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Mini Review

Saccharomyces cerevisiae as A Fusion Inhibitor of Sars-Cov-2

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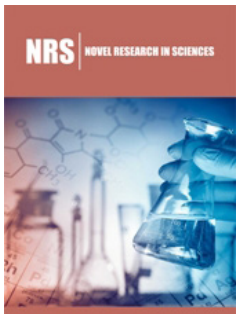
Resume

SARS-CoV-2 interacts with prokaryotic translation elongation factors (eEFs), predominantly eEF1A. This connection occurs at the intracellular level, when the virus is linked to ribosomes, necessary for viral replication. The fungus *Saccharomyces cerevisiae* has an abundance of eEF1A protein, and its dietary supplementation can increase serum protein levels, which, by binding to viruses circulating in the blood, prevent the entry of these cells, thus preventing viral replication; in addition, exposes the virus to the body's humoral immune system. Supplementation through the diet of the fungus *Saccharomyces cerevisiae* would work as a fusion inhibitor drug, a mechanism of action of some antivirals.



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Introduction

The SARS-SoV-2 (covid-19) pandemic killed more than two million people worldwide in 2020. The lack of specific and effective treatment for covid-19, and the absence of a vaccine, are the main causes of this tragedy. Countries with low level of investment in the health system suffer even more with the pandemic. The disparities between regions with better or worse hospital structures can double the mortality rate [1]. WHO data show that mortality per million inhabitants can vary widely beyond countries. Therefore, the use of low-cost treatment is even more important to reduce inequities between countries. The fungus *Saccharomyces cerevisiae* has low cost and simple production, being accessible to all societies. The genus Saccharomyces is a well-known and studied group of yeasts, the most famous representative of the genus being *Saccharomyces cerevisiae*, widely used in bread making, ethanol production and fermented beverages; used in the pharmaceutical industry and in the biomedical field through research an anti-*Saccharomyces cerevisiae* (ASCA).

Discussion

In the search for effective drugs against covid-19, a lot of medicines performs a test called drug repositioning. One known substance is plitidepsin (aplidine), an antitumor produced by the pharmaceutical company Pharma Mar, which is said to be effective against covid-19. Plitidepsin is a blocker of the eEF1A protein and performed 27.5-fold more potent than remdesivir in an in vitro test with cell culture; and in a in vivo test obtained a 99% decrease in viral load [2]. Plitidepsin however has limited approval for clinical use by the Committee for Medicinal Products for Human Use of the European Medicines Agency (Committee for Medicinal Products for Human Use - EMA). The use of the eEF1A protein by SAR-Cov-2 for viral replication is not exclusive to it. Countless viruses use it in the same way [3]. We can mention West Nile Virus (WNV), a single-stranded RNA virus that causes West Nile fever, a member of the Flaviviridae family, more specifically of the Flavivirus genus [4]; the human hepatitis D virus (HDV), also known as the hepatitis Delta virus [5]; the human hepatitis C virus (HCV) [6]; HIV, human immunodeficiency virus [7,8]; HPV, papillomavirus [9]; the human hepatitis B virus (HBV) [10]; in addition to other viruses that attack other species, such as the Bovine Viral Diarrhea virus [11]; the tobacco mosaic virus (TMV) [12]; among so many.

The use of the eEF1A protein for viral replication is known, and it mayn be exploited to inhibit viral replication. EEF1A is an intracellular protein, present in the cytoplasm and nucleus, with translational ARN and pleiotropic properties; its inactivation causes

immunodeficiency, neural and muscular defects, and favors cellular apoptosis [13]. Therefore, drugs that block it will also inhibit biological and necessary activities. However, drugs that simulate it at the seric level do not have adverse effects. Here we propose the use of *Saccharomyces cerevisiae*, a fungus rich in eEF1A proteins [14]. The fungus *Saccharomyces cerevisiae* has eEF1A proteins with a significant degree of homology with humans, and its connection with the HIV virus has been well studied [15,16]. Among the mechanisms for the treatment of viral infections we have the blocking of virus binding, inhibition of DNA / RNA synthesis, inhibition of protein synthesis, inhibition of fusion, inhibition of virus release, inhibition of non-encapsulated viruses and immunomodulation. Administration of *Saccharomyces cerevisiae* via diet would increase serum levels of eEF1A, which would act as an effective antiviral against SARS-Cov-2 by inhibiting fusion. SARS-CoV-2, when it reaches the bloodstream, binds to circulating eEF1A; when binding, it has inhibited its fusion to the cells. Without the possibility of invading cells and replicating, the virus is exposed to the body's huomoral immune response. Thus, circulating eEF1A proteins would work as "traps" for SARS-Cov-2, a mechanism similar to that exercised by antivirals Enfuvirtide and Maraviroc against HIV.

Conclusion

The fungus *Saccharomyces cerevisiae* has the potential to be an effective and low-cost treatment for SARS-Cov-2 infection, by inhibiting virus fusion to human cells, preventing viral replication, while exposing circulating viruses to attack by the body's humoral immune system.

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