

Teicoplanin: an alternative drug for the treatment of coronavirus COVID-19?

Sophie Alexandra Baron, Christian Devaux, Philippe Colson, Didier Raoult,
Jean-Marc Rolain

► **To cite this version:**

Sophie Alexandra Baron, Christian Devaux, Philippe Colson, Didier Raoult, Jean-Marc Rolain. Teicoplanin: an alternative drug for the treatment of coronavirus COVID-19?. International Journal of Antimicrobial Agents, Elsevier, 2020, pp.105944. 10.1016/j.ijantimicag.2020.105944 . hal-02517857

HAL Id: hal-02517857

<https://hal-amu.archives-ouvertes.fr/hal-02517857>

Submitted on 7 May 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

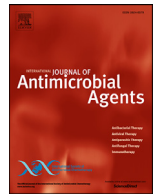
L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.





Contents lists available at ScienceDirect

International Journal of Antimicrobial Agents

journal homepage: www.elsevier.com/locate/ijantimicag

Hot topic

Teicoplanin: an alternative drug for the treatment of COVID-19?

Sophie Alexandra Baron^a, Christian Devaux^b, Philippe Colson^a, Didier Raoult^{a,c},
Jean-Marc Rolain^{a,c,*}^a Aix-Marseille Université, IRD, APHM, MEPHI, Faculté de Médecine et de Pharmacie, 19–21 boulevard Jean Moulin, 13385 Marseille Cedex 05, France^b Aix-Marseille Université, IRD, APHM, VITROME, Faculté de Médecine et de Pharmacie, 19–21 boulevard Jean Moulin, 13385 Marseille Cedex 05, France^c IHU-Méditerranée Infection, 19–21 boulevard Jean Moulin, 13385 Marseille Cedex 05, France

ARTICLE INFO

Article history:

Received 4 March 2020

Accepted 9 March 2020

Available online xxx

Keywords:

SARS-CoV-2

Drug repurposing

Teicoplanin

COVID-19

ABSTRACT

In December 2019, a novel coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged from China causing pneumonia outbreaks, first in the Wuhan region of China and then spread worldwide because of its probable high transmission efficiency. Owing to the lack of efficient and specific treatments and the need to contain the epidemic, drug repurposing appears to be the best tool to find a therapeutic solution. Chloroquine, remdesivir, lopinavir, ribavirin and ritonavir have shown efficacy to inhibit coronavirus in vitro. Teicoplanin, an antibiotic used to treat staphylococcal infections, previously showed efficacy to inhibit the first stage of the Middle East respiratory syndrome coronavirus (MERS-CoV) viral life cycle in human cells. This activity is conserved against SARS-Cov-2, thus placing teicoplanin as a potential treatment for patients with this virus.

© 2020 Elsevier B.V. and International Society of Chemotherapy. All rights reserved.

In December 2019, a novel coronavirus emerged from China causing pneumonia outbreaks, first in the Wuhan region of China and then spread worldwide because of its probable high transmission efficiency [1,2]. This coronavirus, named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (formerly 2019-nCoV), is responsible for respiratory infections including pneumonia, with an estimated mortality rate of approximately 2–2.5%, increasing with age and the presence of underlying diseases. In the first days of March 2020, an estimated 89 068 cases had been confirmed worldwide by the World Health Organization (WHO) (a number likely underestimated due to the existence of asymptomatic carriers) and the epidemic has already left 3046 dead from coronavirus disease 2019 (COVID-19), the majority of them occurring in China. Because COVID-19 is now becoming pandemic, and in the absence of a known validated efficient therapy, efforts of laboratories and medical teams have focused on repurposing US Food and Drug Administration (FDA)-approved drugs to treat the most severe COVID-19 cases. Drug repurposing is an effective way to quickly identify therapeutic drugs with a known safety profile to treat an emerging disease. Chloroquine/hydroxychloroquine, a front-line drug used in the treatment and prophylaxis of malaria as well

as in autoimmune diseases, has been shown to inhibit the replication of several DNA and RNA viruses, including most human coronaviruses [3]. Recently, chloroquine was found to inhibit SARS-CoV-2 in vitro, and its hydroxylated form has been proposed as a possible therapy to treat patients infected with SARS-CoV-2 [4,5]. In this context, other drugs also showed significant efficacy against SARS-Cov-2 in vitro, including remdesivir, lopinavir, ribavirin and ritonavir (<https://drugvirus.info/>) [6].

Teicoplanin, a glycopeptide antibiotic routinely used to treat bacterial infections, was found to be active in vitro against SARS-CoV and has joined the list of molecules that could be used in the therapeutic arsenal against COVID-19 [7]. This antibiotic, currently used in the treatment of Gram-positive bacterial infections, especially staphylococcal infections, has already shown efficacy against various viruses such as Ebola virus, influenza virus, flavivirus, hepatitis C virus and human immunodeficiency virus (HIV) as well as coronaviruses such as Middle East respiratory syndrome coronavirus (MERS-CoV) and SARS-CoV [8,9]. A patent was filed for the treatment of infection caused by MERS-CoV in 2016 [10]. According to Zhou et al., in coronaviruses teicoplanin acts on an early stage of the viral life cycle by inhibiting the low-pH cleavage of the viral spike protein by cathepsin L in the late endosomes, thereby preventing the release of genomic viral RNA and continuation of the virus replication cycle [8]. A recent study by the same authors showed that this activity was conserved against SARS-Cov-2 (the target sequence that serves as the cleavage site for cathepsin L is

* Corresponding author. Present address: Aix-Marseille Université, IRD, APHM, MEPHI, IHU-Méditerranée Infection, Faculté de Médecine et de Pharmacie, 19–21 boulevard Jean Moulin, 13385 Marseille Cedex 05, France. Tel.: +33 4 13 73 24 01.
E-mail address: jean-marc.rolain@univ-amu.fr (J.-M. Rolain).

<https://doi.org/10.1016/j.ijantimicag.2020.105944>

0924-8579/© 2020 Elsevier B.V. and International Society of Chemotherapy. All rights reserved.

conserved among SARS-CoV spike protein) [7]. The concentration of teicoplanin required to inhibit 50% of viruses (IC_{50}) in vitro was 1.66 μ M, which is much lower than the concentration reached in human blood (8.78 μ M for a daily dose of 400 mg) [7]. These preliminary results now need to be confirmed in a randomised clinical trial.

Based on our experience of teicoplanin use in the treatment of infectious diseases, we encourage further investigation of the antiviral effect of this molecule on SARS-CoV-2 and suggest teicoplanin as another potential alternative for the treatment of COVID-19.

Declarations

Funding: This work was supported by the French Government under the 'Investissements d'avenir' (Investments for the Future) programme managed by the Agence Nationale de la Recherche (ANR) [reference: Méditerranée Infection 10-IAHU-03]. This work was supported by Région Provence Alpes Côte d'Azur and European funding FEDER PRIMI.

Competing Interests: None declared.

Ethical Approval: Not required.

References

[1] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020;382:727–33. doi:10.1056/NEJMoa2001017.

- [2] Lai C-C, Shih T-P, Ko W-C, Tang H-J, Hsueh P-R. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and coronavirus disease-2019 (COVID-19): the epidemic and the challenges. *Int J Antimicrob Agents* 2020:105924. doi:10.1016/j.ijantimicag.2020.105924.
- [3] Devaux CA, Rolain J-M, Colson P, Raoult D. New insights on the antiviral effects of chloroquine against coronavirus: what to expect for COVID-19? *Int J Antimicrob Agents* 2020 Forthcoming.
- [4] Wang M, Cao R, Zhang L, Yang X, Liu J, Xu M, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res* 2020;30:269–71. doi:10.1038/s41422-020-0282-0.
- [5] Colson P, Rolain J-M, Raoult D. Chloroquine for the 2019 novel coronavirus SARS-CoV-2. *Int J Antimicrob Agents* 2020:105923. doi:10.1016/j.ijantimicag.2020.105923.
- [6] Ko W-C, Rolain J-M, Lee N-Y, Chen P-L, Huang C-T, Lee P-I, et al. Remdesivir for SARS-CoV-2 pneumonia. *Int J Antimicrob Agents* 2020 Forthcoming.
- [7] Zhang J, Ma X, Yu F, Liu J, Zou F, Pan T, et al. Teicoplanin potently blocks the cell entry of 2019-nCoV. *bioRxiv* 2020 Feb 13. doi:10.1101/2020.02.05.935387.
- [8] Zhou N, Pan T, Zhang J, Li Q, Zhang X, Bai C, et al. Glycopeptide antibiotics potently inhibit cathepsin L in the late endosome/lysosome and block the entry of Ebola virus, Middle East respiratory syndrome coronavirus (MERS-CoV), and severe acute respiratory syndrome coronavirus (SARS-CoV). *J Biol Chem* 2016;291:9218–32. doi:10.1074/jbc.M116.716100.
- [9] Colson P, Raoult D. Fighting viruses with antibiotics: an overlooked path. *Int J Antimicrob Agents* 2016;48:349–52. doi:10.1016/j.ijantimicag.2016.07.004.
- [10] Pan T, Zhou N, Zhang H. Use of teicoplanin anti-Middle East respiratory syndrome coronavirus. WIPO PatentScope; 2015. Publication number: WO/2016/201692 <https://patentscope.wipo.int/search/en/detail.jsf?jsessionid=50F31F08D2ACF24BD9AFE0C123BF028B.wapp2nC?docId=WO2016201692&tab=PCTBIBLIO> [accessed 14 March 2020].