

## Potential antiviral properties of antifungal drugs

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The widespread therapeutic use of antifungal drugs has given rise to multiple interests, and their research and development have become quite rapid, emerging as an active highlight topic [1].

It has been proposed that the efficacy of some antifungal agents may be related to their capacity to induce human cytokine production. This was confirmed when fluconazole was reported to increase CCL3 and CCL4 level in the supernatants of human mononuclear cell cultures [2].

Itraconazole (ITZ) and posaconazole (POS) belong to triazoles that are broad-spectrum antifungal agents, commonly used to prevent and treat several lung fungal infections and other medically significant fungi that cause superficial, subcutaneous, and systemic infections in humans [3]. The mechanisms action of these drugs is by interacting with cytochrome P450 enzymes, via inhibition of particular lanosterol 14 $\alpha$ -demethylase, which is important for biosynthesis in fungal membrane function and growth [4].

Some studies indicate that ITZ may hold promise for the prophylaxis of opportunistic fungal infections in high-risk persons, such as women with persistent recurrent vaginal candidiasis, immunodeficient patients with chronic candidiasis, patients with AIDS, and patients taking immunosuppressive drugs [5]. POS offered successful prophylaxis against invasive fungal infections and was generally well tolerated in patients undergoing chemotherapy for induction–remission [6].

The Coronavirus Disease-2019 (COVID-19) outbreak has become a global health emergency owing to its magnitude, attributed deaths, and its propensity to spread across the world. Until this moment, there is no specific drug to treat this new virus, and organ support in seriously ill individuals and symptomatic treatment are major steps in clinical management. To develop a specific antiviral for treating novel COVID-19 may take a long time for an evaluation. However, some marketed drugs have showed some success in preventing acute respiratory distress syndrome, such as metformin, fibrates, and atorvastatin, besides nutrient supplements [7].

Because viral infections are common and difficult to control, especially RNA viruses with changing mutations, some studies have conducted a series of experiments on the use of some of the available drugs for prevention of viral infections.

POS and ITZ showed an inhibitory effect against the replication of influenza A virus in vitro by using a cell culture model [8]. The potential specificity of the antiviral effect of ITZ and POS may be due to the release of high amounts of type I interferon [9]. Thus, ITZ and POS are promising potential therapies in the

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treatment of influenza and other enveloped viruses, as well as serving as potential prophylactic drug by increasing interferon levels, which is considered a fundamental step in immunity against viral infection.

Regarding enteroviruses (which are nonenveloped icosahedral RNA viruses), ITZ was identified as an effective inhibitor of EV71 replication in the low micromolar range. It also inhibited other enteroviruses including coxsackievirus B3, coxsackievirus A16, enterovirus 68, and poliovirus 1. The suggested mechanism of action is by targeting a specific site(s) in the viral genome, such as a step involved in mRNA translation [10].

Other studies showed that ITZ is capable of inhibiting a wide range of viruses including the hepatitis C virus and poliovirus by exerting an effect on RNA replication [11]. ITZ also acts as an antiviral drug against echovirus 30 by inhibiting the early stages of echovirus 30 replication [12]. Moreover, several combinations of FDA-approved drugs including POS were investigated and were found to act synergistically to block Ebola virus entry and inhibit its infection [13].

## Conclusion

POS and ITZ may potentially hold promise in prophylaxis and treatment of COVID-19. They can act against different viruses by various mechanisms of actions including interfering with viral replication and increasing type I interferons production. In vitro and in vivo studies are recommended to verify the potential antiviral activity of these drugs on SARS-CoV-2.

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## Conflicts of interest

There are no conflicts of interest.

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