. 05, 2021).

5. H. Kawasuji et al., “Transmissibility of COVID-19 depends on the viral load around onset in adult and symptomatic patients,” PLoS ONE, vol. 15, no. 12 December, p. e0243597, Dec. 2020, doi: 10.1371/journal.pone.0243597.
6. C. Bogdan, “Nitric oxide and the immune response NO production in the immune system,” 2001. Accessed: Jul. 05, 2021. [Online]. Available: <https://www-nature-com.proxy1.lib.uwo.ca/articles/ni1001-907.pdf>
7. C. Miller et al., “A phase I clinical study of inhaled nitric oxide in healthy adults,” Journal of Cystic Fibrosis, vol. 11, no. 4, pp. 324–331, Jul. 2012, doi: 10.1016/j.jcf.2012.01.003.
8. N. C. Adusumilli, D. Zhang, J. M. Friedman, and A. J. Friedman, “Harnessing nitric oxide for preventing, limiting and treating the severe pulmonary consequences of COVID-19,” Nitric Oxide, vol. 103, pp. 4–8, 2020, doi: 10.1016/j.niox.2020.07.003.
9. C. McMullin, Bevin; Miller, “The antimicrobial effect of nitric oxide on the bacteria that cause nosocomial pneumonia in mechanically ventilated patients in the intensive care unit - PubMed,” Respiratory Care, 2005. <https://pubmed.ncbi.nlm.nih.gov/16253152/> (accessed Jul. 05, 2021).
10. G. Regev-Shoshani, S. Vimalanathan, B. McMullin, J. Road, Y. Av-Gay, and C. Miller, “Gaseous nitric oxide reduces influenza infectivity in vitro,” Nitric Oxide - Biology and Chemistry, vol. 31, pp. 48–53, May 2013, doi: 10.1016/j.niox.2013.03.007.
11. W. Charnsilpa, R. Takhampanya, T. P. Endy, M. P. Mammen, D. H. Libraty, and S. Ubol, “Nitric oxide radical suppresses replication of wild-type dengue 2 viruses in vitro,” Journal of Medical Virology, vol. 77, no. 1, pp. 89–95, Sep. 2005, doi: 10.1002/jmv.20418.
12. J. O. N. Lundberg, G. Settergren, S. Gelinder, J. M. Lundberg, K. Alving, and E. Weitzberg, “Inhalation of nasally derived nitric oxide modulates pulmonary function in humans,” Acta Physiologica Scandinavica, vol. 158, no. 4, pp. 343–347, 1996, doi: 10.1046/j.1365-201X.1996.557321000.x.
13. “Israel, NZ give interim approval for sale of virus nasal spray firm, company says | Nasdaq.” <https://www.nasdaq.com/articles/israel-nz-give-interim-approval-for-sale-of-virus-nasal-spray-firm-company-says-2021-03-22> (accessed Jul. 05, 2021).
14. “Mortality.” <https://www.openvaers.com/covid-data/mortality> (accessed Jul. 05, 2021).