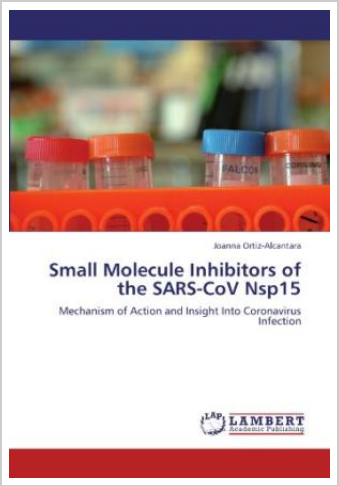

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Small Molecule Inhibitors of the SARS-CoV Nsp15

By Ortiz-Alcantara, Joanna

Condition: New. Publisher/Verlag: LAP Lambert Academic Publishing | Mechanism of Action and Insight Into Coronavirus Infection | The Severe Acute Respiratory Syndrome (SARS) virus encodes several unusual RNA processing enzymes, including Nsp15, an endoribonuclease that cleaves 3 of uridylates through a Ribonuclease A-like mechanism. Crystal structures confirmed that the Nsp15 active site is structurally similar to that of Ribonuclease A. These similarities and our molecular docking analysis lead us to hypothesize that previously characterized Ribonuclease A inhibitors will also inhibit the SARS-CoV Nsp15. Benzopurpurin B, C-467929, C-473872, N-36711, N-65828, N-103018 and Congo red were tested for effects on Nsp15 endoribonuclease activity. A real-time fluorescence assay revealed IC50 values for inhibiting Nsp15 between 0.2 µM and 40 µM. Benzopurpurin B, C-473872, and Congo red are competitive inhibitors, according to kinetic studies and bind SARS-CoV Nsp15 according to a differential scanning fluorimetry assay. Benzopurpurin B also inhibited the Nsp15 orthologs from two other coronaviruses: mouse hepatitis virus (MHV) and infectious bronchitis virus. The three compounds reduced infectivity of MHV in L2 cells by 8 to 26 fold. The more effective drugs also drecreased RNA accumulation in MHV. | Format: Paperback | Language/Sprache: english | 68 pp.

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