

# Antiviral Effects of Sinamaz®: Potentials for COVID-19 Management

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## Dear Editor

Nowadays, viruses are considered the most important infectious agents in human societies. Pathogenic viruses enter the body mainly through the respiratory or digestive systems. Due to urbanization and related lifestyle changes, these viral agents can easily cause epidemics and widespread dangerous pandemics. The most recent example is the COVID-19 pandemic.

The global burden of the COVID-19 pandemic significantly affected societies due to its severe health, economic, and social consequences. It crippled life all around the world and forced countries to take urgent actions (1, 2). In line with the popularity and global acceptance of complementary and alternative medicine (CAM) in recent decades (3), various brands of traditional and complementary medicines have come to the scene to confront the COVID-19 pandemic. In this regard, herbal therapy has shown great potential (4). The goal is to help disease management coincide with conventional medicine. A successful example of such an integrative approach to managing COVID-19 could be Traditional Chinese Medicine (TCM). The efficacy of many TCM drugs in decreasing the side effects of the disease and its better management has been shown in recent investigations (5, 6).

Sinamaz® is a natural product in a nasal drop dosage form manufactured by Sanabel Daroo© Pharmaceutical Corporation, Tehran, Iran. Iran's Food and Drug Administration (IFDA) has approved it to manage the common cold. It is made of black seed (*Nigella sativa*) oil and olive (*Olea europaea*) oil.

Previous studies have shown the anti-inflammatory, anti-microbial, immunomodulatory, and anticoagulant effects of *Nigella sativa* (7). In addition, *in-silico* analyses of *Nigella sativa*'s chief constituents have revealed the high binding affinity of dithymoquinone (DTQ) at the SARS-CoV-2:ACE2 interface in addition to the considerable affinity of the other constituents, including nigelledine, hederagenin, and  $\alpha$ -hederin, with the virus proteins (8, 9). Notably, a recent clinical trial has also revealed that Sinamaz nasal drop could alleviate symptoms and possibly reduce the risk of COVID-19 transmission among close contacts of infected individuals (10).

In a preliminary experimental study evaluating the antiviral effects of Sinamaz®, the following steps were performed: Vero cell line (ATCC® CCL-81™) was cultivated in low-glucose Dulbecco's Modified Eagle's medium (DMEM) and 5% fetal bovine serum in a 48-well cell culture plate. The plate was incubated at 37 degrees Celsius for 48 hours. When the cell reached 85 to 90% confluence, the plate was used for performing toxicity and viral tests.

To evaluate the toxicity of Sinamaz®, the methylthiazol tetrazolium (MTT) assay (Merck, CT01) was performed. Moreover, serial logarithmic dilution of Enterovirus D68, as well as human herpes virus type 1, was prepared from the stock. The 10<sup>2</sup>, 10<sup>4</sup>, and 10<sup>6</sup> cell culture infective dose 50% (CCID<sub>50</sub>) virus was exposed to Sinamaz® solution for 60 seconds, and the virus was transferred to the cell culture plate in 5 replicates.

Results of the MTT assay for toxicity evaluations of Sinamaz® showed very low toxicity in cell culture. Moreover, it was revealed that Sinamaz® could neutralize 10<sup>3</sup> CCID<sub>50</sub> enterovirus and 10<sup>4</sup> CCID<sub>50</sub> HSV-1 after 60 seconds.

Since the nasal cavity is an important entry point for the novel beta coronavirus SARS-CoV-2, which replicates efficiently in the upper respiratory system (7), research for safe and effective nasal disinfectants seems to be justified. On the other hand, the nasal cavity is the access route of the nasal-associated lymphoid tissue (NALT), which has a crucial role in the production of both systemic and mucosal antibodies (11). Accordingly, it can be hypothesized that inactivating a virus, such as SARS-CoV-2, may not only provide protection but also enable the immune system to produce immunoglobulins and memory cells more effectively.

Although this study did not specifically evaluate the anti-SARS-CoV-2 activity of this natural product, it should be investigated in future studies, considering the properties of black seed ingredients.

This natural product seems to have promising viral neutralization activity in cell culture. As a treatment that may control the viral load and inflammatory response, it could be suggested for COVID-19 infection. However, further clinical investigations are needed to evaluate its safety and efficacy in COVID-19 management.

### Conflict of Interest

Mohsen Naseri is the managing director of Sanabel Daroo© Pharmaceutical Corporation. Other authors have nothing to declare.

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