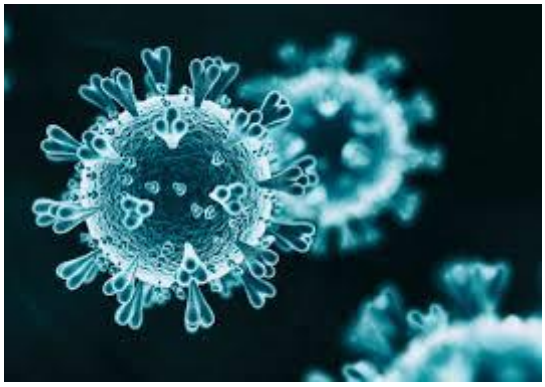
Ritonavir may inhibit exoribonuclease activity of nsp14 from the SARS-CoV-2 virus and potentiate the activity of chain terminating drugs

Computational studies carried out at the DBT's Regional Centre for Biotechnology (RCB), Faridabad suggests that the HIV-1 protease inhibitor named ritonavir might bind to the exoribonuclease active site of the nsp14 protein, prevent association with substrate viral RNA and thus inhibits the proofreading activity of nsp14.



The nsp14 is known to attenuate the inhibitory effect of drugs that function through premature termination of viral genome replication. Hence, ritonavir may potentiate the therapeutic properties of drugs such as remdesivir, favipiravir and ribavirin. A recent clinical involving lopinavir-ritonavir, ribavirin and interferon beta-1b supports the idea that ritonavir can enhance activity of chain terminating drugs. The ability of ritonavir to enhance the activity of remdesivir/favipiravir may be tested at the earliest *in vitro* and *in vivo* and clinical trials may be initiated to assess if the combination results in improved clinical outcomes, especially in patients with severe COVID-19 disease.

SARS-CoV-2 is the causative agent for the ongoing COVID-19 pandemic, and the nsp14 protein of this virus houses a 3' to 5' exoribonuclease activity. This activity is responsible for proofreading progeny RNA and removes errors that arise during genome duplication. Further details of the computational studies conducted at the Regional Centre for Biotechnology can be seen here: https://indiarxiv.org/f5gnq

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