Investigating the antiviral activity of natural product derived compounds and synthetic xanthones against coronaviruses

Gemma Cooper, Bethanie Dean, Timothy J Snape, Maitreyi Shivkumar

Leicester School of Pharmacy, De Montfort University, Leicester UK

In the last 20 years three pandemic coronaviruses have emerged, with many more coronaviruses circulating in animal reservoirs, future spillover into humans is likely. The development of novel pan-coronavirus antivirals is vital to target new emerging coronaviruses and enhance future pandemic preparedness.

Here, we investigated the antiviral activity of a panel of natural product compounds derived from *Swertia chirayita* for their anti-coronavirus activities. A panel of compounds and synthetic xanthones based on *Swerita* bioactive compounds was assessed for antiviral activity against human coronavirus OC43 and 229E, and SARS-CoV-2 pseudoviruses. Infected cell lines were treated with the compounds, and impact on infectivity assessed by quantifying viral titres. Alongside, cytotoxicity of the compounds was determined. The initial screen identified six natural product compounds that display antiviral activity at non-cytotoxic concentrations. While the synthesised xanthones show a significant reduction in viral infectivity, the inhibition was not as potent as seen in the natural xanthone mangiferin. This suggests that the additional complexity of mangiferin and other naturally derived xanthones may contribute to their increased antiviral activities. Our preliminary data investigating the mechanism of action suggests that the hit compounds inhibit the virus at early stages in the viral lifecycle.

The six compounds identified are being carried forward for further investigations. With mechanism of action studies and viral target determination currently ongoing, this work is a step towards identifying novel pan-coronavirus antivirals.