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Possible agent for COVID 19 treatment; Rifampicin

Aydin OC *et al*. Rifampicin to treat COVID-19

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Abstract
Rifampicin is a promising drug for treatment of coronavirus disease 2019 based on its antiviral properties and recent In silico studies. In silico studies can prepare the ground for further studies.

Key Words: Rifampicin; COVID 19; Treatment; In silico; Drug drug interaction; Therapeutic potential

Aydin OC, Aydın S, Barun S. Possible agent for COVID 19 treatment; Rifampicin. *World J Virol* 2022; In press

Core Tip: Rifampicin may be used as a substitute treatment for coronavirus disease 2019 (COVID-19). Despite the fact that it has a variety of medication interactions, none of the important ones for the currently utilised COVID-19 medicines, favipiravir, enoxaparin, and aspirin, have been defined.

TO THE EDITOR

We read the review written by Panayiotakopoulos *et al*[1] with interest. The impacts of the coronavirus disease pandemic of 2019 (COVID-19) are still being felt, and research into this topic continues due to the lack of a precise therapy. It is feasible to repurpose

medications already used for other reasons in the treatment of COVID-19. The authors discussed rifampicin's antiviral capabilities, its potential effects in computer simulations, its safety, and its role in clinical practice. Rifampicin is an antibacterial drug that inhibits DNA-dependent RNA polymerase in M. tuberculosis, and its antiviral activity has been shown on some viruses[2]. On this basis, the potential efficacy of rifampicin as a COVID-19 treatment drug has been demonstrated in in silico research[3]. We concur with the authors' suggestion for more research into the potential use of rifampicin for COVID 19.

In a study in which 20 FDA-approved drugs were screened by molecular docking method in possible drug design for COVID-19, rifampicin showed in silico binding to more than one target protein of SARS-COV2. Other macrocyclic antibiotics showing binding are polymyxin B and bafilomycin A[4]. In another in silico studyof FDA-approved drugs to treat COVID 19 infection, rifampicin has a stronger binding affinity for COVID-19 main protease Mpro[5]. However, these findings are virtual and additional studies are needed for validation.

However, due to the properties of rifampicin, various drug interactions may occur during its possible use. Rifampicin promotes the expression of CYP 3A4 in the small intestine and liver, as noted in the review. Additionally to the work by Panayiotakopoulos *et al*, an essential feature of Rifampicin is that it activates proteins such as the P glycoprotein drug transporter andCYP2C-mediated metabolism[6]. There are possible drug interactions with drugs used for the treatment of COVID-19 and for additional diseases. Favipiravir is one of the antiviral medications used in the treatment of COVID-19. Favipiravir is metabolized mostly *via* aldehyde oxidase and xanthine oxidase[7], the probability of a pharmacological interaction between rifampicin and Favipiravir is low. Lopinavir and ritonavir are two additional widely used antivirals; coadministration of these drugs with rifampin may result in a decrease in the plasma concentrations of ritonavir and lopinavir due to rifampin's induction of CYP450 3A4, the isoenzyme responsible for the metabolic clearance of ritonavir and lopinavir[8]. Remdesivir is widely used in COVID-19 treatment which is metabolized through

hydrolysis reaction to itstriphosphate active form *via* by carboxylesterase 1 (80%), cathepsin A (10%), and CYP3A (10%). Since Rifampicin is a potential inductor of CYP3A4, concomitant administration might increase the metabolism of Remdesivir[9]. Dexamethasone has a strong anti-inflammatory impact and is typically used as an adjunctive treatment for COVID-19 pneumonia. Rifampin may increase corticosteroid hepatic metabolism, hence diminishing their therapeutic impact. Corticosteroids' half-life of elimination has been demonstrated to be shortened by up to 45% when coadministered with rifampin[10,11].

It was suggested that prophylaxis of thrombosis in COVID-19 should include both anticoagulant and antiplatelet medications. Enoxaparin and aspirin are the two most often used anticoagulant and antiplatelet medications[12]. Fortunately, no significant medication interactions between these drugs and rifampicin have been identified to yet. Apixaban and other direct oral anticoagulants can also be utilised. Rifampicin coadministration significantly increased apixaban plasma concentrations. When used orally, approximately 15% of apixaban is metabolised by CYP3A and roughly 6% by CYP1A2 and CYP2J2. The balance (50%) is eliminated unaltered in the form of faeces and urine. A single dose of rifampicin decreased apixaban clearance by 25%. Rifampicin largely influenced apixaban absorption (and/or distribution), which could be attributed to an impairment of intestinal P-glycoprotein[13].

The authors said that rifampicin has been shown to be quite effective in treating COVID-19 in in silico tests. Additionally, multiple medication classes have been examined in silico for the treatment of COVID-19. Melatonin, ramelteon, and agomelatine, for example, have been demonstrated to significantly limit virus entry into cells in investigations. Ramelteon was proven to be the most effective antiviral against SARS-CoV-2[14].

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