Bio/chemoinformatics and formulation insights on the hydroxychloroquine debate on combating COVID-19

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Background: Hydroxychloroquine(HCQ) is undergoing several clinical trials for evaluating its efficacy and safety as an antiviral. Yet, there is still a great debate about their efficacy in combating COVID-19. We hereby, hypothesize the success of the intranasal and the pulmonary routes through a gelatin matrix to overcome a lot of its pharmacodynamic and pharmacokinetic challenges and to increase their local concentrations at the sites of initial viral entry while minimizing the side effects.

Methods: Molecular dynamic simulation of a gelatin matrix was performed. Molecular docking of HCQ on this simulated carrier and on mucin as well as various receptors including Angiotensin-converting enzyme 2 (ACE-2), heparin sulphate proteoglycan and Phosphatidylinositol binding clathrin assembly protein (PICALM), which are expressed in the lung and intranasal tissues and represent initial sites of attachment of the viral particles to the surface of respiratory cells was accomplished.

Results: Molecular docking on the gelatin-simulated matrix proposed high loading and a sustained release profile. Moreover, strong binding to all the investigated receptors was obtained.

Conclusions: The presented data provide insight into the rational for an intranasal or pulmonary HCQ formulation aiming for a sustained prophylaxis effect and/or a treatment strategy against COVID-19 pandemic viral infection.