Understanding the binding mode and binding interactions of novel main protease pyridyl ester derivatives with SARS-CoV-2 using molecular docking calculations

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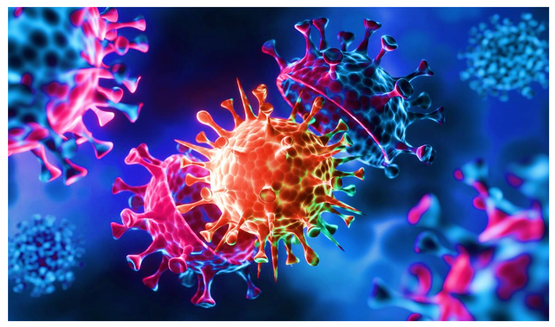
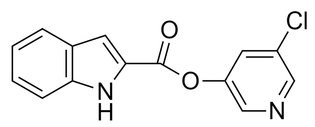
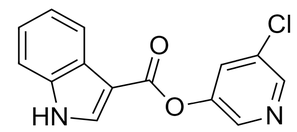
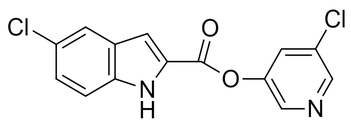
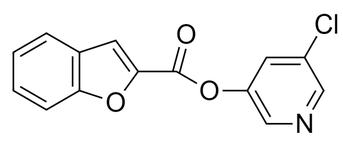
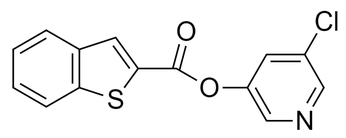
INTRODUCTION



Currently, the infectious disease, COVID-19 disease caused by SARS-CoV-2 virus is spreading over a large number. Resulting in major health problems main protease (M^{pro}) enzymes have been investigated as a primary drug development target to inhibit SARS-CoV-2 virus. In this work, we attempted to elucidate the binding mode, binding interaction and binding energy for novel 5-halopyridin-3-yl 1*H*-indole-carboxylates derivatives using molecular docking calculation

MATERIAL & METHODS

Table 1 Structure and biological activities of 5-halopyridin-3-yl 1*H*-indole-carboxylates

Cpd.	Structure	IC_{50} (μM)
1		0.0247 ± 0.0044
2		21.7 ± 0.0
3		0.0342 ± 0.0021
4		0.00541 ± 0.00032
5		0.0261 ± 0.0051

Structures and biological activities of five compounds against M^{pro} SARS-CoV-2 for this study were taken from literatures (Angew. Chem. Int. Ed. 2021, 60, 10423-10429). The chemical structures of these inhibitors were constructed using the standard tools available in GaussView 5.08 program and were then fully optimized using the M062X/6-31G(d,p) method implemented in Gaussian 09 program.

Molecular docking was performed to investigate the binding mode, binding interactions and binding energy of the selected inhibitors. The molecules were docked into M^{pro} SARS-CoV-2 (PDB code: 7P51) using Maestro 10.2 program.

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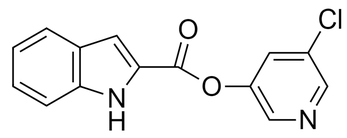
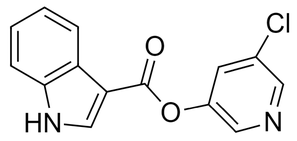
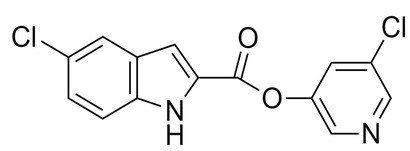
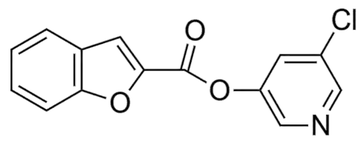
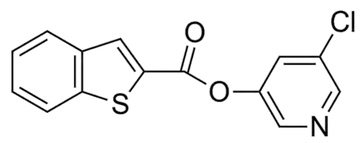
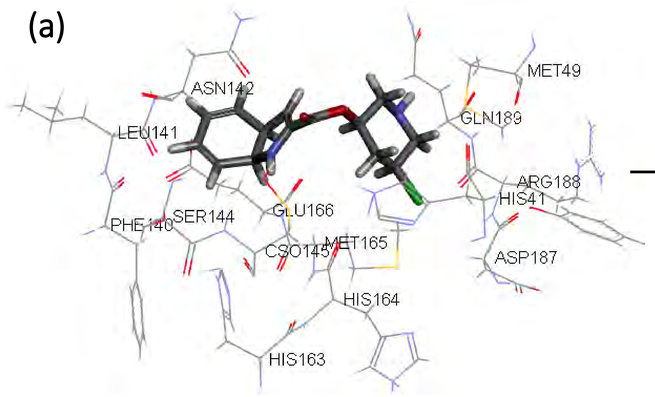
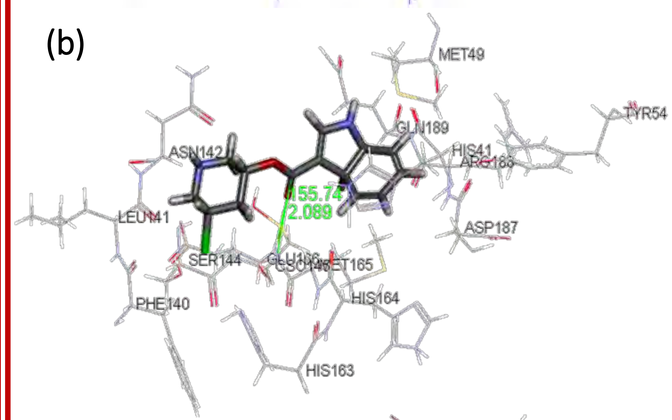
- Faculty of Science, Ubon Ratchathani University
- Faculty of Science, Nakhon Phanom University
- Faculty of Science, Kasetsart University
- National Nanotechnology Center (NANOTEC)

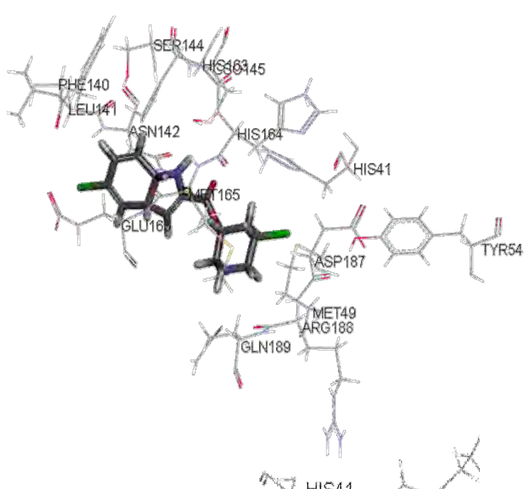
RESULTS

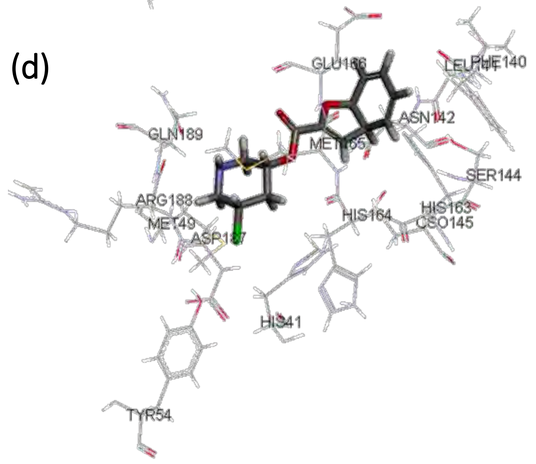
Table 2 The binding energy of 5-halopyridin-3-yl 1*H*-indole-carboxylates form molecular docking calculations.

Cpd.	Structures	Binding energy (kcal/mol)
1		-6.851
2		-6.677
3		-6.407
4		-6.314
5		-6.116









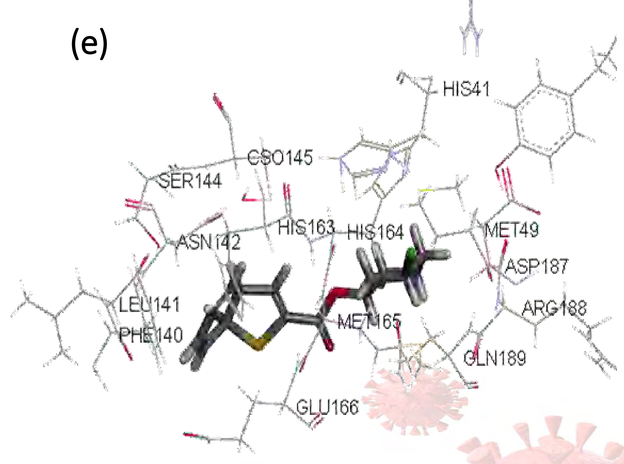


Figure 1. The binding mode and binding interactions of the compounds 1-5 (a) – (e), respectively. Green line indicate hydrogen bond interaction.

CONCLUSION

- ✓ The hydrogen bond interactions were found between carbonyl group of compound 2 with Glu166 and Cys145 residues
- ✓ The hydrophobic interactions were found between all compounds with Met49, Phe140, Leu141, and Met165 residues
- ✓ Our findings could provide understanding binding interactions that possibly apply to the ligand design of novel and highly potent anti-M^{pro} SAR-CoV-2.