Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to Editors

Aminoglycosides and their potential as SARS-CoV-2 antivirals

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To the Editor,

Chalichem et al. propose that aminoglycosides may be worthy of investigation as SARS-CoV-2 antivirals given their potential for defensin modulation [1]. The use of these agents as anticoronavirus treatments has some history and adds strength to their unique hypothesis.

The aminoglycosides hygromycin B (hygB) and neomycin were shown capable of inhibiting murine hepatitis virus (MHV) *in vitro* [2]. Others found hygB activity against bovine coronavirus and feline coronavirus [3,4]. These interests were extended by demonstrating that hygB also inhibited MHV replication in chronic infection models [5]. Although eukaryotic cells are generally impermeable to aminoglycosides, hygB concentrations increased intracellularly during active viral infection [2,6]. Similar enhancement of aminoglycoside uptake was also ascribed to E protein viroporin activity for SARS-CoV-1 [7].

Additional science continues to favour potential roles for aminoglycosides as antivirals [8,9]. Both tobramycin and kanamycin attract to SARS-CoV-2 stem-loop II motif in docking studies [8]. Yet others find reason to believe that paromomycin could inhibit spike protein and/or the main protease of SARS-CoV-2 [9].

Electrostatic RNA binding of aminoglycosides has long been known, and they can function as inhibitors of eukaryotic ribosomes. Though usually excluded from intracellular environments, these antibiotics may enter active sites of viral replication in a time-accrued fashion thus potentially being more selectively effective when antiviral activity is desirable. It is unclear as to whether antiviral effects occur due to inhibition of eukaryotic functions or to mechanisms more closely related to viral replication. Inhibitory concentrations required *in vitro* are achievable *in vivo* by intramuscular or intravenous administration similar to the clinical use otherwise for human pharmacotherapy. The challenge nevertheless is to find antiviral efficacy in the therapeutic window given that there are generally narrow therapeutic indices. There is potential however in such a narrow window for aminoglycosides to complicate existing COVID-19-related pathology (e.g., renal dysfunction). Animal models for SARS-CoV-2 infection provide an abundance of opportunity for assessment. Ongoing analysis of repurposed drugs as coronavirus antivirals has considerable merit [10]. If only partially effective as single therapies, any benefit could be additive to other partially effective treatments. Despite advances in vaccinology, moderate to severe COVID-19 infections will continue. Even if vaccines are highly efficacious, the establishment of SARS-CoV-2 as a common endemic respiratory coronavirus will attract demand for coronavirus antivirals to be used in niche situations [11].

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Declaration of Competing Interest

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