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Enovid™, a therapy delivered intranasally, developed by SaNOtize, a Vancouver based company with strong ties to Israel, was recently shown to be **highly effective in reducing viral load of SARS-CoV-2 in positive tested patients**. Given that the nasal passage is often the primary entry point for SARS-CoV-2, interventions administered intranasally could be highly effective in limiting spread of COVID-19 infection. **enovid™** could be such an intervention.

Independent testing laboratories have confirmed that enovid™ inactivated SARS-CoV-2 virus *in-vitro* in under 2 minutes (including it's variants – alpha and Gamma. Delta variant in testing) and significantly reduced SARS-CoV-2 in infected hamsters. External laboratory testing validated that this treatment also inactivated Influenza viruses and other respiratory viruses such as RSV and Rhinovirus.

SaNOtize together with Ashford and St Peter's Hospitals NHS Foundation Trust in Surrey, UK, recently completed a randomised, double blinded, placebo controlled trial and showed that **enovid™** represents a safe and effective virucidal treatment. This treatment can prevent the infection and transmission of COVID-19, shorten its course, and prevent the progression of the disease. Specifically, in this clinical trial, that evaluated about 80 confirmed cases of COVID-19, **SaNOtize's early treatment for COVID-19 significantly reduced the level of SARS-CoV-2**, as compared to placebo. The average viral log reduction in the first 24 hours of treatment was 1.362, which corresponds to a **decline of about 95%.** Within 72 hours, the viral load dropped by **more than 99%**. The majority of these patients had been infected with the UK variant, which is considered a variant of concern. The study concluded that **enovid™ accelerated clearance of SARS-CoV-2 by a factor of 16-fold versus the placebo saline nasal spray** (as compared to 4-5 fold shown in monoclonal antibody testing), and it presents supporting evidence for the use of enovid™ for prevention or treatment of patients with recent or established SARS-CoV-2 RNA infection. Since this is a non specific virucidal treatment, it can be effective against a wide range of variants and different viruses.

Given that enovid™ can easily be self-administered as a nasal spray and act as "**hand sanitizer for your nose**", consideration should be given to its role as an affordable, highly scalable, public health measure for **prevention** of COVID-19 and other similar airborne viral contagions such as influenza.

Mechanism of Action for the prevention and Treatment of COVID-19

enovid™ formulation is highly effective at reducing viral load because it has multiple mechanisms of action that make it the ideal prevention and treatment for early COVID-19 or other respiratory infections like the flu and common cold.
enovid™ formulation creates a physical and chemical barrier in the nose. The gelling agent creates a mechanical barrier which traps viruses within the nasal cavity and prevents them from further entry into the respiratory tract causing infection. The first chemical barrier is established by the acid, which lowers the pH in the nasal cavity and creates a hostile environment for the virions. The second chemical barrier is created by the short (about 5 min) burst of nitric oxide (NO) which enhances the hostile environment. During this time, NO rapidly destroys the shape of spikes/protrusions of any virions present, through a process called nitrosylation, rendering the key-like viral portion required to enter the cell useless. The other unique mechanism of action of enovid™ is that the NO molecule blocks the ACE-2 receptor, preventing the virion from fusing to the host cell. This is important because even though NO is produced for a short period of time, its effects have a long-lasting protection against viral entry preventing infection of the host cell.

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Akaberi[1], a well-respected researcher, was quoted recently saying "To our knowledge, **nitric oxide is the only substance shown so far to have a direct effect on SARS-CoV-2"**

Nitric oxide is a natural molecule produced by our body and it is widely regarded to possess antimicrobial properties. It has been approved, for two decades, as an inhalation treatment for newborn babies with pulmonary hypertension, using pressurized gas cylinders. The nitric oxide dose from **enovid™** is different from the newborn therapy in at least two notable ways. First, **enovid™** is being administered **topically** with a liquid made out of compounds approved by the FDA for use in food products, and secondly, enovid™ daily NO dose is 0.5% of that approved for the newborns.

The rationale to evaluate enovid™ in nasal spray for treating COVID-19 is based on its non-systemic, topical NO releasing capability showing strong virucidal activity. Delivery of NO releasing liquid to the nasal cavity is supported in a recent study that concluded "given that nasal carriage is likely to be a key feature of transmission, drugs/vaccines administered intranasally could be highly effective in limiting spread of COVID-19 infection".[2]

enovid™ could be used daily, for prevention of infection, supported by the strong human data of reducing viral load in the nose. enovid™ could also potentially be used to prevent the progression of the disease, in the first few days of symptoms. Daily use of enovid™ will very likely prevent infections.

Safety

Nitric oxide gas inhaled continuously in a concentration of 20 parts per million (ppm) for 14 days has been approved as a drug to treat newborn babies with pulmonary hypertension, safely, for almost two decades. Nitric Oxide is also a natural molecule, produced in every system in our body. enovid™, delivered as nasal spray, has a localized effect and produces nitric oxide at 0.5% of what is approved for treating "blue babies".

Further, the compounds used to create the nasal spray are food grade materials in a daily concentration under the Average Daily Intake guidelines. There were no adverse health events recorded in over 2000 treatments given in the UK trial (with positive tested patients), or in over 7,000 self-administered treatments given to healthy volunteers in earlier Canadian clinical trial.

Approval

enovid™ was given an interim approval, by the MOH, as a medical device, in Israel and in Bahrain. It is also going through approval processes in other countries. Fast track approvals are available. Sales of enovid™ will commence in Israel in first early July 2021. **enovid™ is currently being manufactured in Israel, by Nextar at a capacity of 10,000 bottles a day with scale up planned.**

https://www.youtube.com/watch?v=R2I3lnKlSxQ

References

1 Akaberi D, et al. (2020). Mitigation of the replication of SARS-CoV-2 by nitric oxide in vitro. *Redox Biology 37*.

2 Sungnak, W. *et al.* SARS-CoV-2 entry factors are highly expressed in nasal epithelial cells together with innate immune genes. *Nat Med* **26**, 681-687, doi:10.1038/s41591-020- 0868-6 (2020).