Broad-spectrum antiviral activity of naproxen: from Influenza A to SARS-CoV-2 Coronavirus

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Abstract: There is an urgent need for specific antiviral drugs directed against SARS-CoV-2 both to prevent the most severe forms of COVID-19 and to reduce viral excretion and subsequent virus dissemination; in the present pandemic context, drug repurposing is a priority. Targeting the nucleoprotein N of the SARS-CoV-2 coronavirus in order to inhibit its association with viral RNA could be a strategy to impeding viral replication and possibly other essential functions associated with viral N. The antiviral properties of naproxen, belonging to the NSAID family, previously demonstrated against Influenza A virus, were evaluated against SARS-CoV-2. Naproxen binding to the nucleoprotein of SARS-CoV-2 was shown by molecular modeling and fluorescence spectroscopy. In VeroE6 cells and reconstituted human primary respiratory epithelium models of SARS-CoV-2 infection, naproxen inhibited viral replication and protected the bronchial epithelia against SARS-CoV-2 induced-damage. The benefit of naproxen addition to the standard of care is tested in an on-going clinical study. https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001301-23/FR; NCT04325633

Naproxen binds to viral nucleoproteins (N) in silico and in vitro

Naproxen was identified in a virtual screening (using a library of compounds selected from Sigma) targeting N

Dual effect of naproxen:
- Antiviral effect: inhibition of transcription/replication of the virus by targeting the nucleoprotein
- Well-known anti-inflammatory effect: Inhibition of cyclo-oxygenase COX (NSAID) and prostaglandin synthesis; COX1: inhibition of thrombosis; COX2: inhibition of inflammation & pain

Naproxen inhibits SARS-CoV-2 replication in VeroE6 cells (A,B) and in a model of reconstituted epithelium (C) and protects the epithelium against viral-induced damage (D)


Efficacy of Addition of Naproxen in the Treatment of critically ill Patients Hospitalized for COVID-19 Infection

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