**Literature search for small molecule inhibitors for CHIKV nsP2 helicase and protease**

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| **CHIKV nsP2 protease** | | |
| MBZM-N-IBT, a Novel Small Molecule, Restricts Chikungunya Virus Infection by Targeting nsP2 Protease Activity *In Vitro*, *In Vivo*, and *Ex Vivo* - **2022** | | 10.1128/aac.00463-22 |
|  | IC50: 31.96 μM (nsP2-CT)  Kd: 6.14 ± 0.58 μM  SI: > 21 | |
| Riboflavin, a Potent Neuroprotective Vitamin: Focus on Flavivirus and Alphavirus Proteases - **2022** | | 10.3390/microorganisms10071331 |
|  | IC50: 93 ± 5.7 nM  Kd: 2.8 ± 0.7 µM  CC50: 72.31 μM | |
| 1,3-Thiazolbenzamide Derivatives as Chikungunya Virus nsP2 Protease Inhibitors - **2021** | | 10.1021/acsomega.0c06191 |
| **10** | EC50: 13.1 μM  CC50: > 1000 μM |  |
| **10c** | EC50: 9.3 μM  CC50: > 100 μM |
| Novel Analogues of the Chikungunya Virus Protease Inhibitor: Molecular Design, Synthesis, and Biological Evaluation - **2021** | | 10.1021/acsomega.1c00625 |
| **D160a** | EC50: 26.8 μM  CC50: > 100 μM |  |
| **D160d** | EC50: 4.8 μM  CC50: > 100 μM |
| Design and Validation of Novel Chikungunya Virus Protease Inhibitors - **2016** | | 10.1128/aac.01421-16 |
| **1c** | EC50: 50 μM  CC50: > 200 μM  SI: > 4 |  |
| **3** | EC50: 33 μM  CC50: > 200 μM  SI: > 6 |
| **8** | EC50: 1.5 μM  CC50: > 200 μM  SI: > 133.3 |
| **11** | EC50: 25 μM  CC50: > 200 μM  SI: > 8 |
| Chikungunya virus inhibition by peptidomimetic inhibitors targeting virus-specific cysteine protease - **2018** | | 10.1016/j.biochi.2018.04.004 |
| **PEP-I** |  |  |
| **PEP-II** |

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| **CHIKV small molecules 2022-2023 – no insight to MoA** | | | |
| Discovery and development of labdane-oxindole hybrids as small-molecule inhibitors against chikungunya virus infection - **2022** | | | 10.1016/j.ejmech.2022.114110 |
|  | EC50: 1.55 μM  CC50: 129.6 μM  SI: 83 | | |
| Computer-Aided Design and Synthesis of (Functionalized quinazoline)–(α-substituted coumarin)–arylsulfonate Conjugates against Chikungunya Virus - **2022** | | | 10.3390/ijms23147646 |
|  | EC50: 3.84 μM  CC50: 72.3 μM  SI: 18.8 | | |
| Cationic Perylene Antivirals with Aqueous Solubility for Studies *In Vivo* - **2022** | | | 10.3390/ph15101178 |
|  | EC50 (CHIKV): 0.99 ± 0.15 μM  EC50 (SARS-CoV-2): 1.45 ± 0.95 μM  CC50 (VERO): > 100 μM  CC50 (MDCK): 69 ± 27 μM | | |
|  | EC50 (CHIKV): 0.47 ± 0.16 μM  EC50 (SARS-CoV-2): 11.3 ± 1.8 μM  CC50 (VERO): > 100 μM  CC50 (MDCK): > 100 μM | | |
|  | EC50 (CHIKV): < 0.016 μM  EC50 (SARS-CoV-2): 0.075 ± 0.018 μM  CC50 (VERO): 98 ± 17 μM  CC50 (MDCK): 62 ± 24 μM | | |
|  | EC50 (CHIKV): 0.55 ± 0.33 μM  EC50 (SARS-CoV-2): 1.28 ± 0.40 μM  CC50 (VERO): > 100 μM  CC50 (MDCK): > 100 μM | | |
| 5-(Perylen-3-ylethynyl)uracil as an antiviral scaffold: Potent suppression of enveloped virus reproduction by 3-methyl derivatives *in vitro* - **2023** | | | 10.1016/j.antiviral.2022.105508 |
|  |  | EC50: 0.43 ± 0.10 μM  SI: > 120 | |
|  | EC50: 0.11 ± 0.03 μM  SI: > 470 | |
|  | EC50: 0.43 ± 0.10 μM  SI: > 120 | |
|  | EC50: 0.38 ± 0.18 μM  SI: > 130 | |
|  | EC50: 0.38 ± 0.18 μM  SI: > 130 | |
|  | EC50: 0.88 ± 0.75 μM  SI: > 50 | |
|  | EC50: 1.1 ± 0.7 μM  SI: > 40 | |
|  | EC50: 0.88 ± 0.75 μM  SI: > 50 | |
|  | EC50: 0.09 ± 0.04 μM  SI: > 530 | |
|  | EC50: 3.2 ± 0.7 μM  SI: > 15 | |
|  | | EC50: 1.1 ± 0.5 μM  SI: > 50 | |
| Synthesis and Anti-Chikungunya Virus (CHIKV) Activity of Novel 1,4-Naphthoquinone Sulfonamide and Sulfonate Ester Derivatives - **2022** | | | 10.21577/0103-5053.20220010 |
|  | EC50: 0.97 ± 0.2 μM  CC50: 281 ± 2.5 μM  SI: 289 | | |
|  | EC50: 1.18 ± 0.16 μM  CC50: 540 ± 3.7 μM  SI: 457 | | |
|  | EC50: 0.77 ± 0.1 μM  CC50: 322 ± 6.6 μM  SI: 418 | | |
|  | EC50: 0.88 ± 0.1 μM  CC50: 352 ± 4.3 μM  SI: 400 | | |
|  | EC50: 1.25 ± 0.2 μM  CC50: 478 ± 6.2 μM  SI: 382 | | |