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OPINION

Quinacrine, an Old Drug with Potentially usefull in the Treatment for COVID-19

The novel β -coronavirus 2019-nCoV or SARS CoV-2 emerged in the city of Wuhan in China, and it is the causal agent of coronavirus disease 2019 (COVID-19) that trigger the current pandemic (1). The high speed of dissemination, the emergence of new genomic variants and the shortage of low-cost and effective treatments make it urgent to find new treatment strategies for the SARS-CoV-2 outbreak (2). Quinacrine (Qx), an aminoacridine used as an antimalarial drug, was proposed as an antiviral molecule against several viruses including Ebola and Zika (3,4), and listed among the top 16 repurposable drugs against SARS-CoV (5). Moreover, its effectiveness against SARS-CoV-2 has been demonstrated *in vitro* showing a half-maximum effective concentration (EC_{50}) range 0.58–1.88 mmol (6,7).

Among the mechanisms by which Qx induces antiviral effects highlight: a) its ability to intercalate DNA and RNA, thus inhibiting virus replication (8); b) it can increase the pH into the acidic organelles, and c) it can inhibit autophagy (9). Also, Qx is a potent inhibitor of phospholipase A2, diminishing cysteinyl leukotrienes levels and modulating Th1/Th2 response. Additionally, Qx can inhibit the secretion of proinflammatory cytokines and Toll-Like Receptors 7 and 9, molecules involved in the cytokine storm produced in severe COVID-19 patients (9,10).

Regarding its potential use in patients, Qx has been daily administrated (100 mg/daily by oral route) for extended periods proven to be well tolerated with few adverse effects even in children (nausea and vomiting). The most frequent and significant adverse effects were dermatitis and corneal edema; however, these effects were reversed when the drug was discontinued (9,11). Recently, Qx has been tested in several cancer trials (NCT01839955, NCT00417274, NCT01844076) and prion disease (NCT00183092, NCT00104663). Moreover, it was found that the maximum tolerated dose of Qx was 100 mg twice daily per 21 d in a colorectal cancer study (12).

The vast knowledge about the medical use of Qx and its corroborated efficacy inhibiting virus including SARS-CoV-2 makes Qx a viable candidate to be repurposing and clinical tested in COVID-19 patients of any age range.

Considering its pharmacokinetics and set up a record of wellbeing, the safest dose reported, even in children is 100 mg/day for 7 d (13,14), which would allow reaching Qx levels in lung tissue above the anti-SARS-CoV-2 EC_{50} reported (6).

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Conflict of Interest

The author declares that there is no conflict of interest.

Supplementary Materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.arcmed.2021.06.002](https://doi.org/10.1016/j.arcmed.2021.06.002).

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References

- 1 Wang C, Horby PW, Hayden FG, et al. A novel coronavirus outbreak of global health concern. *Lancet* 2020;395:470–473.
- 2 Penarrubia L, Ruiz M, Porco R, et al. Multiple assays in a real-time RT-PCR SARS-CoV-2 panel can mitigate the risk of loss of sensitivity

- by new genomic variants during the COVID-19 outbreak. *Int J Infect Dis* 2020;97:225–229. doi:10.1016/j.ijid.2020.06.027.
- 3 Sotelo J. Could an aminoacridine interfere with the cellular mechanisms involved in the process of human immunodeficiency virus infection? *Med Hypotheses* 1996;47:43–47.
 - 4 Lane TR, Comer JE, Freiberg AN, et al. Repurposing Quinacrine against Ebola Virus Infection *In vivo*. *Antimicrob Agents Chemother* 2019;63 e01142–e0119. doi:10.1128/AAC.01142-19.
 - 5 Zhou Y, Hou Y, Shen J, et al. Network-based drug repurposing for novel coronavirus 2019-nCoV/SARS-CoV-2. *Cell Discov* 2020;6:14.
 - 6 Salas Rojas M, Silva Garcia R, Bini E, et al. Quinacrine, an Antimalarial Drug with Strong Activity Inhibiting SARS-CoV-2 Viral Replication *In vitro*. *Viruses* 2021;13:121. doi:10.3390/v13010121.
 - 7 Han Y, Duan X, Yang L, Nilsson-Payant BE, Wang P, Duan F, et al. Identification of SARS-CoV-2 inhibitors using lung and colonic organoids. *Nature* 2021;589:270–275.
 - 8 Gasparian AV, Neznanov N, Jha S, et al. Inhibition of encephalomyocarditis virus and poliovirus replication by quinacrine: implications for the design and discovery of novel antiviral drugs. *J Virol* 2010;84:9390–9397.
 - 9 Pineda B, Perez de la Cruz V, Hernandez Pando R, et al. Quinacrine as a potential treatment for COVID-19 virus infection. *Eur Rev Med Pharmacol Sci* 2021;25:556–566.
 - 10 Vaninov N. In the eye of the COVID-19 cytokine storm. *Nat Rev Immunol* 2020;20:277.
 - 11 Parmer LG. Blood and bone marrow concentration of atabrine and its role in aplastic anemia. *J Lab Clin Med* 1948;33:827–832.
 - 12 Winer A, Denlinger CS, Vijayvergia N, et al. First-in-Human Phase 1b Trial of Quinacrine Plus Capecitabine in Patients With Refractory Metastatic Colorectal Cancer. *Clin Colorectal Cancer* 2021;20:e43–e52.
 - 13 Ehsanian R, Van Waes C, Feller SM. Beyond DNA binding - a review of the potential mechanisms mediating quinacrine's therapeutic activities in parasitic infections, inflammation, and cancers. *Cell Commun Signal* 2011;9:13.
 - 14 Craft JC, Murphy T, Nelson JD. Furazolidone and quinacrine. Comparative study of therapy for giardiasis in children. *Am J Dis Child* 1981;135:164–166.