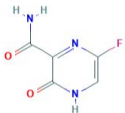
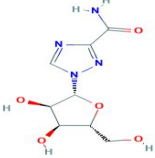
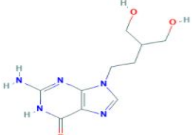
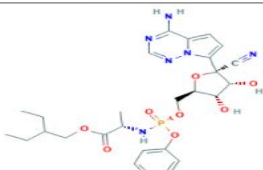
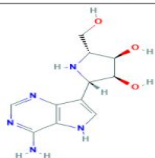
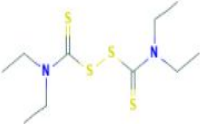
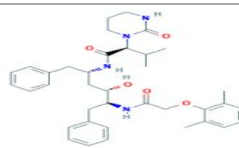
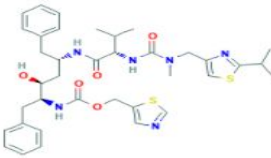
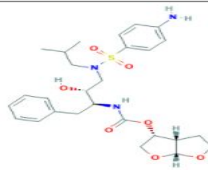
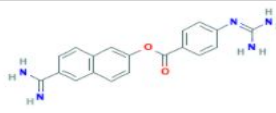

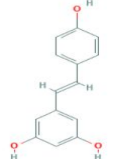
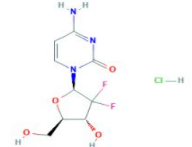
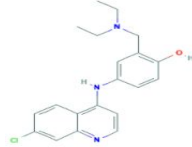
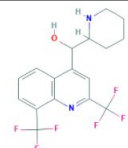
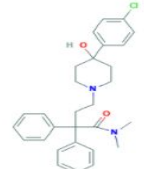
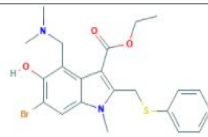
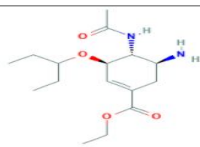
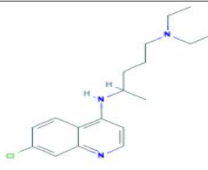
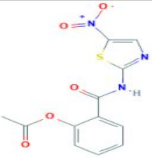
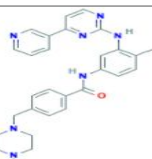
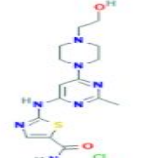
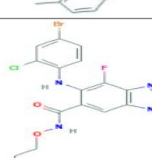
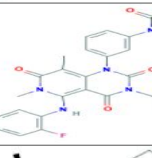
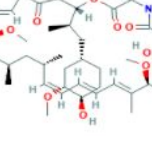
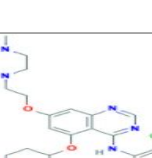
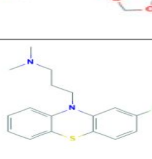
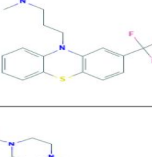
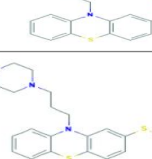
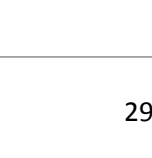


| Name | Binding Energy (kcal/mol) | SARS-CoV N residues interacting with ligands | Infectious diseases | References | 2D Structures |
|-------------|---------------------------|--|--|-------------|---|
| Favipiravir | -5.55 | Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Trp132, Val133, Ala134 | 2019-nCoV; Influenza | 1,2 |  |
| Ribavirin | -6.72 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Gly71, Tyr123, Ile131, Trp132, Val133, Ala134, Thr135, Glu136 | 2019-nCoV, MERS-CoV, SARS-CoV, RSV, HCV | 2-8 |  |
| Penciclovir | -6.23 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Gly71, Tyr123, Ile131, Trp132, Val133, Ala134 | 2019-nCoV | 2 |  |
| Remdesivir | -6.71 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Ile131, Trp132, Val133, Ala134, Thr166, Leu167, Pro168, | 2019-nCoV, MERS-CoV, SARS-CoV | 1,2,9-11 |  |
| Galidesivir | -6.64 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Ile131, Trp132, Val133, Ala134, Thr135 | Broad-spectrum (e.g. SARSCoV, MERSCoV, IAV) | 12 |  |
| Disulfiram | -4.47 | Phe66, Pro67, Arg68, Gly69, Gln70, Ile84, Tyr123, Trp132, Val133, Ala134, Thr135, Glu136, Gly137, Ala138 | MERS-CoV, SARS-CoV | 13 |  |
| Lopinavir | -7.62 | Leu64, Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Gly124, Ile130, Ile131, Trp132, Val133, Ala134, Thr135, Glu136, Gly137, Ala138 | 2019-nCoV; MERS-CoV, SARS-CoV; HCoV-229E; HIV, HPV | 11,14-17 |  |
| Ritonavir | -6.67 | Asp63, Leu64, Lys65, Phe66, Pro67, Arg68, Gly69, Arg89, Trp108, Tyr123, Gly124, Ala125, Asn126, Lys127, Asp128, Gly129, Ile130, Ile131, Trp132, Val133, Ala134 | 2019-nCoV, MERS-CoV | 11,14,16,17 |  |
| Darunavir | -8.19 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Gly71, Tyr123, Gly124, Ala125, Asn126, Lys127, Ile130, Ile131, Trp132, Val133, Ala134 | 2019-nCoV | - |  |

Appendix A. Supplementary Material

| | | | | | | |
|----|---------------------------|-------|---|-------------------------------------|------------|---|
| 1 | | | | | | |
| 2 | | | | | | |
| 3 | Nafamostat | -9.35 | Phe66, Pro67, Arg68, Gly69, Gln70, Gly71, Tyr123, Gly124, Ala125, Asn126, Lys127, Asp128, Gly129, Ile130, Ile131, Trp132, Val133, Ala134 | 2019-nCoV, MERS-CoV | 2,18 |  |
| 4 | | | | | | |
| 5 | | | | | | |
| 6 | | | | | | |
| 7 | | | | | | |
| 8 | | | | | | |
| 9 | Cobicistat | -5.59 | Glu62, Asp63, Leu64, Lys65, Phe66, Pro67, Arg68, Tyr123, Gly124, Ala125, Asn126, Lys127, Asp128, Gly129, Ile130, Ile131, Trp132, Val133, Pro168 | 2019-nCoV | - |  |
| 10 | | | | | | |
| 11 | | | | | | |
| 12 | | | | | | |
| 13 | | | | | | |
| 14 | | | | | | |
| 15 | Resveratrol | -6.90 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Ile131, Trp132, Val133, Ala134 | MERS-CoV | 19 |  |
| 16 | | | | | | |
| 17 | | | | | | |
| 18 | | | | | | |
| 19 | | | | | | |
| 20 | | | | | | |
| 21 | Gemcitabine hydrochloride | -6.55 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Ile131, Trp132, Val133, Ala134 | MERS-CoV, SARS-CoV | 20 |  |
| 22 | | | | | | |
| 23 | | | | | | |
| 24 | | | | | | |
| 25 | | | | | | |
| 26 | Amodiaquine | -7.94 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Gly124, Ala125, Asn126, Lys127, Ile130, Ile131, Trp132, Val133, Ala134 | MERS-CoV, SARS-CoV | 20 |  |
| 27 | | | | | | |
| 28 | | | | | | |
| 29 | | | | | | |
| 30 | | | | | | |
| 31 | | | | | | |
| 32 | Mefloquine | -7.77 | Leu161, Pro162, Gln163, Gly164, Thr165, Thr166, Leu167, Pro168, Lys169, Phe171, Tyr172, Ala173 | MERS-CoV, SARS-CoV | 20 |  |
| 33 | | | | | | |
| 34 | | | | | | |
| 35 | | | | | | |
| 36 | | | | | | |
| 37 | Loperamide | -8.30 | Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Gly124, Asn126, Lys127, Asp128, Gly129, Ile130, Ile131, Trp132, Val133, Ala134 | MERS-CoV, SARS-CoV HCoV-229E | 15 |  |
| 38 | | | | | | |
| 39 | | | | | | |
| 40 | | | | | | |
| 41 | | | | | | |
| 42 | Arbidol (Umifenovir) | -7.49 | Leu64, Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Gly124, Ala125, Asn126, Lys127, Asp128, Gly129, Ile130, Ile131, Trp132, Val133, Ala134 | 2019-nCoV; Influenza virus; | - |  |
| 43 | | | | | | |
| 44 | | | | | | |
| 45 | | | | | | |
| 46 | | | | | | |
| 47 | | | | | | |
| 48 | | | | | | |
| 49 | Oseltamivir | -6.23 | Phe66, Pro67, Arg68, Gly69, Gln70, Ile84, Tyr123, Trp132, Val133, Ala134, Thr135, Glu136, Gly137, Ala138, Leu139, Asn140 | 2019-nCoV; Influenza virus; | - |  |
| 50 | | | | | | |
| 51 | | | | | | |
| 52 | | | | | | |
| 53 | | | | | | |
| 54 | | | | | | |
| 55 | Chloroquine | -6.99 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Gly124, Ala125, Asn126, Lys127, Ile130, Ile131, Trp132, Val133, Ala134 | 2019-nCoV; SARS-CoV; MERS-CoV | 2,15,21,22 |  |
| 56 | | | | | | |
| 57 | | | | | | |
| 58 | | | | | | |
| 59 | | | | | | |
| 60 | | | | | | |

| | | | | | |
|-------------------|--------|---|--|-------|---|
| Nitazoxanide | -7.75 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Gly124, Ala125, Asn126, Lys127, Ile130, Ile131, Trp132, Val133, Ala134 | Broad-spectrum (e.g. coronaviruses, 2019-nCoV) | 2,23 |  |
| Imatinib mesylate | -8.89 | Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Trp132, Val133, Ala134, Thr135, Glu136, Gly137, Ala138, Leu139, Asn140 | MERS-CoV, SARS-CoV | 20,24 |  |
| Dasatinib | -8.94 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Ile131, Trp132, Val133, Ala134, Thr135, Glu136, Gly137, Ala138 | MERS-CoV, SARS-CoV | 20 |  |
| Selumetinib | -7.51 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Ile130, Ile131, Trp132, Val133, Ala134 | MERS-CoV, SARS-CoV | 25 |  |
| Trametinib | -9.45 | Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Ile131, Trp132, Val133, Ala134 | MERS-CoV, SARS-CoV | 25 |  |
| Rapamycin | -11.87 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Ile84, Pro122, Tyr123, Gly124, Ala125, Asn126, Ile130, Ile131, Trp132, Val133, Ala134, Thr135, Glu136, Gly137, Ala138, Asn140 | MERS-CoV | 25 |  |
| Saracatinib | -10.40 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Gly124, Ile131, Trp132, Val133, Ala134, Thr135, Glu136, Gly137, Ala138, | MERS-CoV | 26 |  |
| Chlorpromazine | -6.53 | Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Trp132, Val133, Ala134, Thr135, Glu136, Gly137 | SARS-CoV, MERS-CoV | 15,20 |  |
| Triflupromazine | -6.32 | Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Trp132, Val133, Ala134, Thr135, Glu136, Gly137 | SARS-CoV, MERS-CoV | 15,20 |  |
| Fluphenazine | -6.30 | Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Trp132, Val133, Ala134, Thr135, Glu136, Gly137 | SARS-CoV, MERS-CoV | 15,20 |  |
| Thiethylperazine | -7.68 | Lys65, Phe66, Pro67, Arg68, Gly69, Gln70, Tyr123, Gly124, Ala125, Asn126, Lys127, Ile130, Ile131, Trp132, Val133, Ala134 | SARS-CoV, MERS-CoV | 15,20 |  |

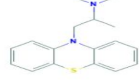
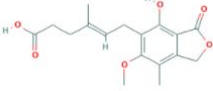
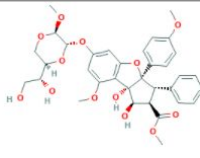
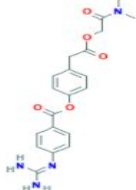
| | | | | | | | |
|-------------------|-------|---|--|--------------------------------|---|-------|---|
| Promethazine | -6.46 | Phe66, Gly69, Trp132, Thr135, Glu136 | Pro67, Gln70, Val133, Ala134, | Arg68, Tyr123, Ala134, | SARS-CoV, MERS-CoV | 15,20 |  |
| Mycophenolic acid | -7.88 | Lys65, Arg68, Tyr123, Val133, Ala134, | Phe66, Gly69, Ile131, | Pro67, Gln70, Trp132, | MERS-CoV, HBV, HCV | 27,28 |  |
| Silvestrol | -7.71 | Arg68, Gly71, Ile74, Ser78, Gln83, Gly137, Pro162, Thr165 | Gly69, Val72, Asn75, Ser79, Thr135, Glu136, | Gln70, Pro73, Thr76, Pro80, | MERS-CoV, HCoV-229E, EBOV, Picornaviridae | 29 |  |
| Camostat | -9.85 | Lys65, Gly69, Ala125, Ile131, Ala134, Gly137, Ala138 | Phe66, Tyr123, Asn126, Trp132, Thr135, Glu136, | Arg68, Gly124, Ile130, Val133, | SARS-CoV, MERS-CoV, HCoV-229E | 30 |  |

TABLE S1 List of the binding energy, important interactions with residues at the active site, published pharmaceutical data

| Complexes | Initial Total Energy (kcal/mol) | Initial Potential Energy (kcal/mol) | Final Total Energy (kcal/mol) | Final Potential Energy (kcal/mol) | RMSF value of residues in main interaction (nm) | RMSD value of protein Ca atoms (Å) | RMSD value of whole protein (Å) |
|---|---------------------------------|-------------------------------------|-------------------------------|-----------------------------------|--|------------------------------------|---------------------------------|
| <i>SARS-CoV-2 N-NTD & Rapamycin</i> | -2.417,08 | -3.980,43 | -2.517,21 | -4.110,04 | <i>Phe66:0.77, Arg68:0.72, Gly69:0.63, Tyr123:1.32, Ile131:0.53, Trp132:0.84, Val133:0.73, Ala134:0.52</i> | 2.26 | 2.53 |
| <i>SARS-CoV-2 N-NTD & Saracatinib</i> | -2.623,80 | -4.144,73 | -2.688,01 | -4.172,02 | <i>Phe66:0.61, Arg68:0.62, Gly69:0.54, Tyr123:1.19, Ile131:0.99, Trp132:0.83, Val133:0.46, Ala134:0.48</i> | 2.09 | 2.40 |
| <i>SARS-CoV-2 N-NTD & Camostat</i> | -2.769,50 | -4.212,74 | -2.832,14 | -4.300,04 | <i>Phe66:0.89, Arg68:0.96, Gly69:0.60, Tyr123:0.85, Ile131:0.42, Trp132:0.50, Val133:0.41, Ala134:0.72</i> | 2.70 | 3.06 |
| <i>SARS-CoV-2 N-NTD & Trametinib</i> | -2.665,45 | -4.168,43 | -2.740,94 | -4.240,19 | <i>Phe66:0.54, Arg68:0.97, Gly69:0.61, Tyr123:0.88, Ile131:0.54, Trp132:0.55, Val133:0.49, Ala134:0.69</i> | 1.87 | 2.27 |
| <i>SARS-CoV-2 N-NTD & Nafamostat</i> | -2.594,47 | -4.086,61 | -2.876,42 | -4.335,22 | <i>Phe66:0.93, Arg68:0.66, Gly69:0.68, Tyr123:0.95, Ile131:0.56, Trp132:0.44, Val133:0.60, Ala134:0.44</i> | 2.18 | 2.46 |

TABLE S2 MD simulation calculations of total and potential energy for five selected complexes. The RMSF value of main interaction residues and RMSD value of protein structures.

| Rapamycin | | |
|-----------------------------|------------------------------|------------------|
| Donor | Acceptor | Occupancy |
| <i>Tyr123-Side-CE2</i> | <i>Rapamycin-Side-C64</i> | 100% |
| <i>Trp132-Side-CD1</i> | <i>Rapamycin-Side-C46</i> | 100% |
| <i>Trp132-Side-CD1</i> | <i>Rapamycin-Side-C62</i> | 100% |
| <i>Lys65-Side-CE</i> | <i>Rapamycin-Side-C19</i> | 100% |
| <i>Lys65-Side-CE</i> | <i>Rapamycin-Side-C20</i> | 100% |
| <i>Asn126-Side-ND2</i> | <i>Rapamycin-Side-C10</i> | 100% |
| <i>Asn126-Side-ND2</i> | <i>Rapamycin-Side-O11</i> | 100% |
| <i>Rapamycin-Side-C58</i> | <i>Ala134-Main-O</i> | 100% |
| <i>Rapamycin-Side-C28</i> | <i>Val133-Main-CA</i> | 100% |
| <i>Rapamycin-Side-C19</i> | <i>Lys65-Main-CA</i> | 100% |
| <i>Rapamycin-Side-C57</i> | <i>Lys65-Main-CA</i> | 100% |
| <i>Rapamycin-Side-C22</i> | <i>Lys65-Side-CB</i> | 100% |
| <i>Rapamycin-Side-C18</i> | <i>Lys65-Side-CE</i> | 100% |
| Saracatinib | | |
| Donor | Acceptor | Occupancy |
| <i>Trp132-Side-CB</i> | <i>Saracatinib-Side-O13</i> | 100% |
| <i>Trp132-Main-N</i> | <i>Saracatinib-Side-O13</i> | 100% |
| <i>Trp132-Main-N</i> | <i>Saracatinib-Side-C21</i> | 100% |
| <i>Ile130-Side-CG1</i> | <i>Saracatinib-Side-C21</i> | 100% |
| <i>Ile131-Side-CG2</i> | <i>Saracatinib-Side-CL30</i> | 100% |
| <i>Val133-Main-CA</i> | <i>Saracatinib-Side-N11</i> | 100% |
| <i>Ile131-Main-CA</i> | <i>Saracatinib-Side-C2</i> | 100% |
| <i>Ala134-Side-CB</i> | <i>Saracatinib-Side-O31</i> | 100% |
| <i>Arg68-Side-NE</i> | <i>Saracatinib-Side-C26</i> | 100% |
| <i>Saracatinib-Side-C33</i> | <i>Tyr123-Side-CZ</i> | 100% |
| <i>Saracatinib-Side-C38</i> | <i>Trp132-Side-CG</i> | 100% |
| <i>Saracatinib-Side-C38</i> | <i>Trp132-Side-CD1</i> | 100% |
| <i>Saracatinib-Side-C10</i> | <i>Arg68-Main-CA</i> | 100% |
| Camostat | | |
| Donor | Acceptor | Occupancy |
| <i>Glu136-Main-CA</i> | <i>Camostat-Side-N22</i> | 100% |
| <i>Trp132-Side-CB</i> | <i>Camostat-Side-C29</i> | 100% |
| <i>Trp132-Side-CD1</i> | <i>Camostat-Side-O9</i> | 100% |
| <i>Ile131-Main-CA</i> | <i>Camostat-Side-C8</i> | 100% |
| <i>Ile131-Main-CA</i> | <i>Camostat-Side-O7</i> | 100% |
| <i>Trp132-Main-N</i> | <i>Camostat-Side-C8</i> | 100% |
| <i>Lys65-Side-CB</i> | <i>Camostat-Side-C1</i> | 100% |
| <i>Camostat-Side-N25</i> | <i>Tyr123-Side-CE2</i> | 100% |
| <i>Camostat-Side-C29</i> | <i>Phe66-Side-CB</i> | 100% |

| | | |
|--------------------------|-----------------------|------|
| <i>Camostat-Side-C29</i> | <i>Phe66-Main-CA</i> | 100% |
| <i>Camostat-Side-C10</i> | <i>Pro67-Main-N</i> | 100% |
| <i>Camostat-Side-C6</i> | <i>Ile131-Side-CB</i> | 100% |

Trametinib

| Donor | Acceptor | Occupancy |
|----------------------------|----------------------------|------------------|
| <i>Lys65-Side-CD</i> | <i>Trametinib-Side-N17</i> | 100% |
| <i>Val133-Side-CG2</i> | <i>Trametinib-Side-C33</i> | 100% |
| <i>Ile131-Side-CG2</i> | <i>Trametinib-Side-F24</i> | 100% |
| <i>Ile131-Side-CD1</i> | <i>Trametinib-Side-F24</i> | 100% |
| <i>Phe66-Main-N</i> | <i>Trametinib-Side-C10</i> | 100% |
| <i>Phe66-Main-N</i> | <i>Trametinib-Side-O29</i> | 100% |
| <i>Trp132-Main-N</i> | <i>Trametinib-Side-C20</i> | 100% |
| <i>Trp132-Side-CD1</i> | <i>Trametinib-Side-I25</i> | 100% |
| <i>Ile131-Main-CA</i> | <i>Trametinib-Side-C21</i> | 100% |
| <i>Gly69-Main-N</i> | <i>Trametinib-Side-N34</i> | 100% |
| <i>Gly69-Main-CA</i> | <i>Trametinib-Side-C32</i> | 100% |
| <i>Gly69-Main-CA</i> | <i>Trametinib-Side-C31</i> | 100% |
| <i>Ala134-Side-CB</i> | <i>Trametinib-Side-C6</i> | 100% |
| <i>Val133-Main-CA</i> | <i>Trametinib-Side-C12</i> | 100% |
| <i>Val133-Main-CA</i> | <i>Trametinib-Side-O30</i> | 100% |
| <i>Ala134-Main-N</i> | <i>Trametinib-Side-C12</i> | 100% |
| <i>Ala134-Main-N</i> | <i>Trametinib-Side-O30</i> | 100% |
| <i>Trametinib-Side-N17</i> | <i>Lys65-Side-CD</i> | 100% |
| <i>Trametinib-Side-C33</i> | <i>Lys65-Main-C</i> | 100% |
| <i>Trametinib-Side-C33</i> | <i>Phe66-Main-N</i> | 100% |
| <i>Trametinib-Side-C22</i> | <i>Gly129-Main-O</i> | 100% |
| <i>Trametinib-Side-C36</i> | <i>Glu136-Side-OE2</i> | 100% |
| <i>Trametinib-Side-C1</i> | <i>Arg68-Main-C</i> | 100% |
| <i>Trametinib-Side-C31</i> | <i>Trp132-Main-C</i> | 100% |
| <i>Trametinib-Side-C31</i> | <i>Val133-Main-N</i> | 100% |

Nafamostat

| Donor | Acceptor | Occupancy |
|----------------------------|----------------------------|------------------|
| <i>Gly129-Main-N</i> | <i>Nafamostat-Side-N26</i> | 100% |
| <i>Lys65-Main-CA</i> | <i>Nafamostat-Side-C22</i> | 100% |
| <i>Ile131-Side-CD1</i> | <i>Nafamostat-Side-C10</i> | 100% |
| <i>Ile131-Side-CD1</i> | <i>Nafamostat-Side-C9</i> | 100% |
| <i>Ile131-Side-CB</i> | <i>Nafamostat-Side-O14</i> | 100% |
| <i>Val133-Main-CA</i> | <i>Nafamostat-Side-C1</i> | 100% |
| <i>Val133-Main-CA</i> | <i>Nafamostat-Side-C4</i> | 100% |
| <i>Arg68-Main-CA</i> | <i>Nafamostat-Side-C1</i> | 100% |
| <i>Arg68-Side-CG</i> | <i>Nafamostat-Side-C3</i> | 100% |
| <i>Gly69-Main-N</i> | <i>Nafamostat-Side-C11</i> | 100% |
| <i>Nafamostat-Side-N25</i> | <i>Asp63-Side-CB</i> | 100% |
| <i>Nafamostat-Side-N25</i> | <i>Asp63-Side-CG</i> | 100% |
| <i>Nafamostat-Side-C4</i> | <i>Phe66-Side-CB</i> | 100% |
| <i>Nafamostat-Side-C1</i> | <i>Val72-Main-N</i> | 100% |
| <i>Nafamostat-Side-N12</i> | <i>Gly71-Main-C</i> | 100% |
| <i>Nafamostat-Side-N12</i> | <i>Gly71-Main-O</i> | 100% |

| | | |
|---------------------------|------------------------|------|
| <i>Nafamostat-Side-C7</i> | <i>Tyr123-Side-CE2</i> | 100% |
| <i>Nafamostat-Side-C3</i> | <i>Ala134-Main-O</i> | 100% |

TABLE S3 Occupancy values of H-bond interactions between SARS-CoV-2 residues and compounds below 5.0 Å

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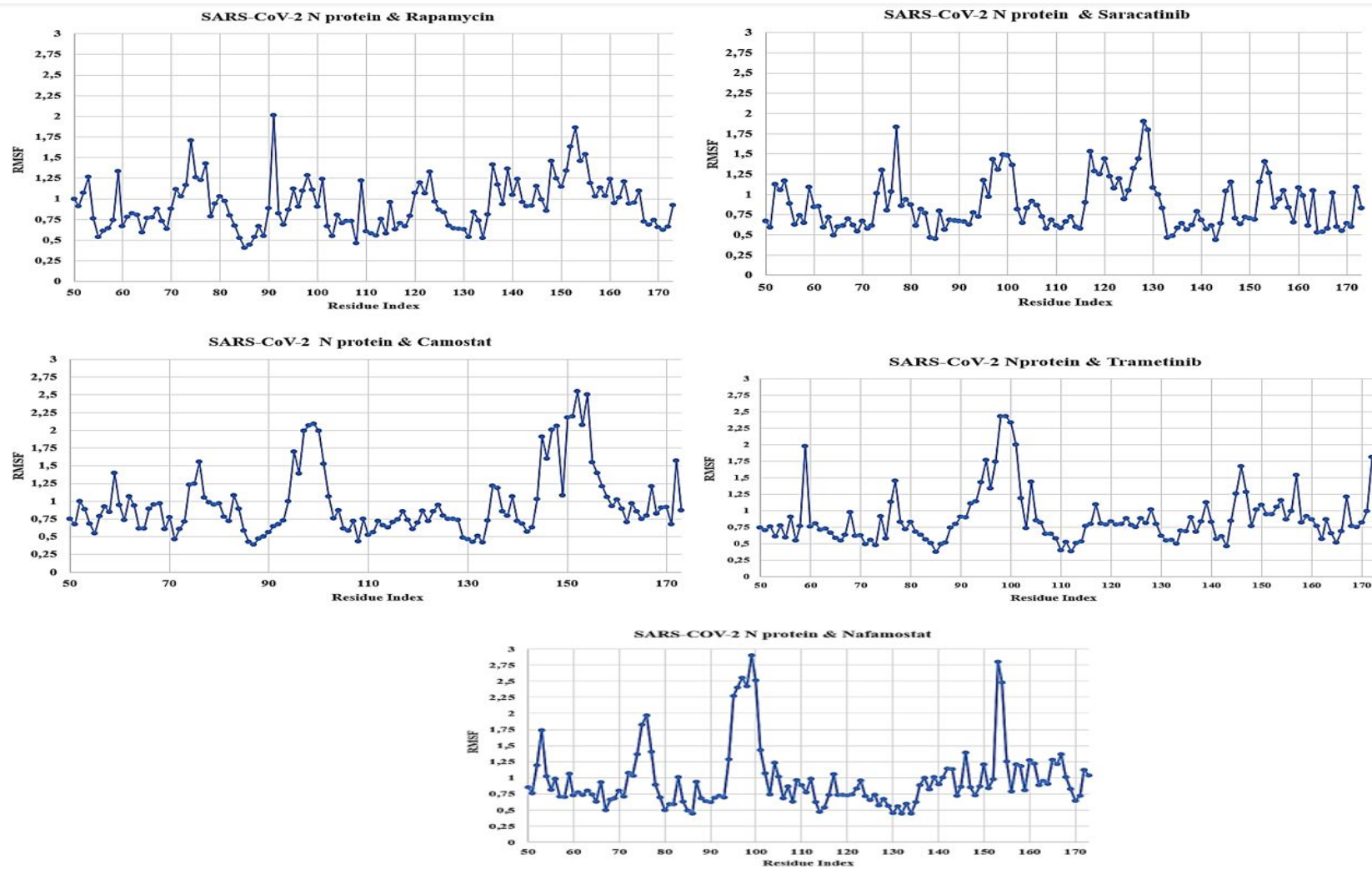


FIGURE S1 RMSF profile of SARS-CoV-2 N protein in the complex structures

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