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LETTER TO THE EDITOR

Potentially repurposing adamantanes for COVID-19

To the Editor,

The impressive array of clinical trials outlined by Zhang et al[1] in a short format speaks well towards the impetus of finding effective antiviral chemotherapy for COVID-19. Early reports of the potential efficacy of chloroquine in such clinical studies illustrates also the rapid progress that can be made in the current era.[2] The latter theme, in particular, emerges from previous knowledge that chloroquine has been active in vitro against SARS-CoV, feline infectious peritonitis virus, bovine coronavirus, human coronavirus 229E, and human coronavirus OC43 using a variety of test methods.[3-7]

Although not commonly discussed, adamantanes should also be reassessed at least in preliminary in vitro studies for the various human coronaviruses. Early study with an amantadine analog showed some promise in a dose-response effect for human coronavirus 229E.[8] Other modest antiviral effects have been shown for amantadine, rimantadine, memantine, and bananin in models for bovine coronavirus, mouse hepatitis virus, human coronavirus OC43, and SARS-CoV.[3,9-12] Despite the latter, others have proposed poor activity of amantadine for SARS-CoV and feline infectious peritonitis virus.[13,14] The latter studies, however, should not preempt an assessment of adamantanes for COVID-19 on several grounds. Viral susceptibility in these reports had varied considerably in the test methodology, and no consistent standard has yet emerged for coronavirus testing in particular. In vitro outcomes are not always predictive one way or another for in vivo outcome. The human pharmacology for several adamantanes has already been well-studied and provides some starting point for any related clinical trials. Continued derivation of further adamantane analogs has potential. Even modest antiviral effects may have some use if additive or synergistic combinations of antivirals emerge.

Whether for chloroquine or any adamantane that may prove useful, laboratory surveillance for the subsequent evolution of resistance is imperative given the experience of some other RNA viruses (eg, influenza A) to evolve amantadine/rimantadine resistance. Having many laboratories worldwide that are currently capable of assessing COVID-19 or other coronavirus susceptibilities in vitro, the extension of analysis to the adamantane family on an expanded basis is only one step away and deserves further consideration in short order.

CONFLICT OF INTERESTS

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Nevio Cimolai MD, FRCP(C)

Faculty of Medicine, Children's and Women's Health Centre of British Columbia, The University of British Columbia, Vancouver, British Columbia, Canada

Correspondence

Dr. Nevio Cimolai MD, FRCP(C), Faculty of Medicine, Children's and Women's Health Centre of British Columbia, The University of British Columbia, 4480 Oak Street, Vancouver, BC V6H3V4, Canada.

Email: ncimolai@mail.ubc.ca

ORCID

Nevio Cimolai http://orcid.org/0000-0003-2743-0556

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