

World Journal of *Virology*

World J Virol 2022 September 25; 11(5): 221-393



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ABOUT COVER

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The primary aim of *World Journal of Virology* (*WJV*, *World J Virol*) is to provide scholars and readers from various fields of virology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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INDEXING/ABSTRACTING

The *WJV* is now abstracted and indexed in PubMed, PubMed Central, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Yu-Xi Chen*; Production Department Director: *Xiang Li*; Editorial Office Director: *Jin-Lai Wang*.

NAME OF JOURNAL

World Journal of Virology

ISSN

ISSN 2220-3249 (online)

LAUNCH DATE

February 12, 2012

FREQUENCY

Bimonthly

EDITORS-IN-CHIEF

Mahmoud El-Bendary, En-Qiang Chen

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2220-3249/editorialboard.htm>

PUBLICATION DATE

September 25, 2022

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INSTRUCTIONS TO AUTHORS

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<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Possible agent for COVID-19 treatment: Rifampicin

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Specialty type: Pharmacology and pharmacy

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): D
Grade E (Poor): 0

P-Reviewer: Gupta S, United States; Varshney K, Australia

Received: April 20, 2022

Peer-review started: April 20, 2022

First decision: June 8, 2022

Revised: June 20, 2022

Accepted: August 25, 2022

Article in press: August 25, 2022

Published online: September 25, 2022



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Abstract

Rifampicin is a promising drug for the treatment of coronavirus disease 2019 based on its antiviral properties and recent *in silico* studies. *In silico* studies can serve as a foundation for further studies.

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

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

Citation: Aydin OC, Aydin S, Barun S. Possible agent for COVID-19 treatment: Rifampicin. *World J Virol* 2022; 11(5): 391-393

URL: <https://www.wjgnet.com/2220-3249/full/v11/i5/391.htm>

DOI: <https://dx.doi.org/10.5501/wjv.v11.i5.391>

TO THE EDITOR

We read the review written by Panayiotakopoulos and Papadimitriou[1] with interest.

The impacts of the coronavirus disease 2019 (COVID-19) pandemic 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 for 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 *Mycobacterium tuberculosis*, and its antiviral effect 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 United States Food and Drug Administration (FDA)-approved drugs were screened by molecular docking method in a possible drug design for COVID-19, rifampicin showed *in silico* binding to more than one target protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). Other macrocyclic antibiotics showing binding are polymyxin B and bafilomycin A[4]. In another *in silico* study of FDA-approved drugs to treat COVID-19 infection, rifampicin has stronger binding affinity for the COVID-19 main protease Mpro[5]. However, additional studies are needed for validation.

Due to the properties of rifampicin, various drug-drug interactions (DDIs) may occur during its possible use. Rifampicin promotes the expression of cytochrome p450 3A4 (CYP3A4) in the small intestine and liver, as noted in the review. Additionally, according to the work by Panayiotakopoulos and Papadimitriou[1], an essential feature of rifampicin is that it activates proteins such as the P glycoprotein (P-gp) drug transporter and CYP2C-mediated metabolism[6]. There are possible DDIs with drugs used for the treatment of COVID-19 and for additional diseases. Favipiravir is one of the antiviral medications used for the treatment of COVID-19. It is metabolized mostly *via* aldehyde oxidase and xanthine oxidase[7], and 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 for COVID-19 treatment, which is metabolized through hydrolysis reaction to its triphosphate active form *via* by carboxylesterase 1 (80%), cathepsin A (10%), and CYP3A (10%). Since rifampicin is a potential inducer 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 is shortened by up to 45% when co-administered with rifampin [10,11].

It has been 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. 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 influences apixaban absorption (and/or distribution), which could be attributed to an impairment of intestinal P-gp[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].

FOOTNOTES

Author contributions: Aydin S, Aydin OC and Barun S conceived the study; Aydin S, Aydin OC and Barun S were responsible for designing, materials and supervision; Aydin S, Aydin OC and Barun S did the literature search, wrote the manuscript, and reviewed the manuscript critically; All authors have read and approved the final manuscript.

Conflict-of-interest statement: The authors have no conflicts of interest to declare.

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S-Editor: Gong ZM

L-Editor: Filipodia

P-Editor: Gong ZM

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