Electronic Supplementary Material (ESI) for RSC Advances.

Supporting information

Binding of Inhibitors to the Monomeric and Dimeric SARS-CoV-2 Mpro

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Table S1. The binding pose of ligands to SARS-CoV-2 Mpro via PyMOL.

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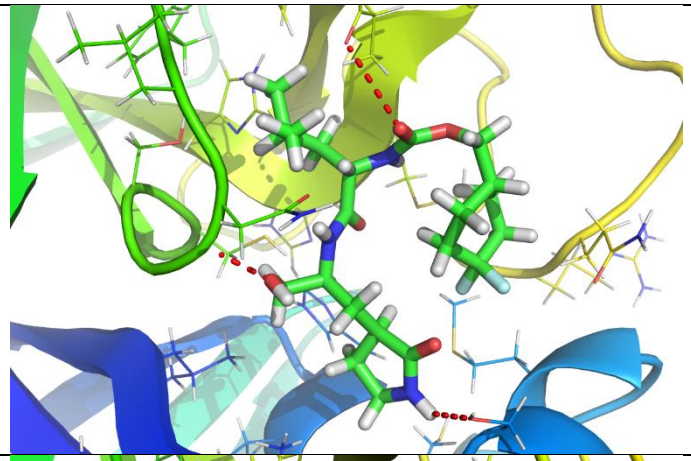
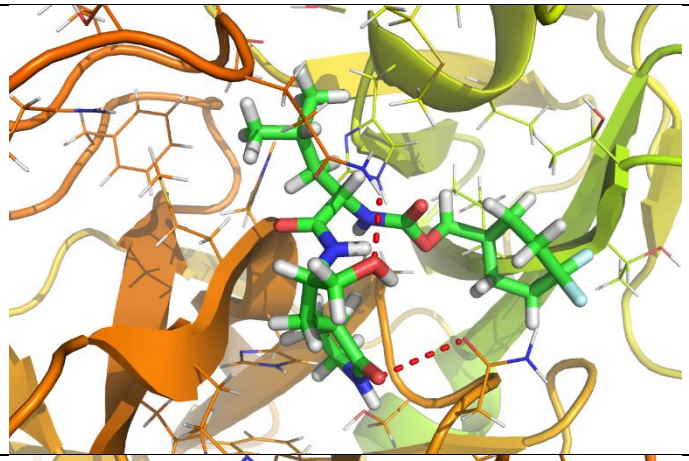
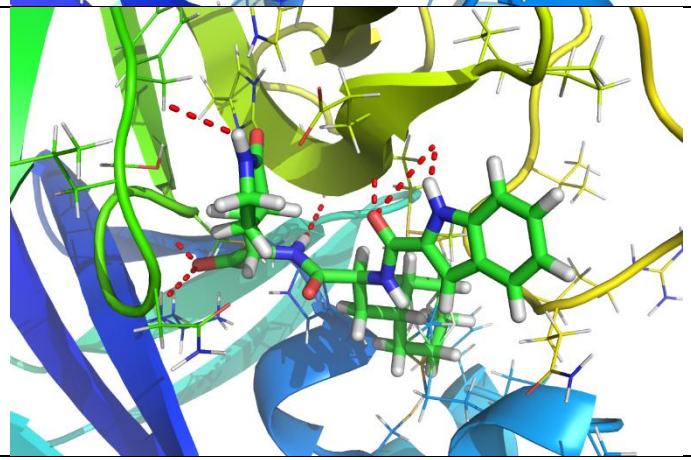
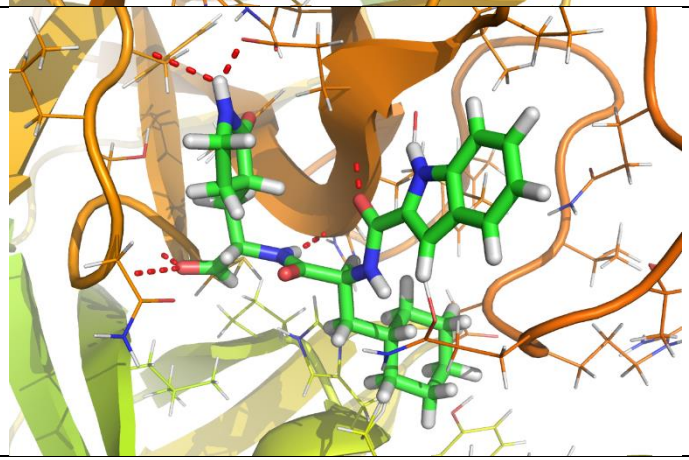
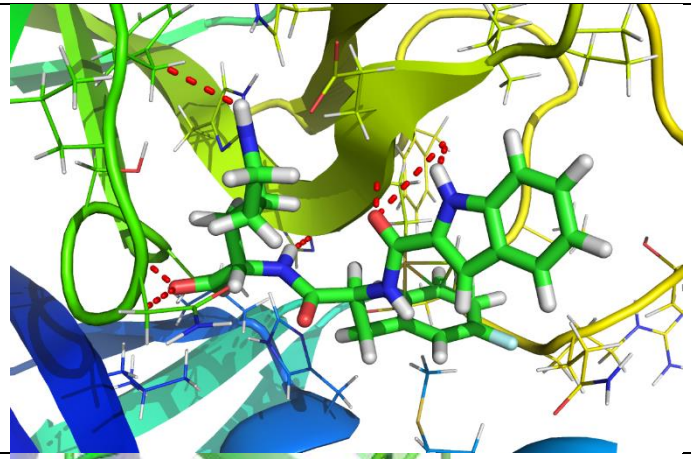
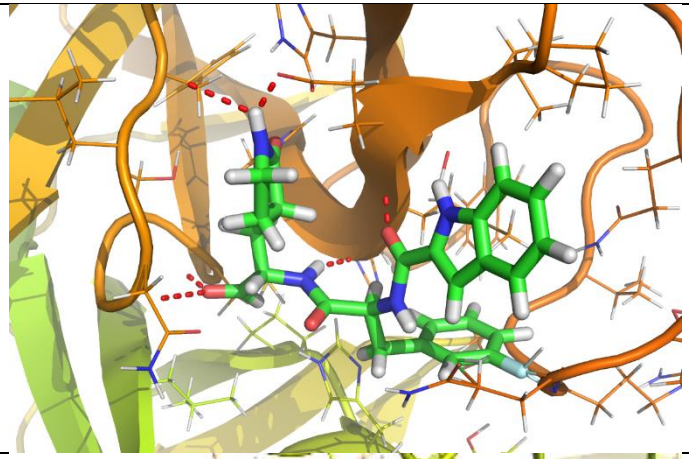
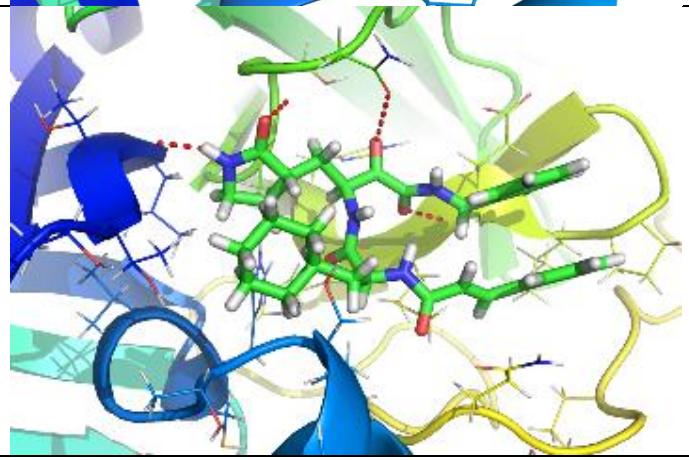
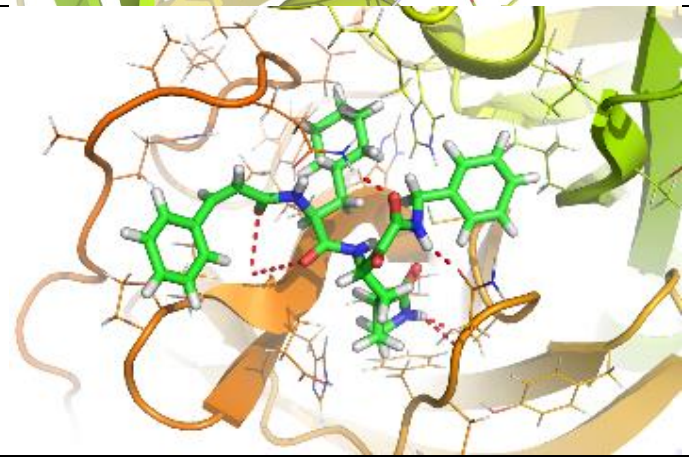
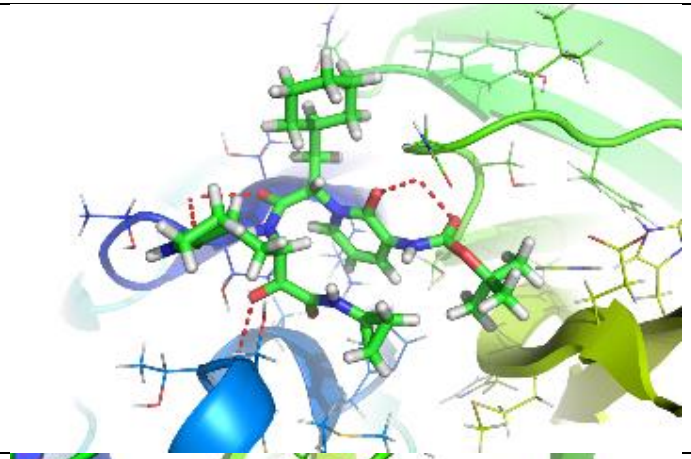
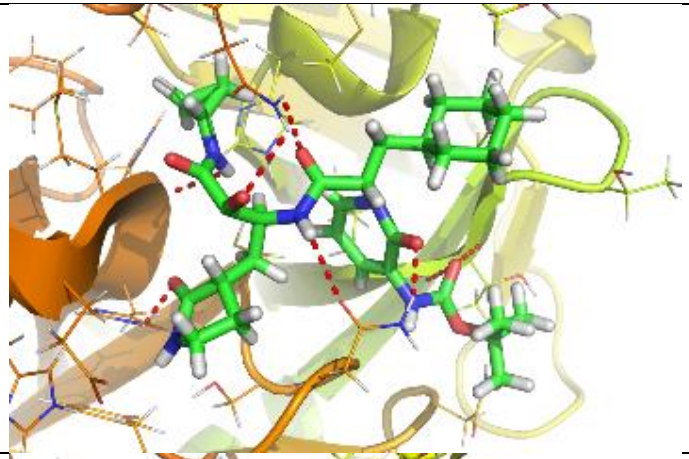
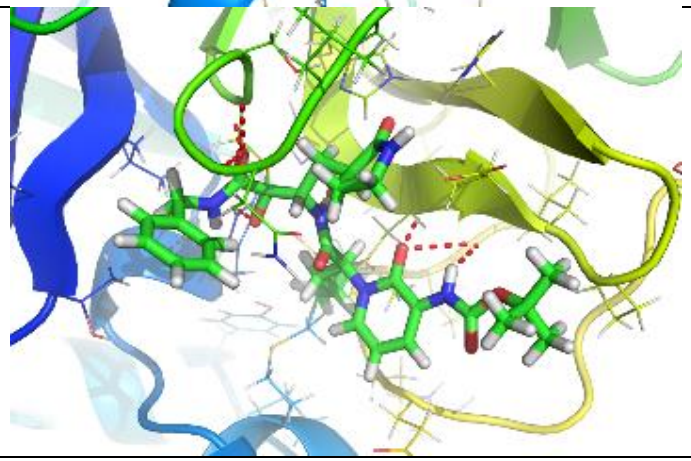
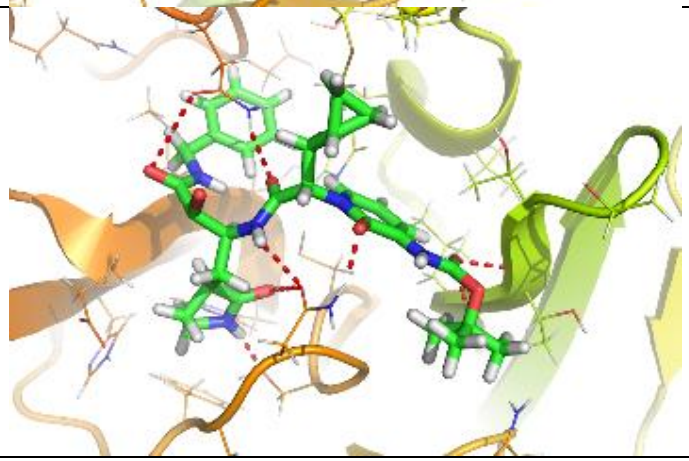
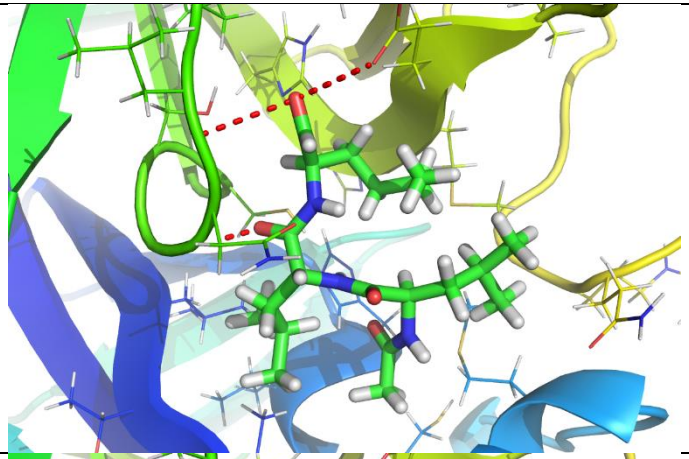
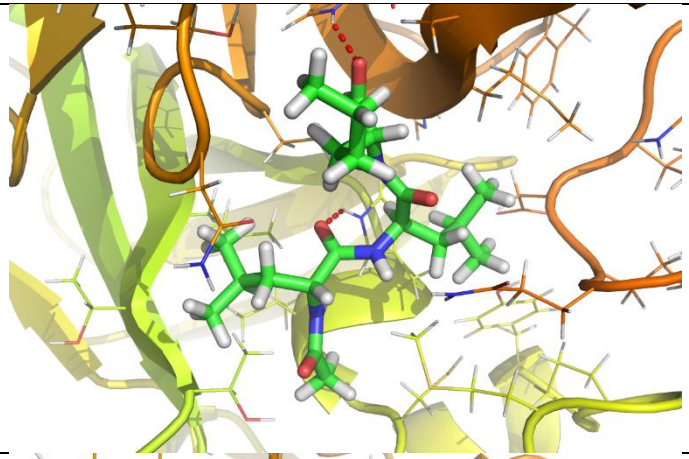
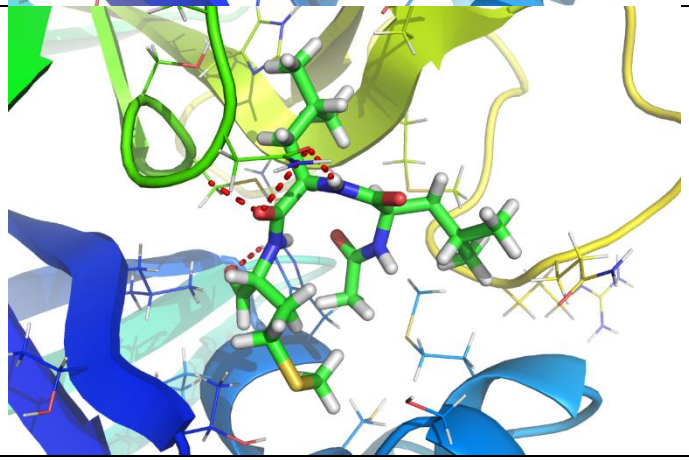
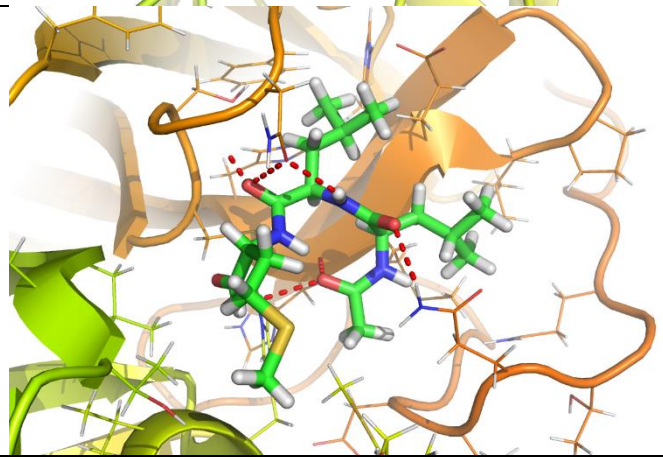
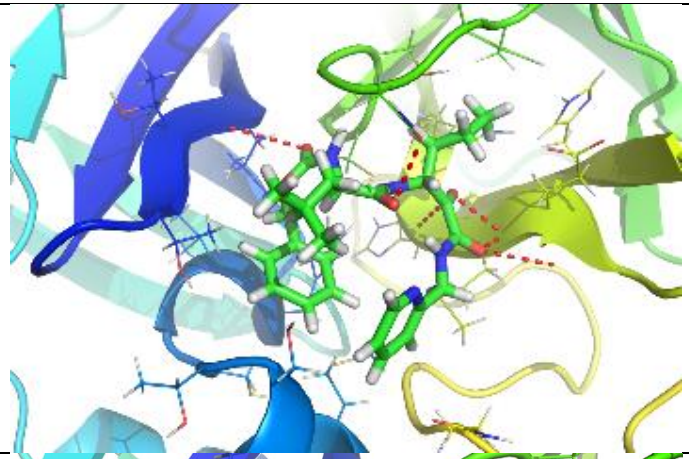
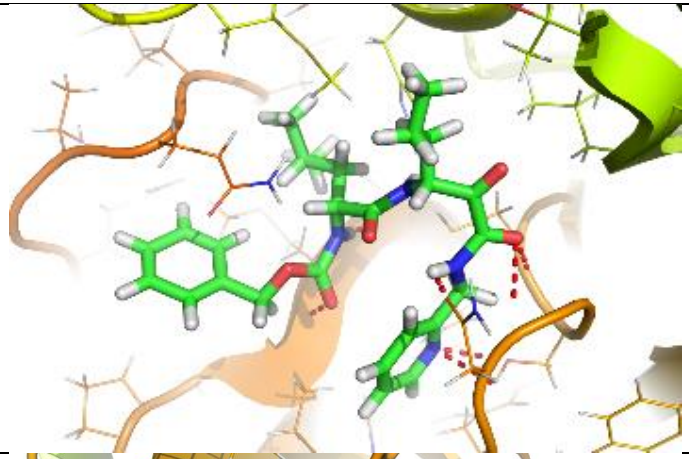
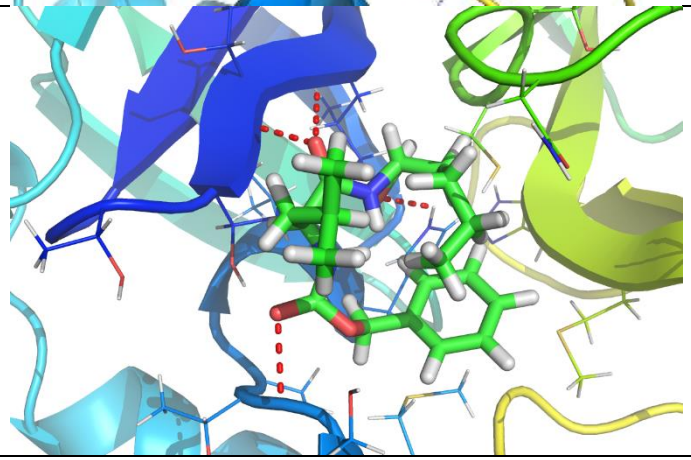
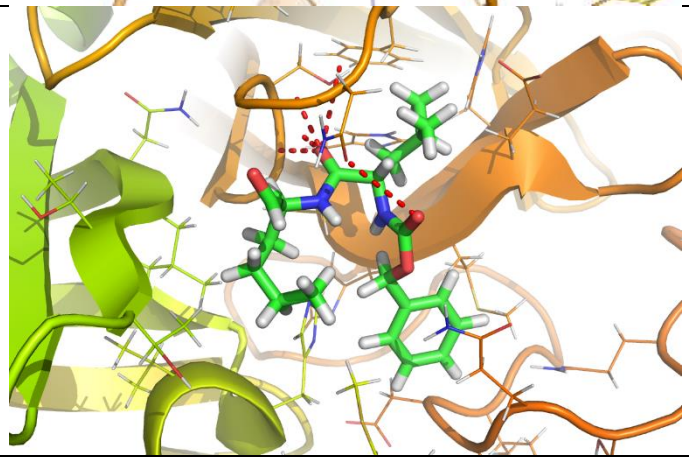
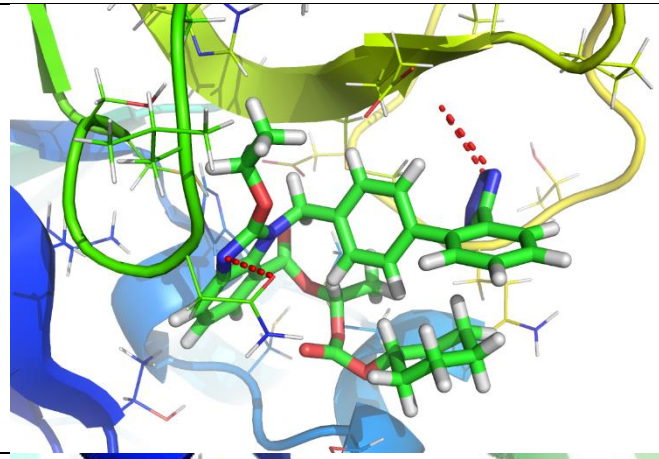
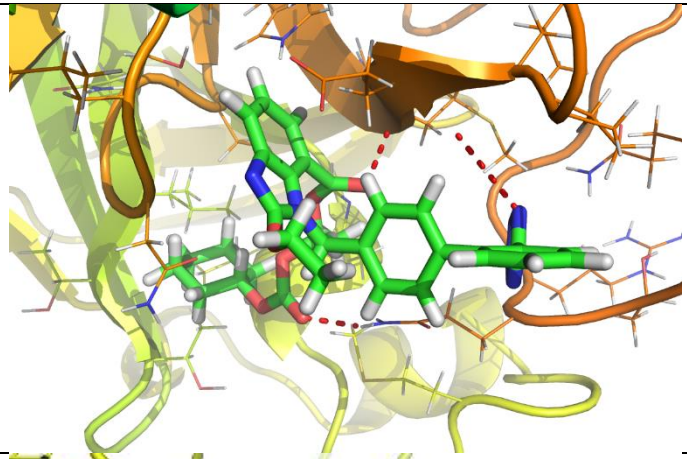
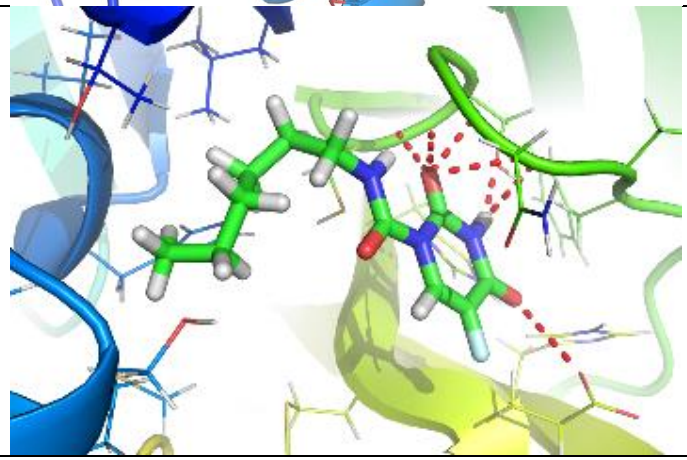
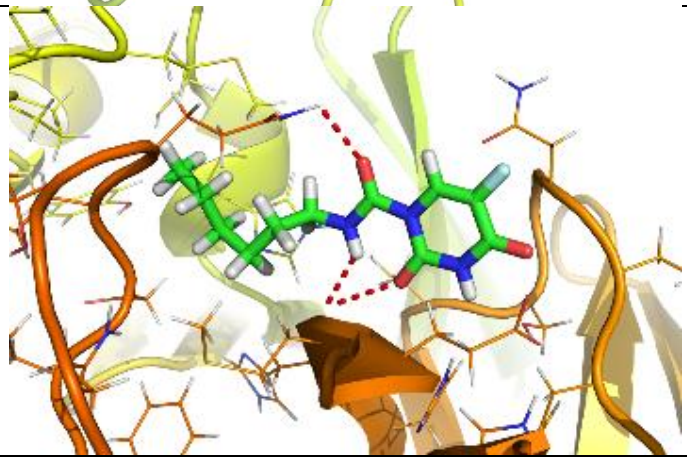
7J		
11a		

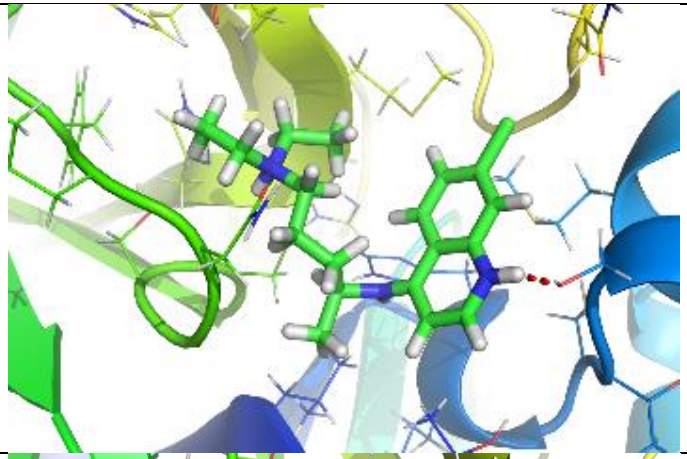
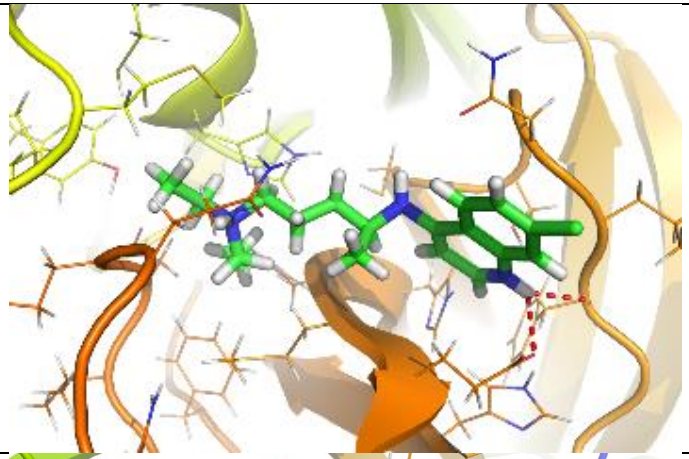
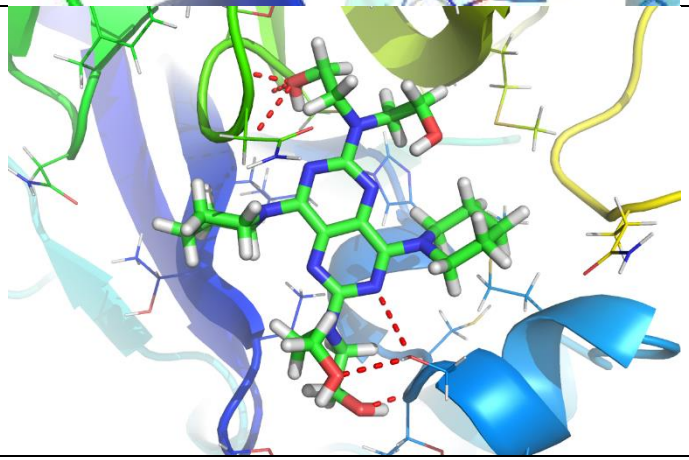
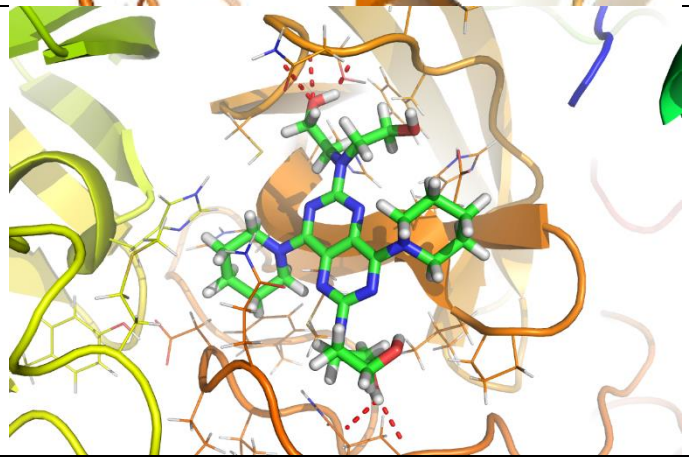
11b		
11r		

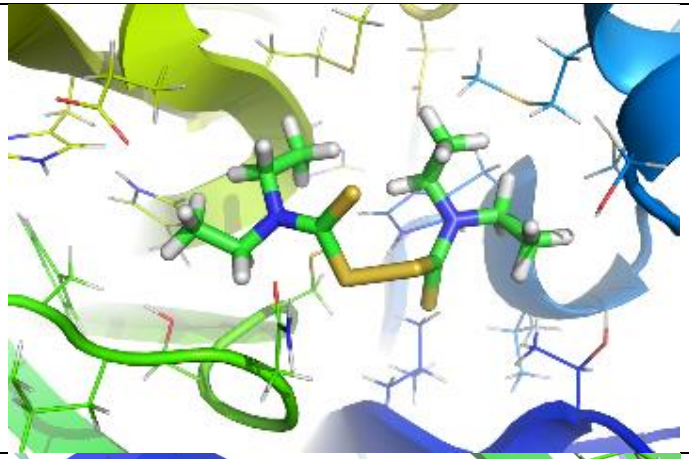
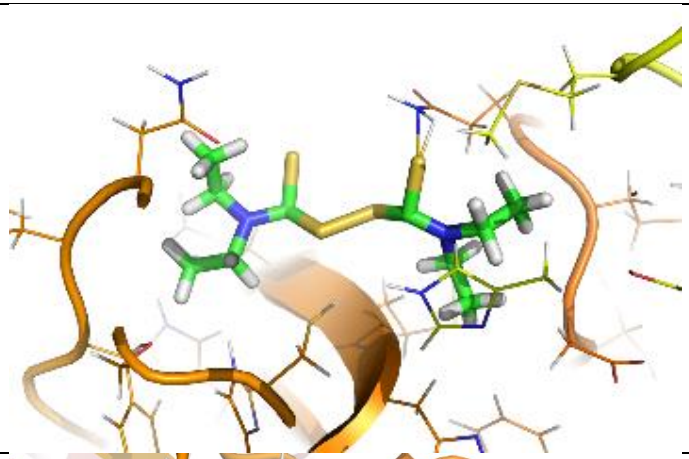
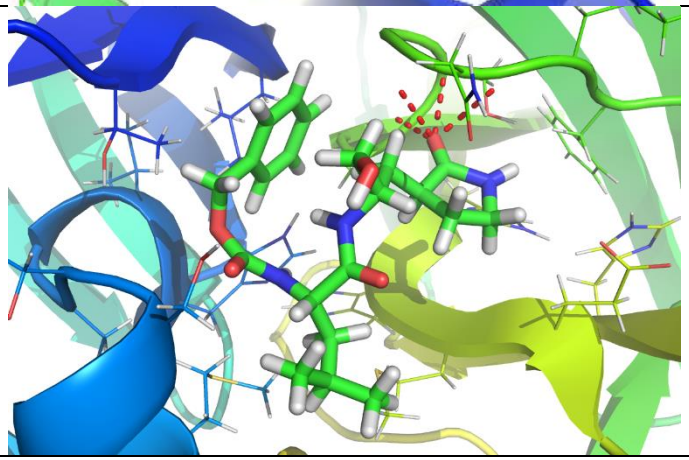
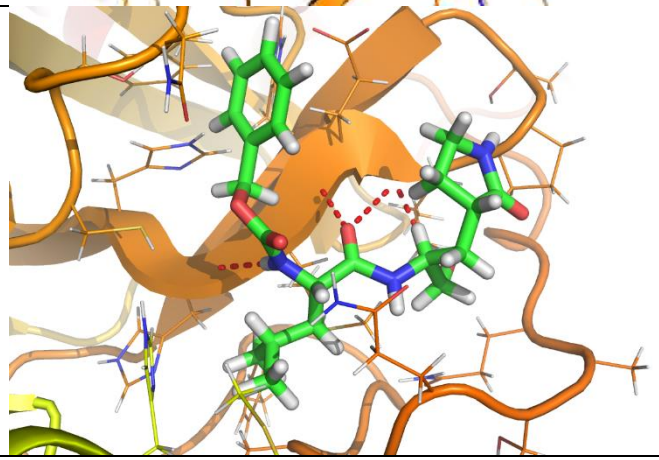
13a		
13b		

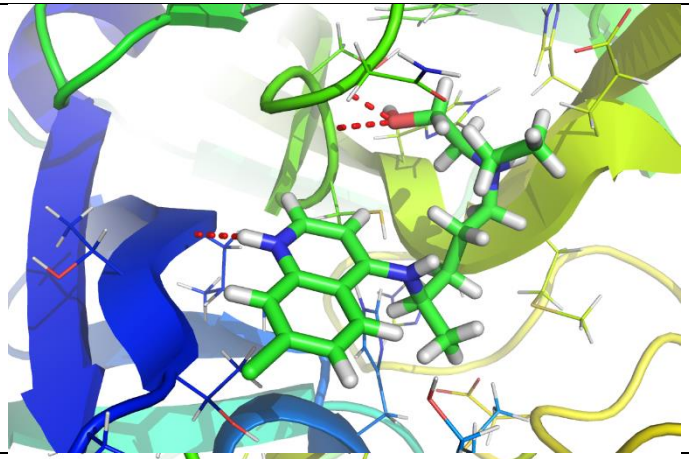
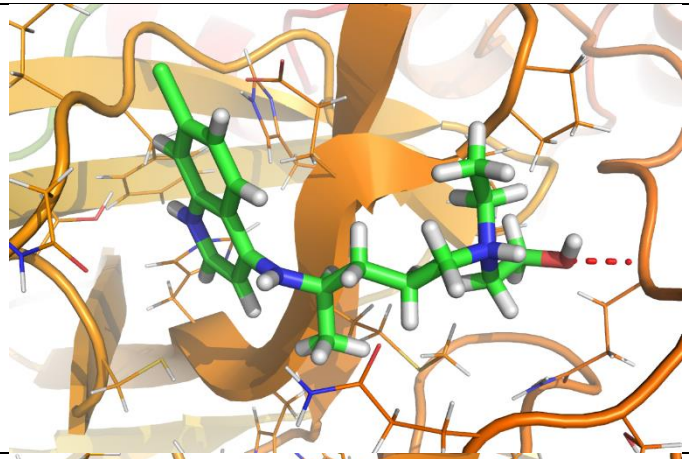
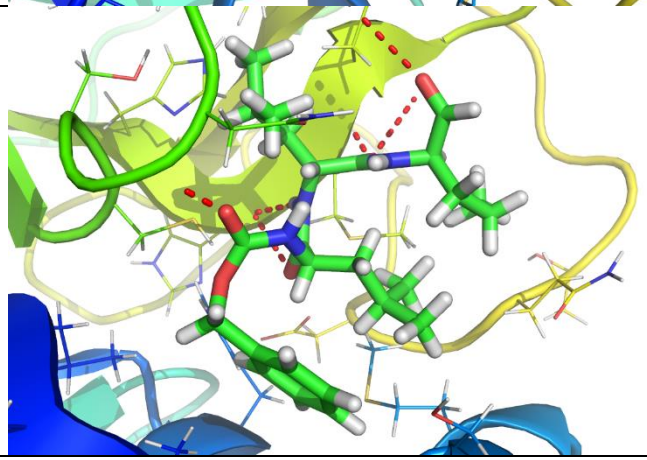
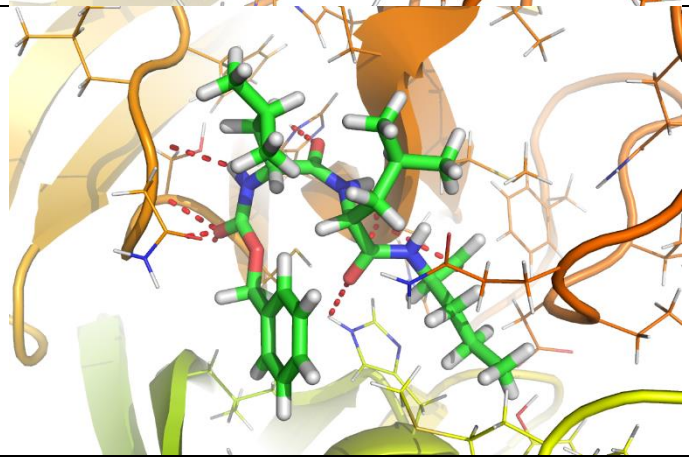
Calpain inhibitor I		
Calpain inhibitor II		

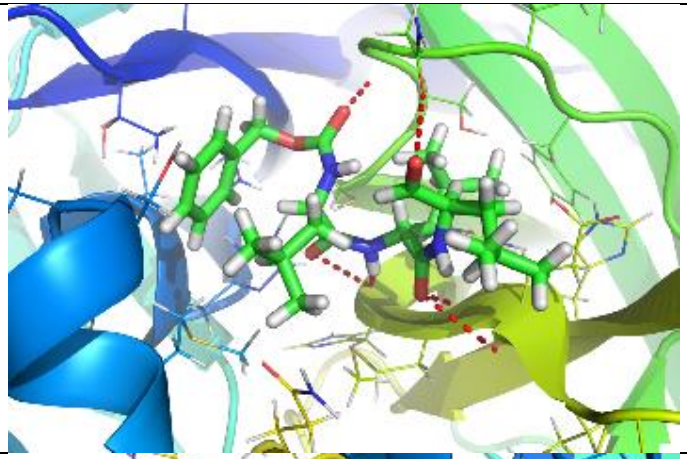
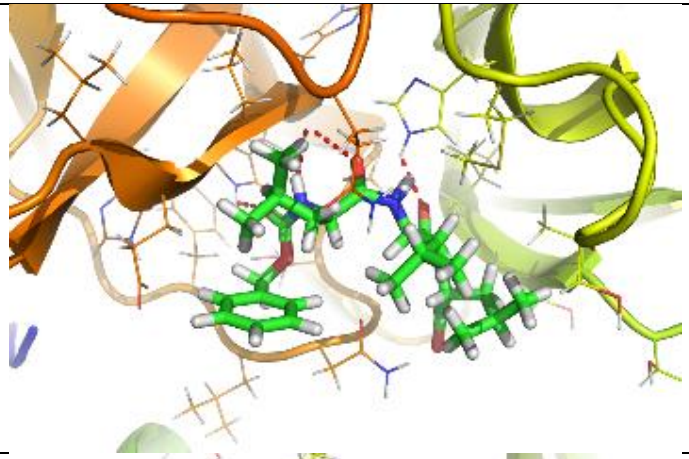
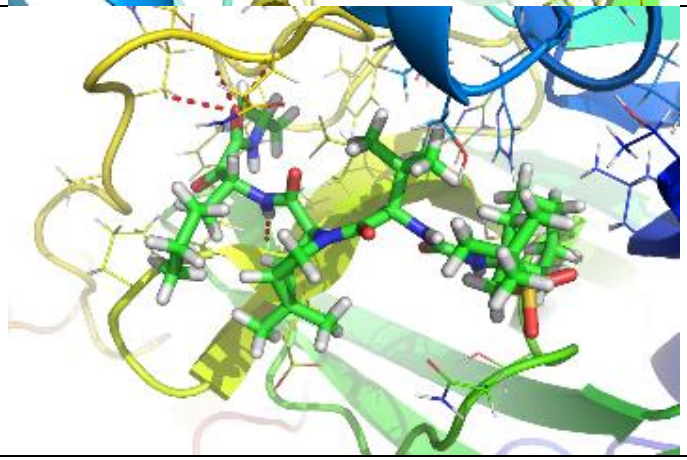
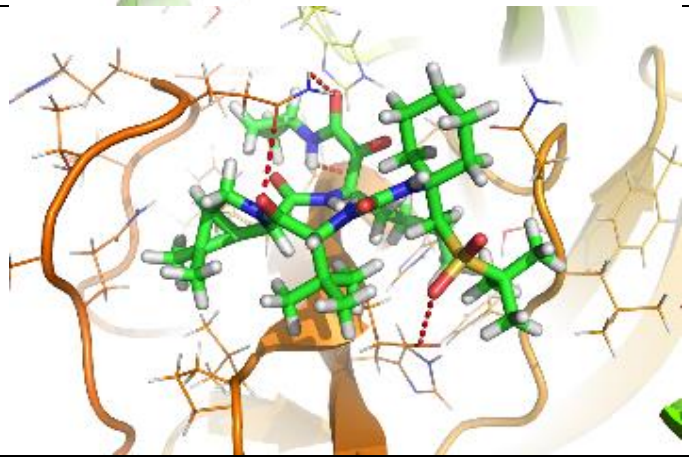
Calpain inhibitor XII		
Calpeptin		

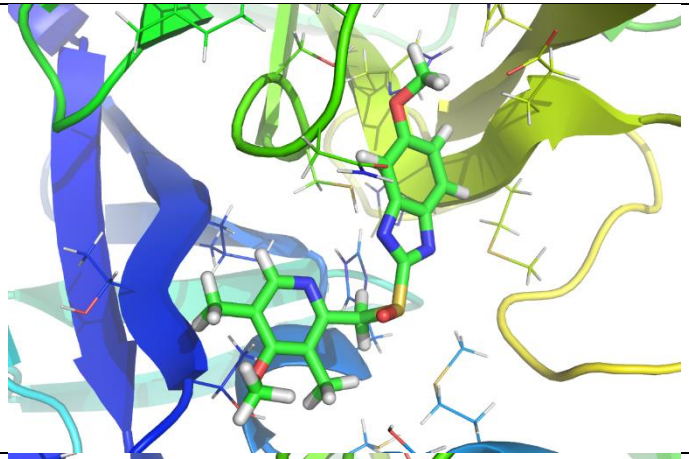
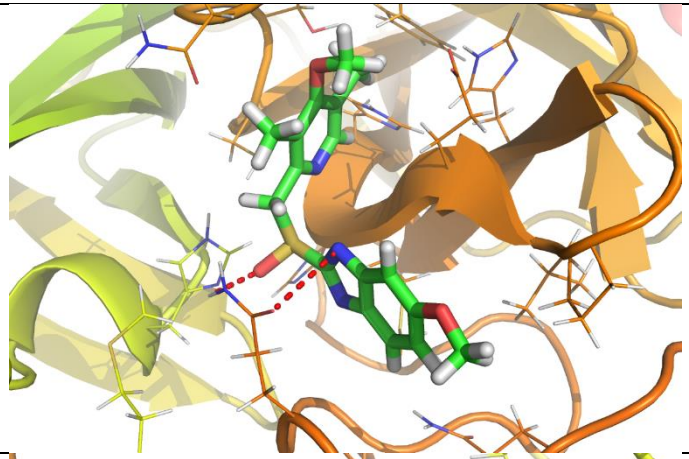
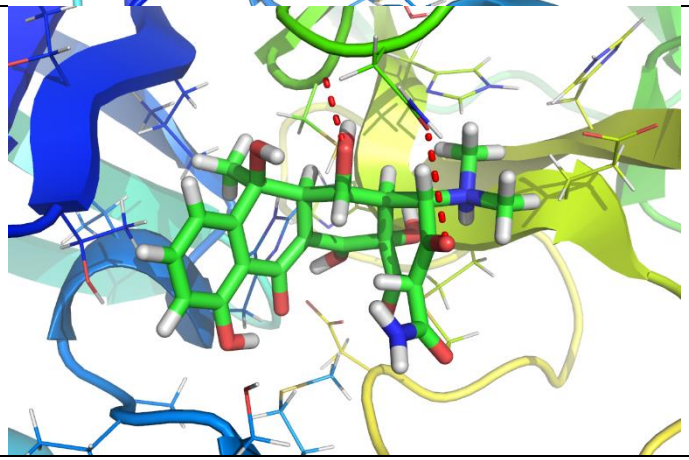
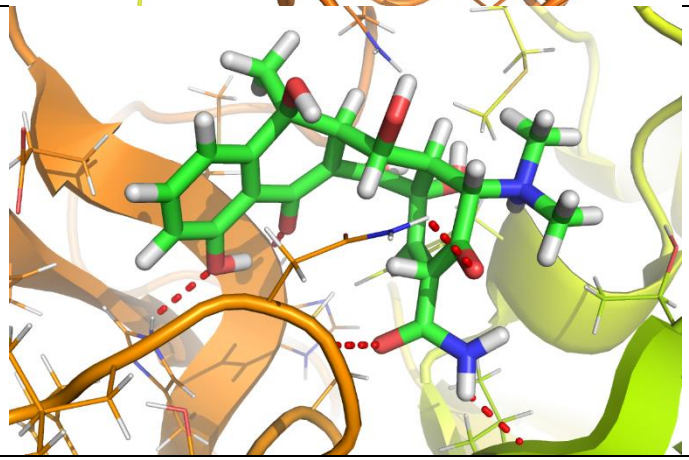
Candesartan cilexetil		
Carmofur		

Chloroquine		
Dipyridamole		

Disulfiram		
GC-373		

Hydroxychloroquine		
MG-115		

MG-132		
Narlaprevir		

Omeprazole		
Oxytetracycline		

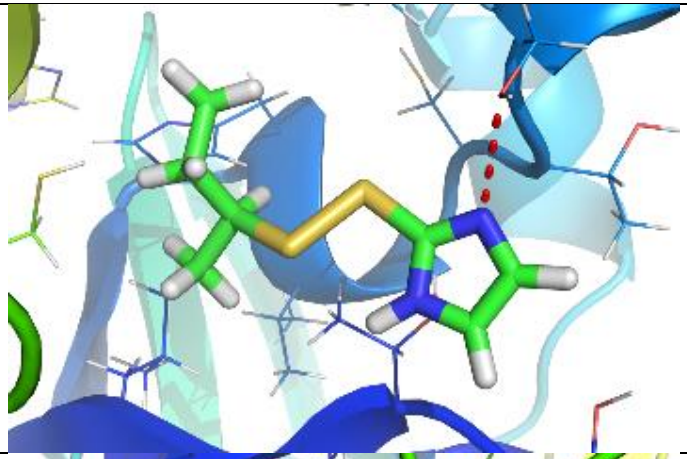
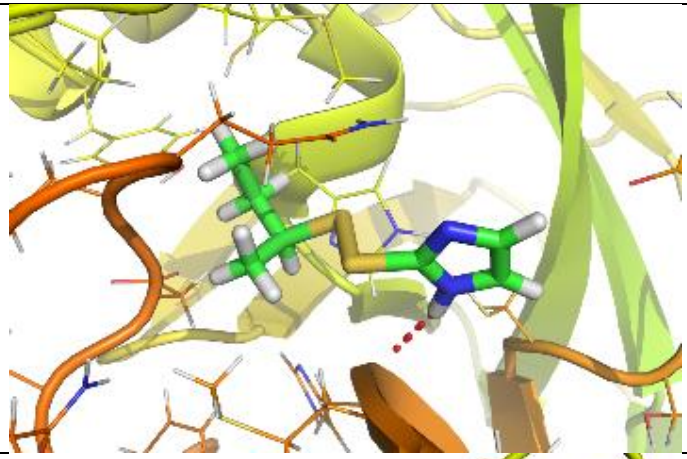
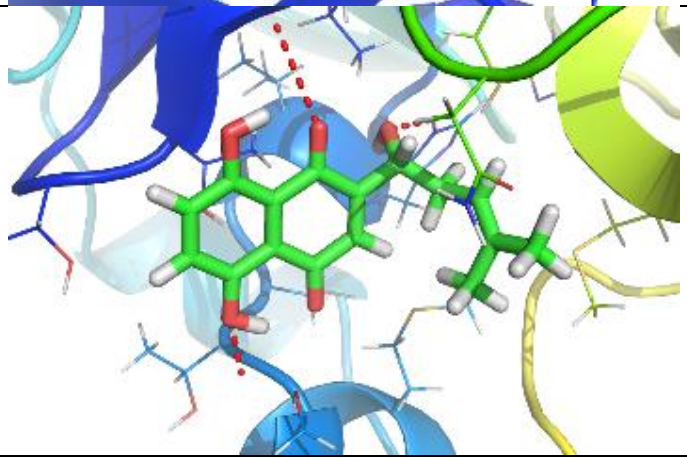
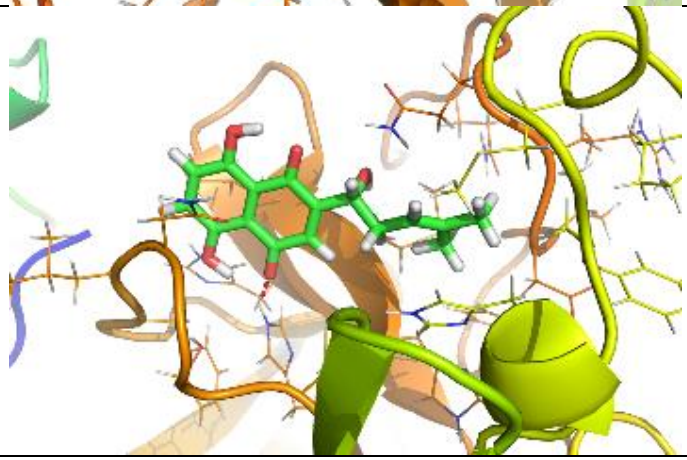
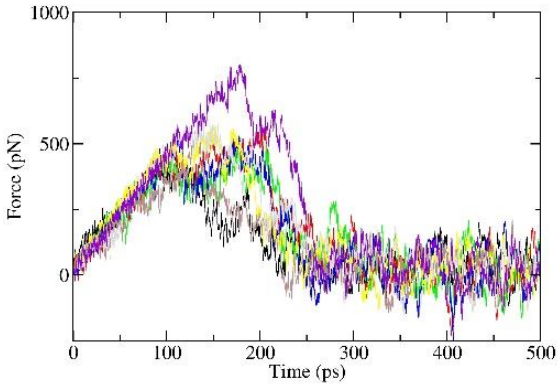
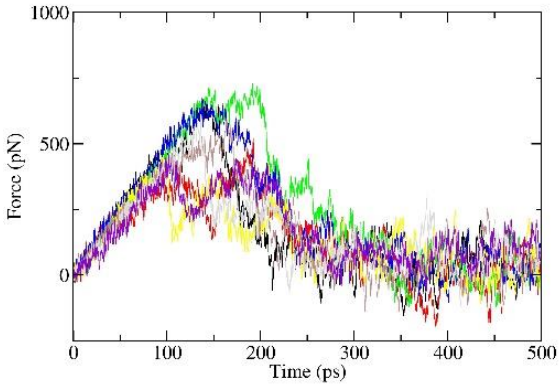
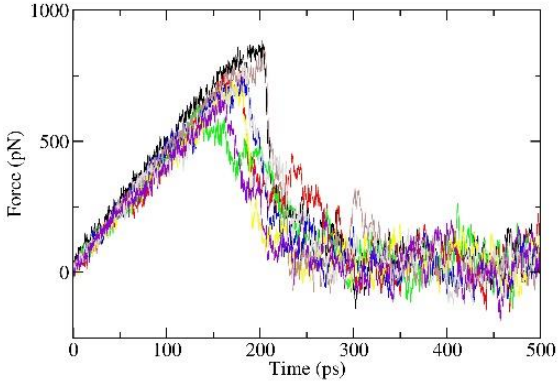
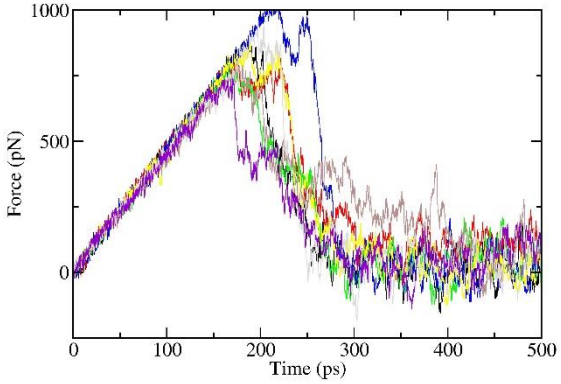
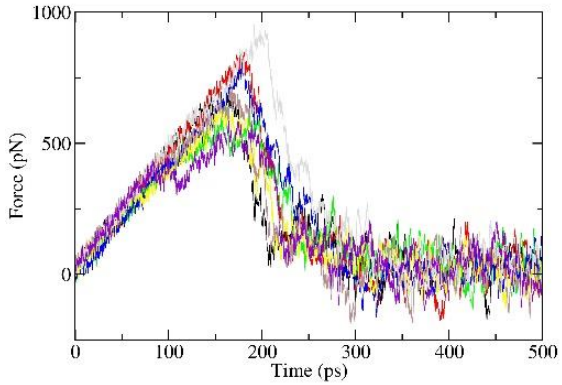
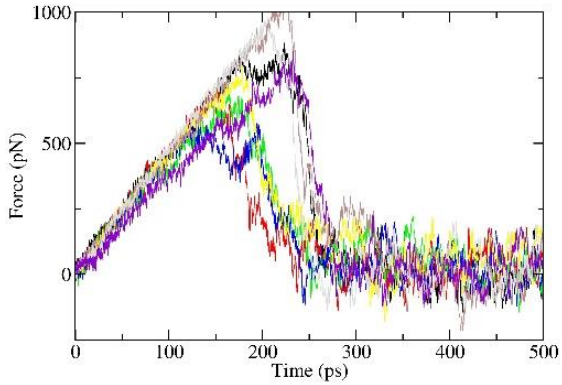
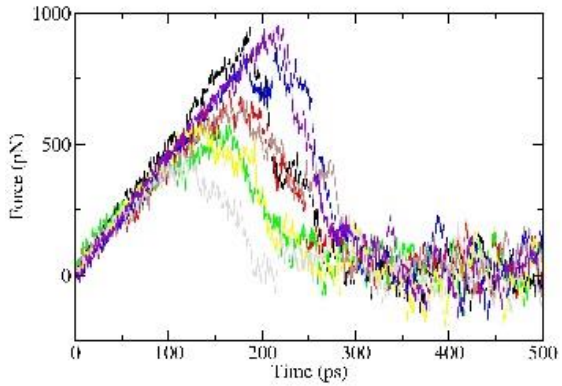
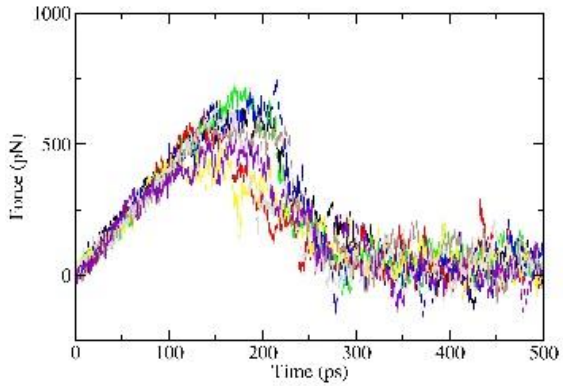
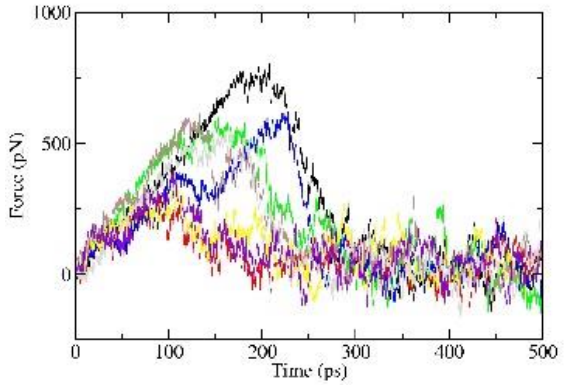
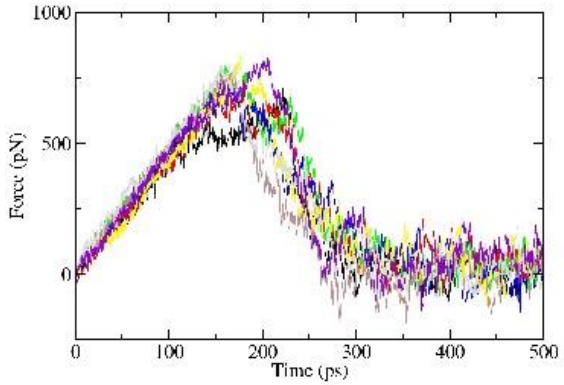
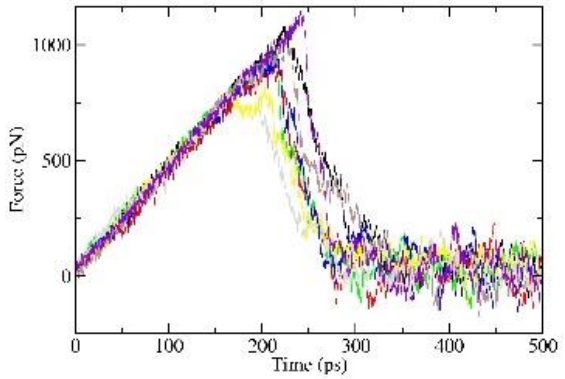
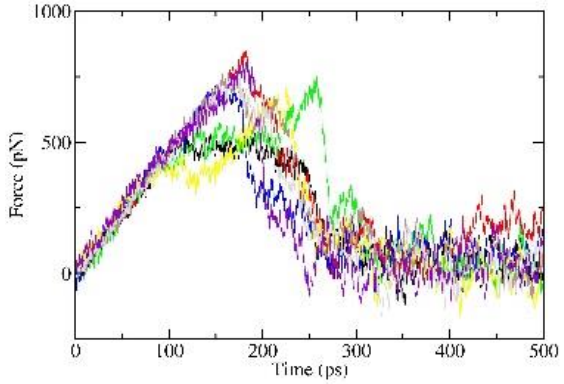
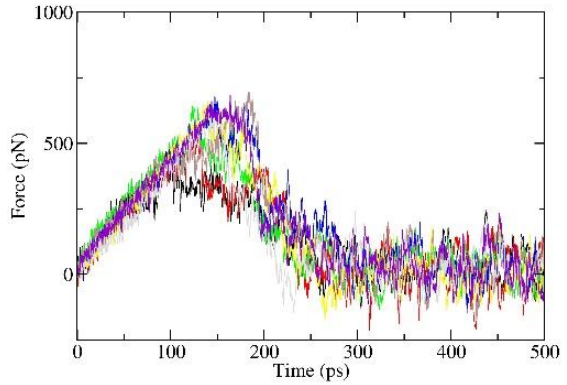
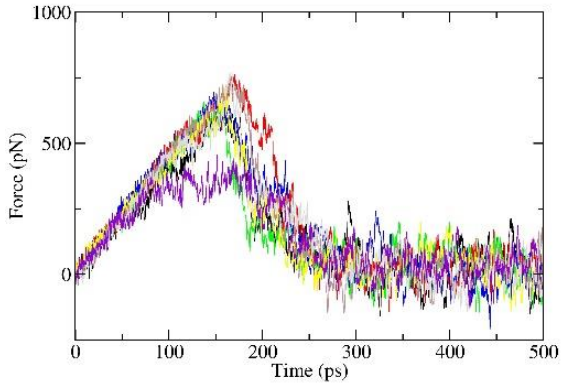
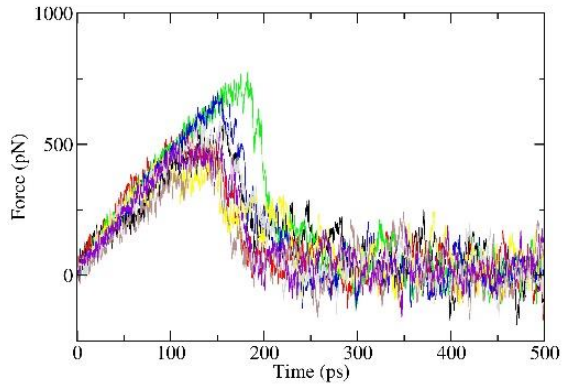
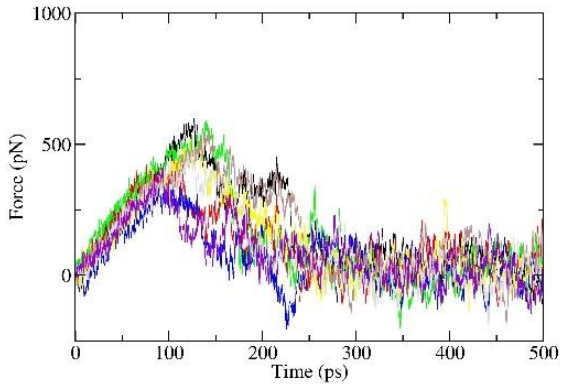
PX-12		
Shikonin		

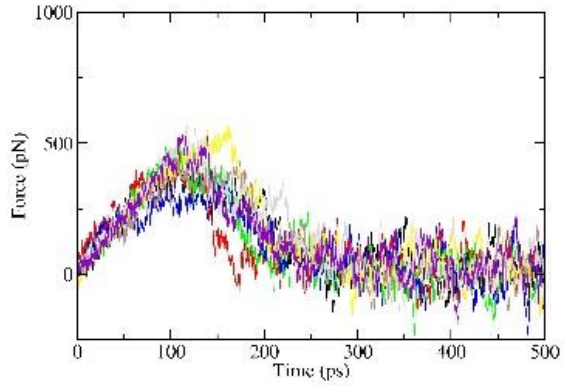
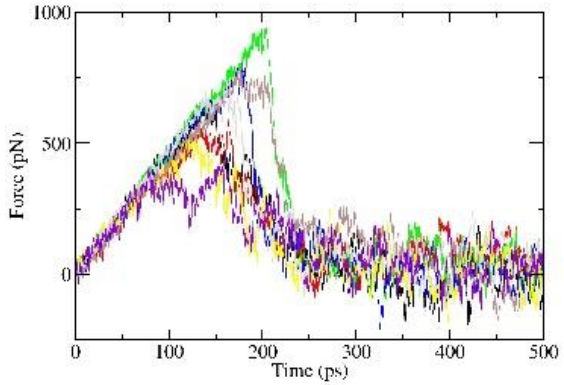
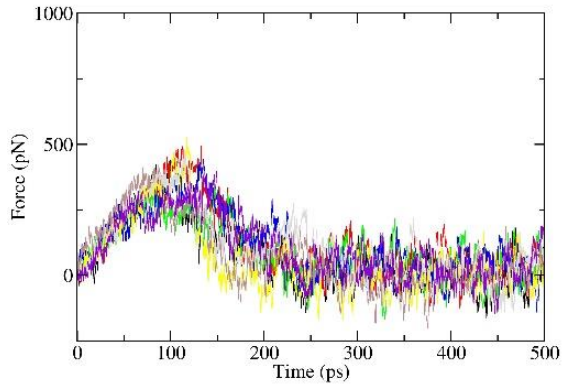
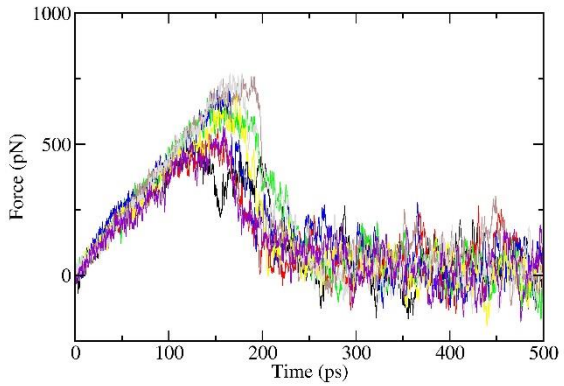
Table S2. The Pulling Force in Time Evolution.

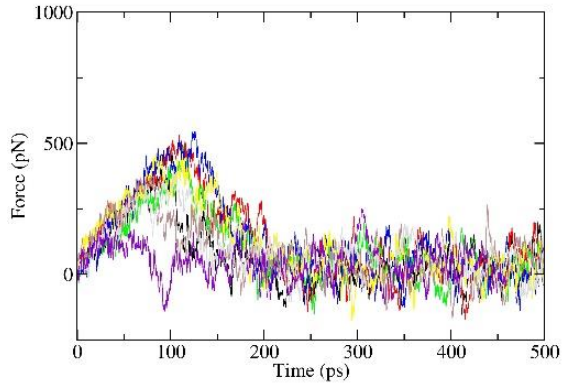
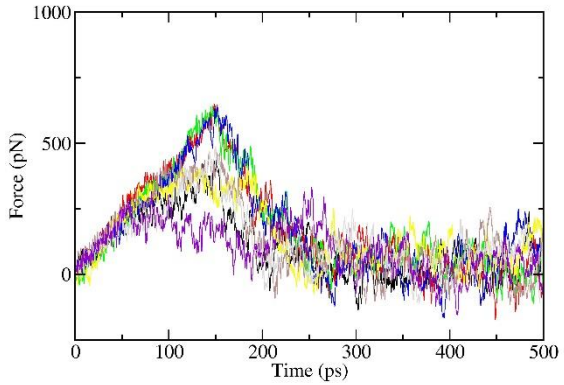
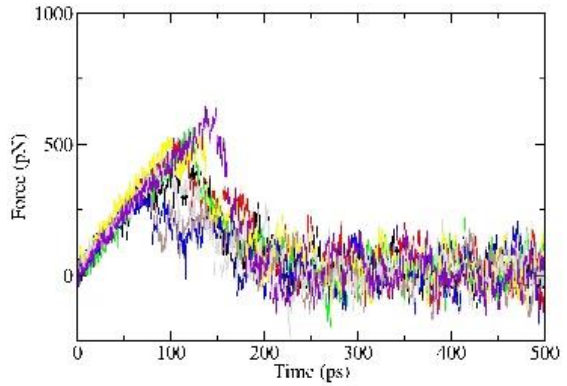
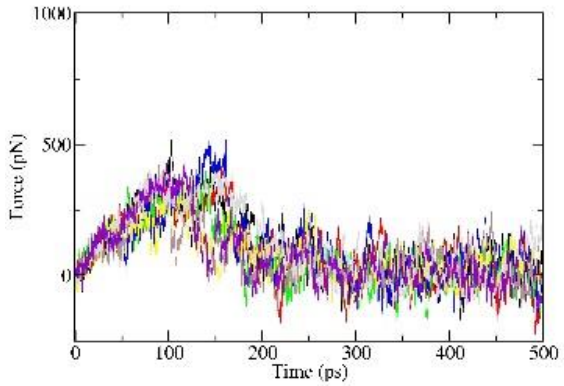
Name	Monomer	Dimer
7J		
11a		

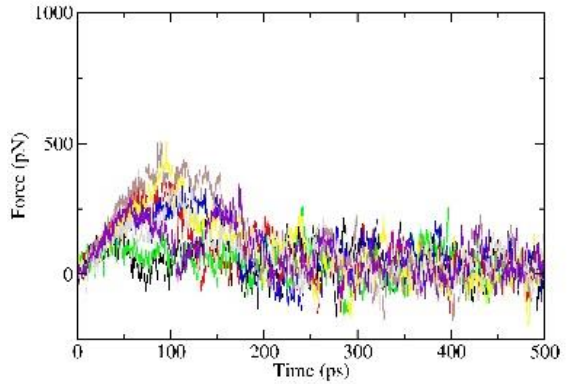
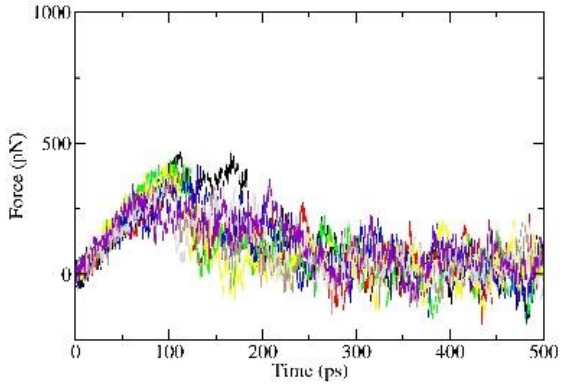
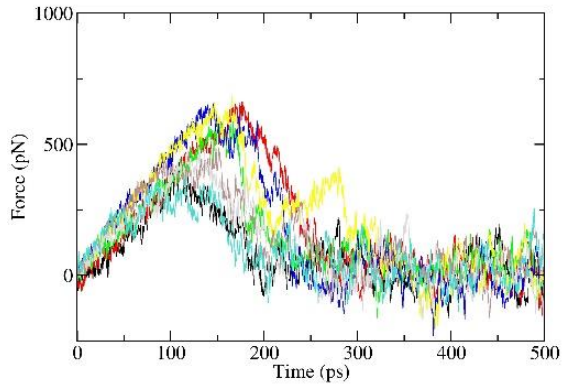
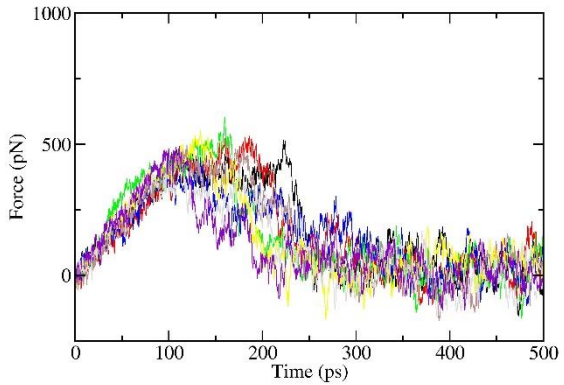
11b	 1000 500 0 Force (pN) 0 100 200 300 400 500 Time (ps)	 1000 500 0 Force (pN) 0 100 200 300 400 500 Time (ps)
11r	 1000 500 0 Force (pN) 0 100 200 300 400 500 Time (ps)	 1000 500 0 Force (pN) 0 100 200 300 400 500 Time (ps)

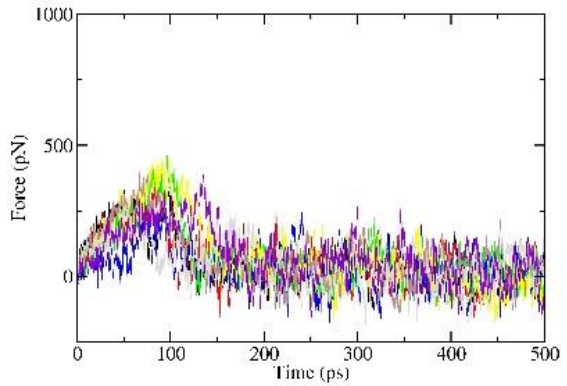
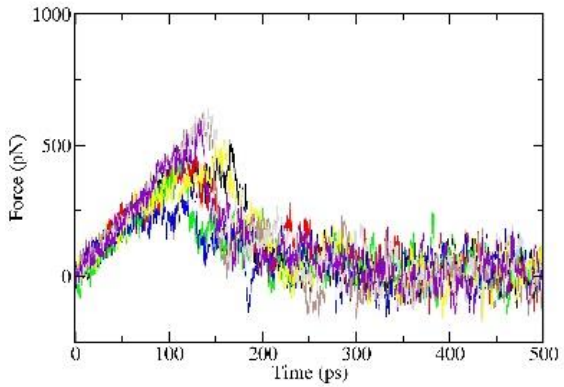
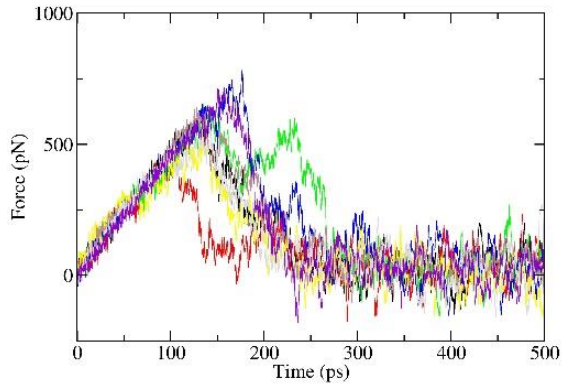
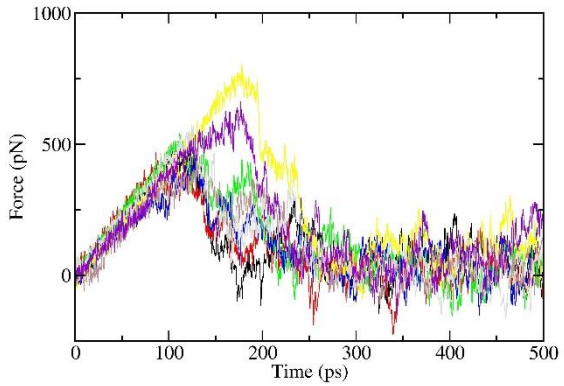
13a	 1000 500 0 Force (pN) 0 100 200 300 400 500 Time (ps)	 1000 500 0 Force (pN) 0 100 200 300 400 500 Time (ps)
13b	 1000 500 0 Force (pN) 0 100 200 300 400 500 Time (ps)	 1000 500 0 Force (pN) 0 100 200 300 400 500 Time (ps)

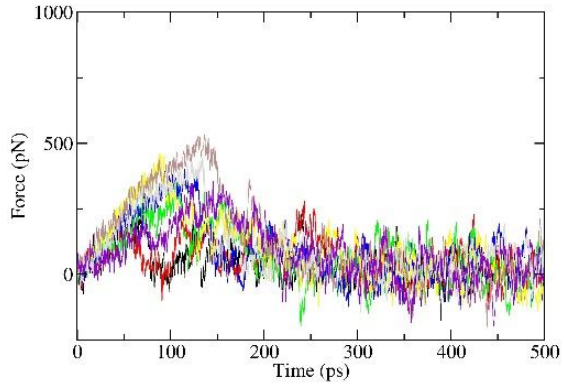
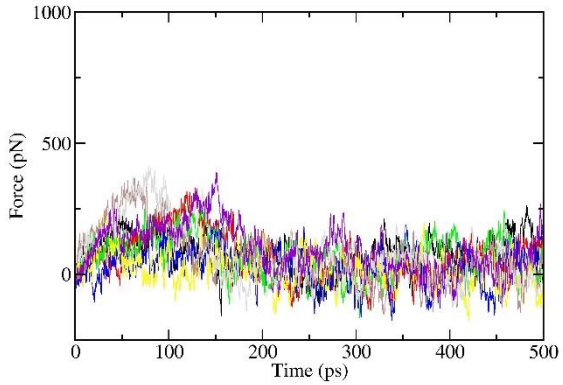
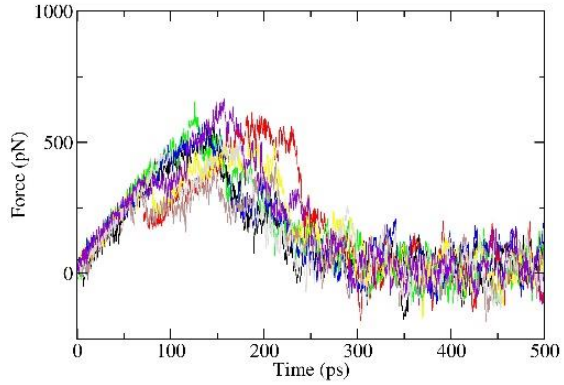
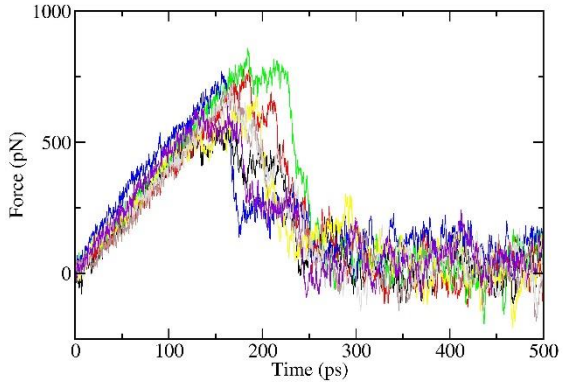
Calpain inhibitor I		
Calpain inhibitor II		

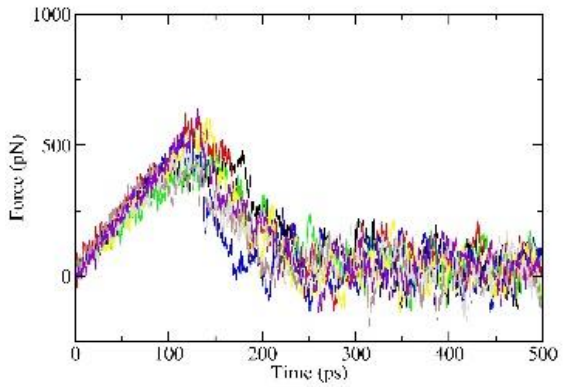
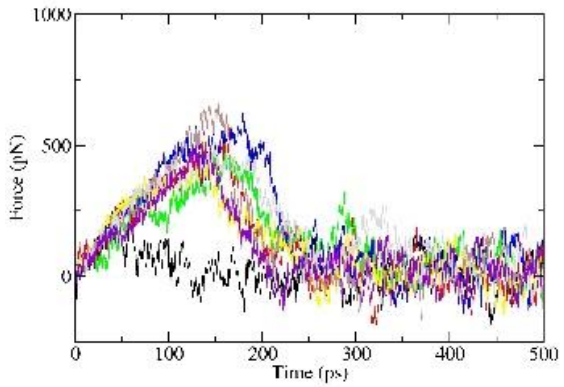
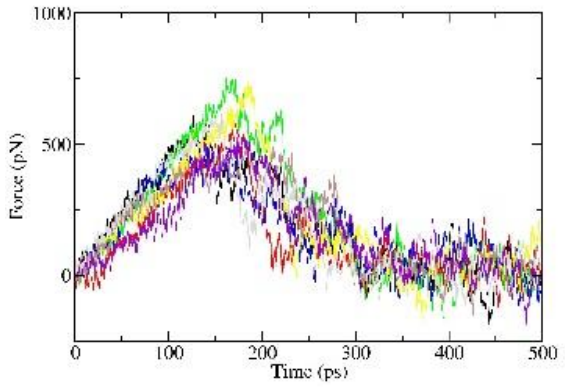
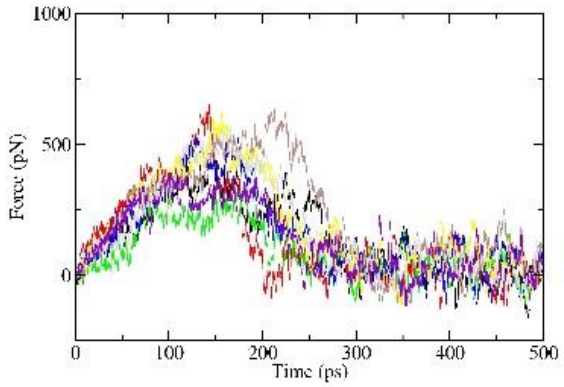
Calpain inhibitor XII		
Calpeptin		

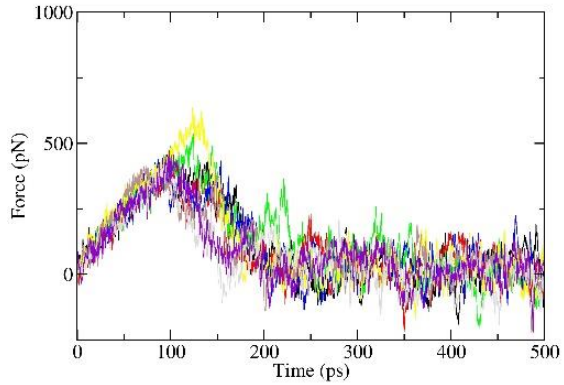
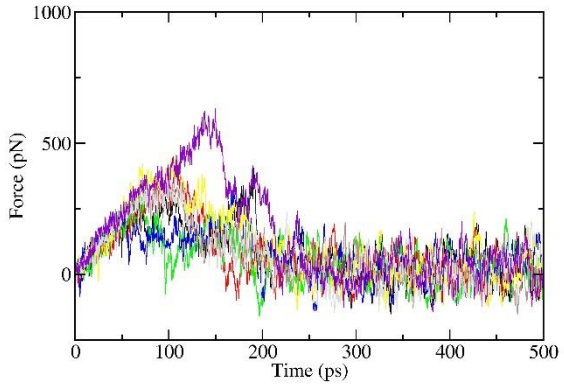
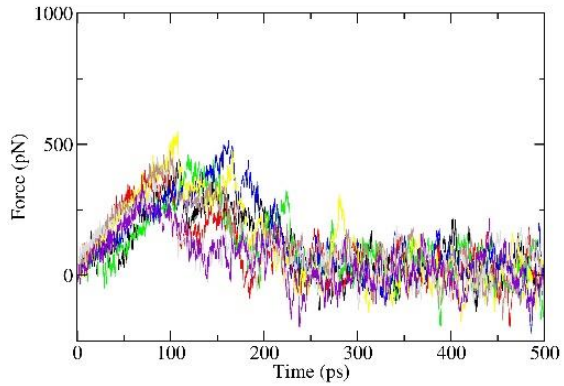
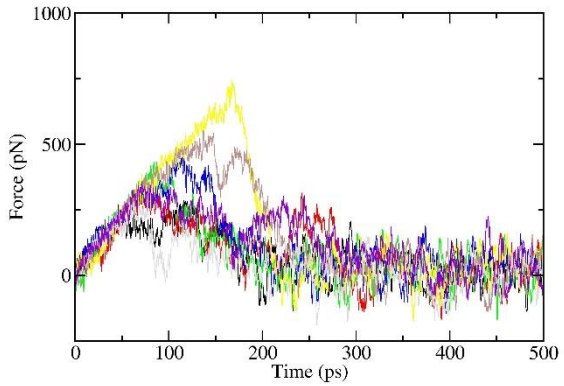
Candesartan cilexetil		
Carmofur		

Chloroquine		
Dypyradimole		

Disulfiram		
GC-373		

Hydroxychloroquine		
MG-115		

MG-132		
Narlaprevir		

Omeprazole		
Oxytetracycline		

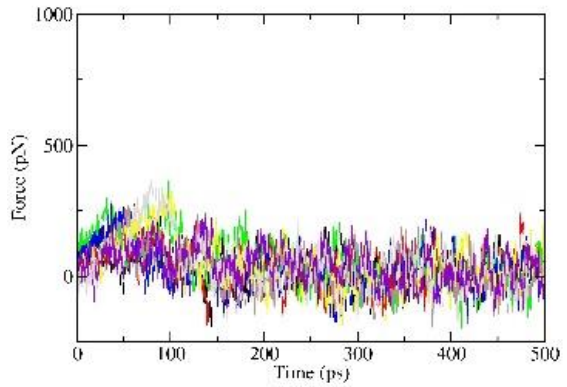
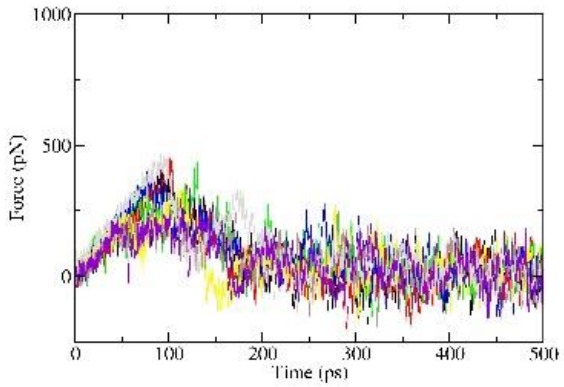
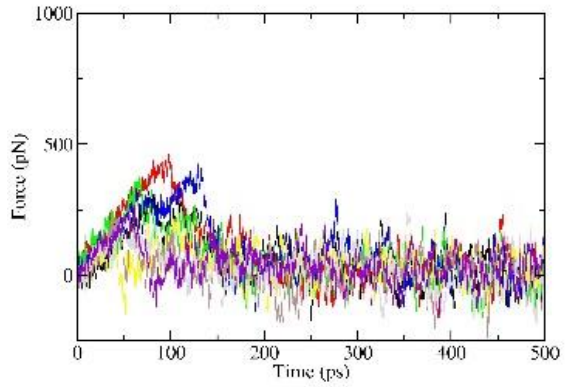
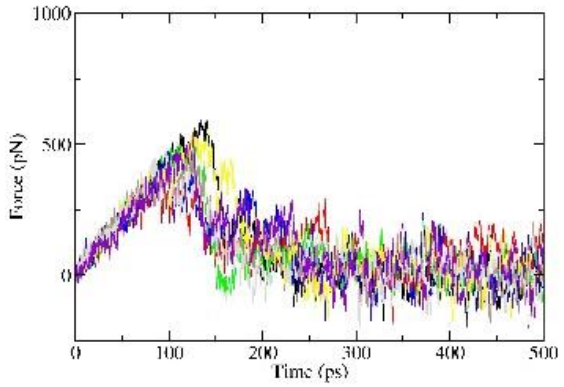
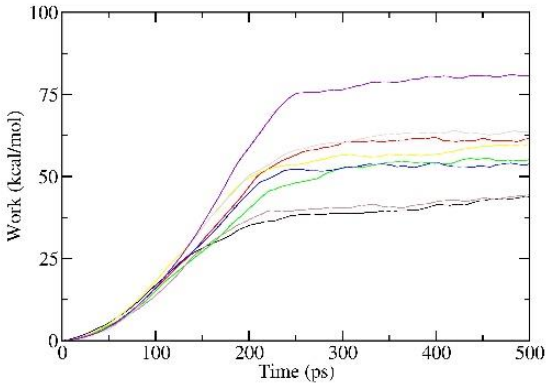
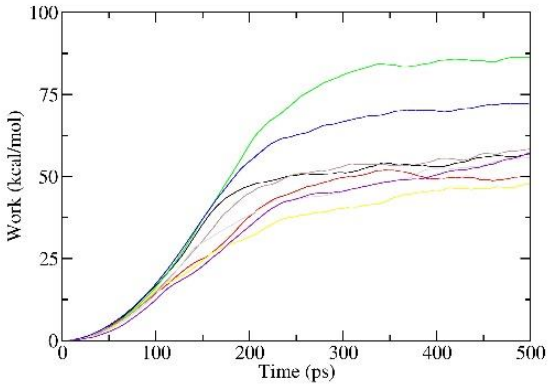
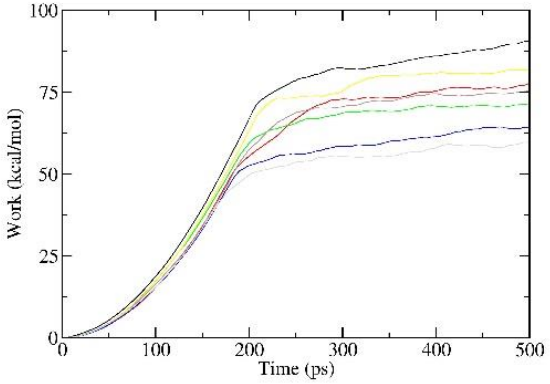
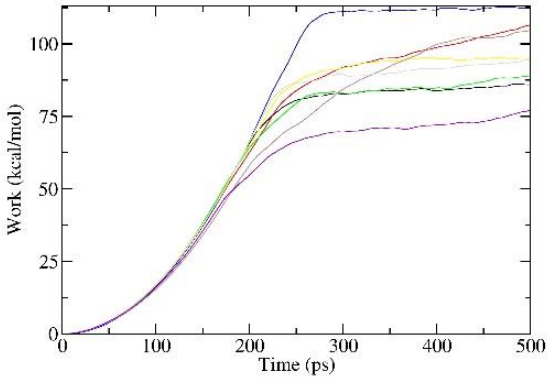
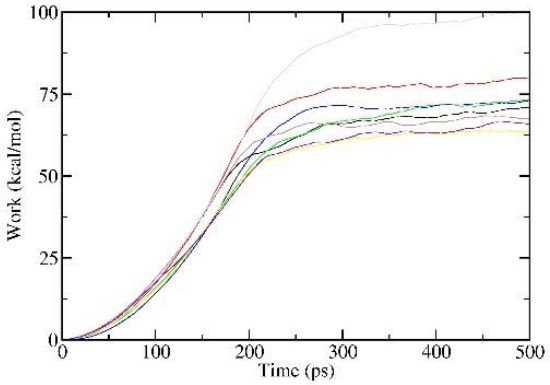
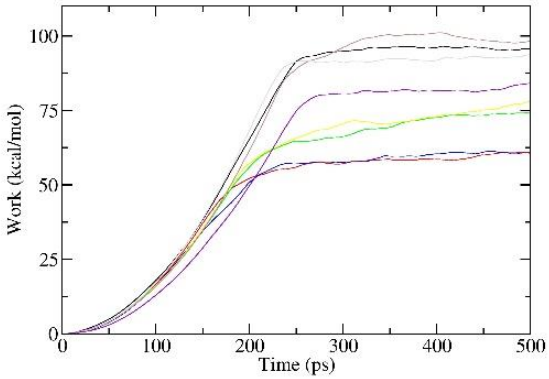
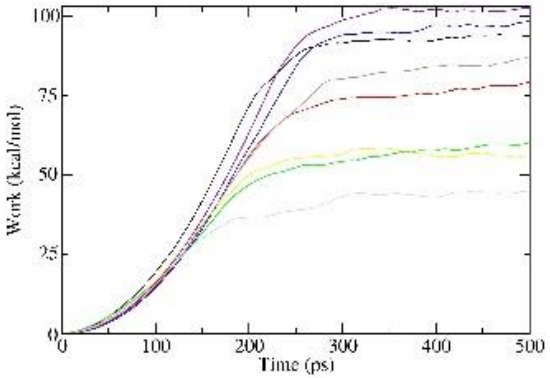
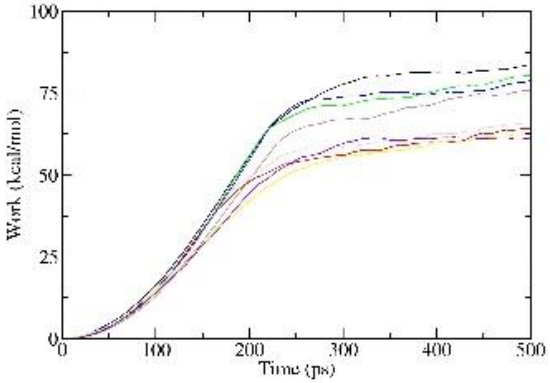
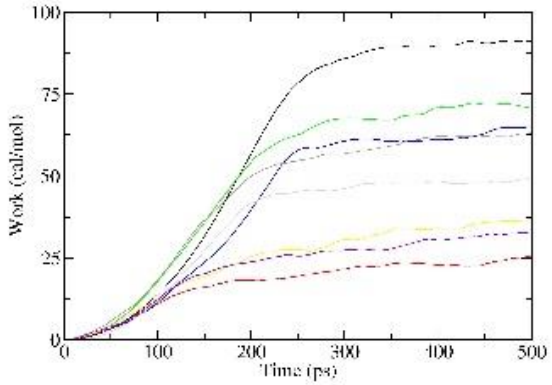
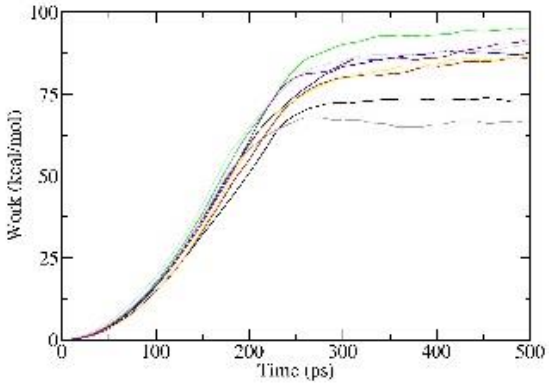
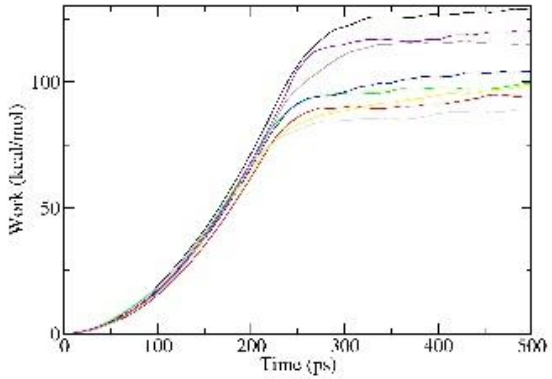
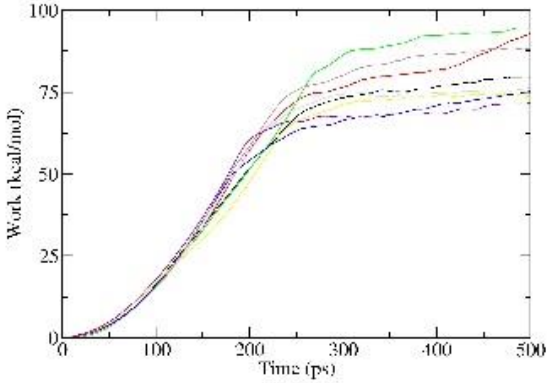
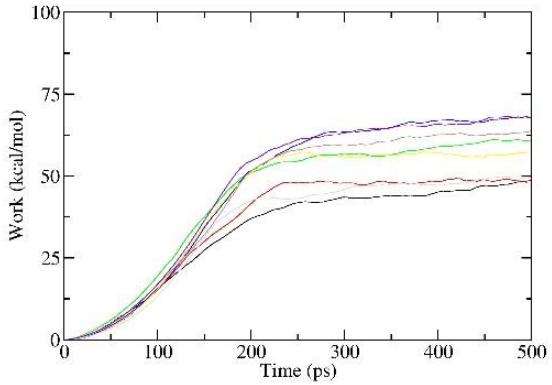
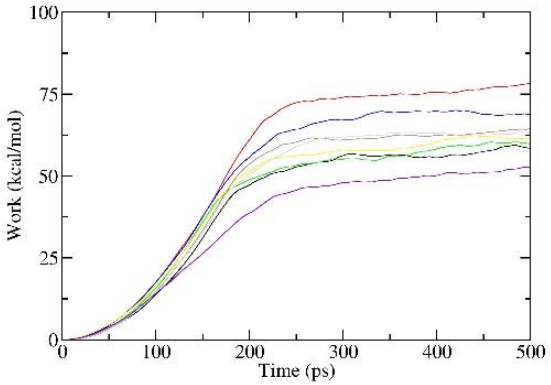
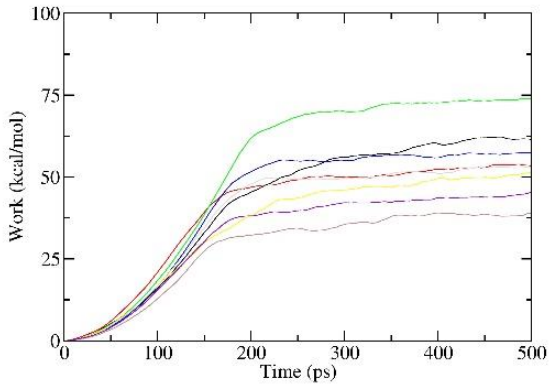
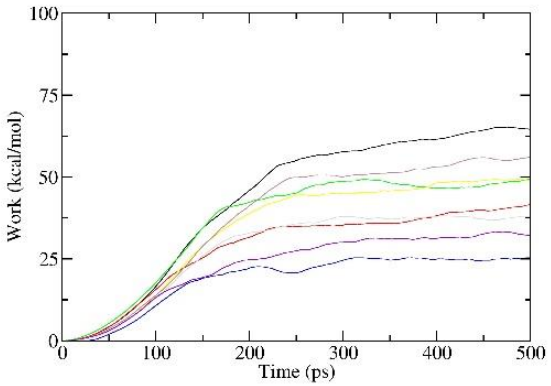
PX-12		
Shikonin		

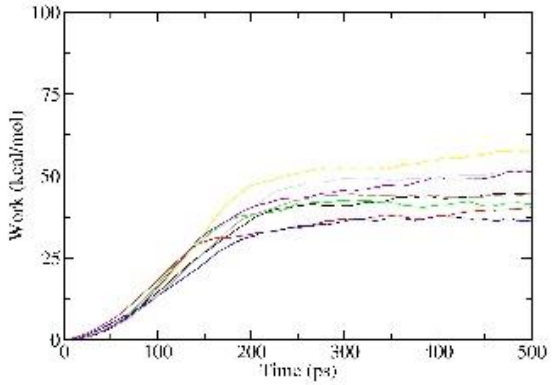
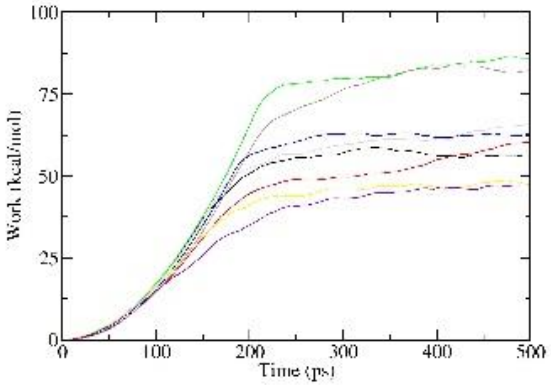
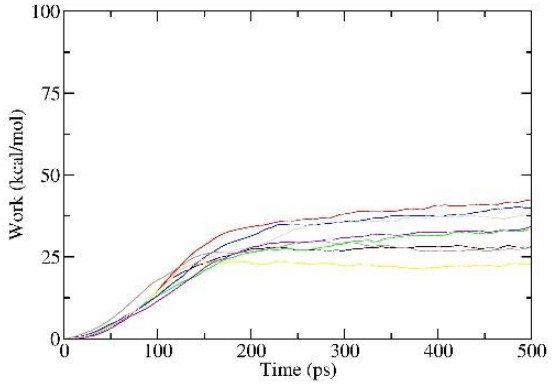
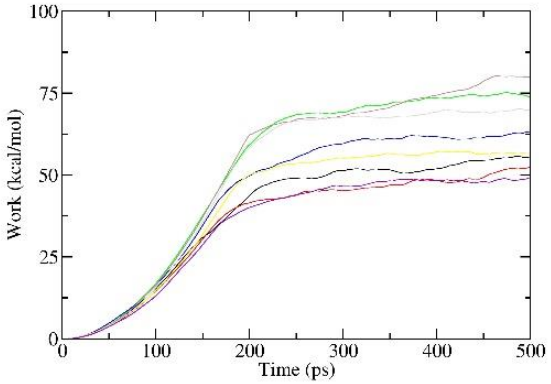
Table S3. The Pulling Work in Time Dependence over 8 Independent SMD Trajectories.

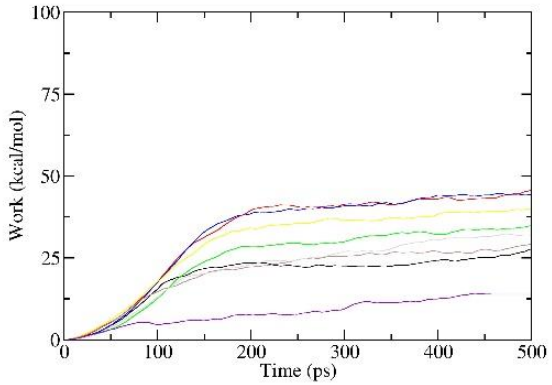
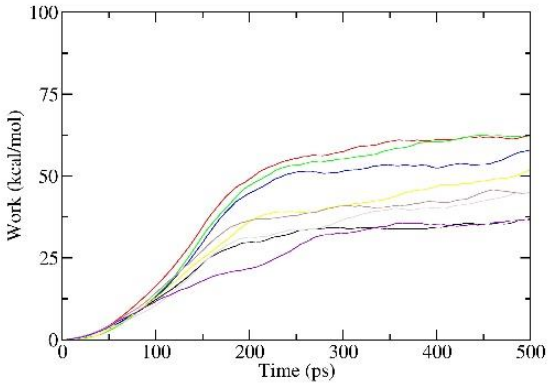
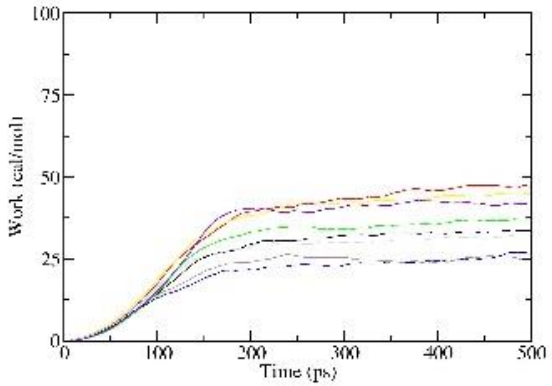
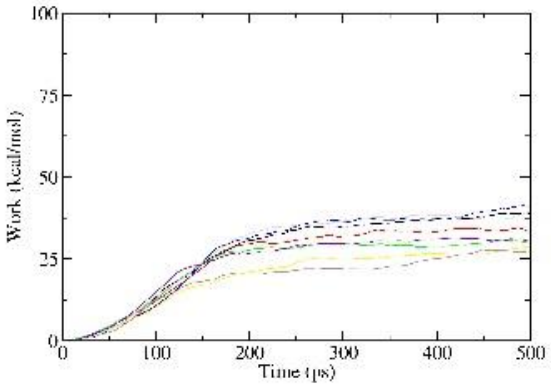
Name	Monomer	Dimer
7J		
11a		

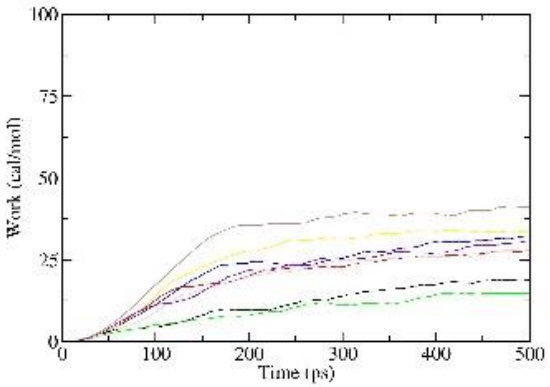
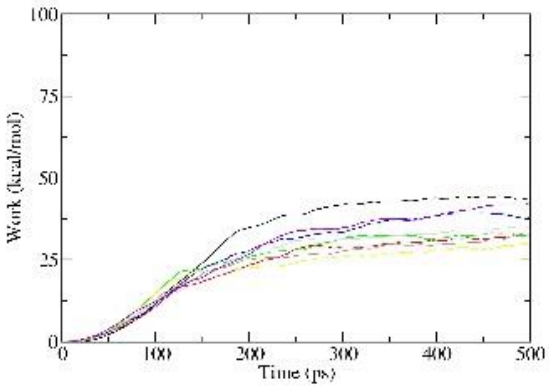
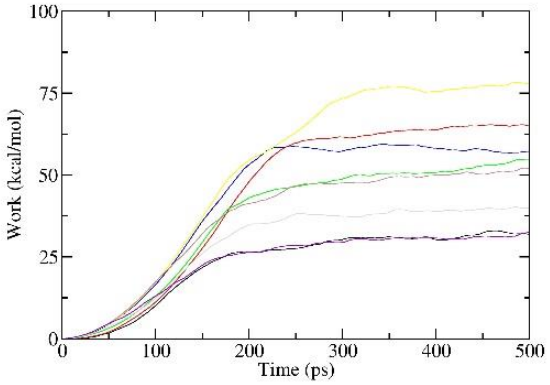
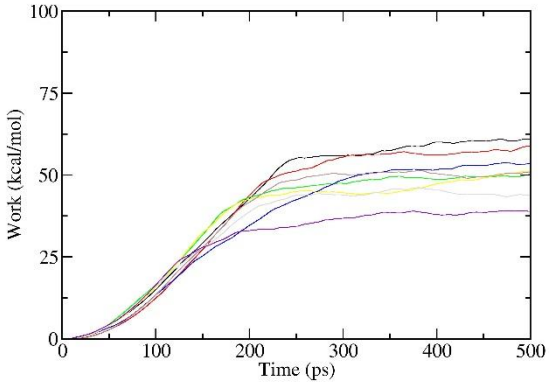
11b	 Work (kcal/mol) Time (ps)	 Work (kcal/mol) Time (ps)
11r	 Work (kcal/mol) Time (ps)	 Work (kcal/mol) Time (ps)

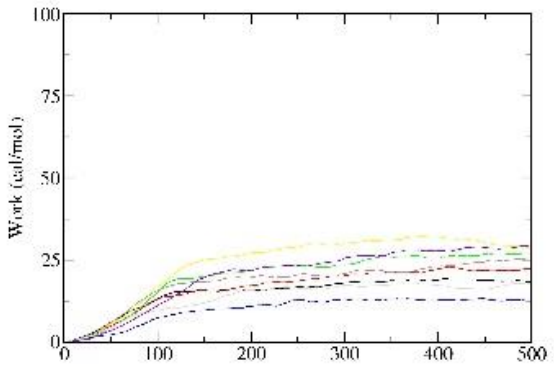
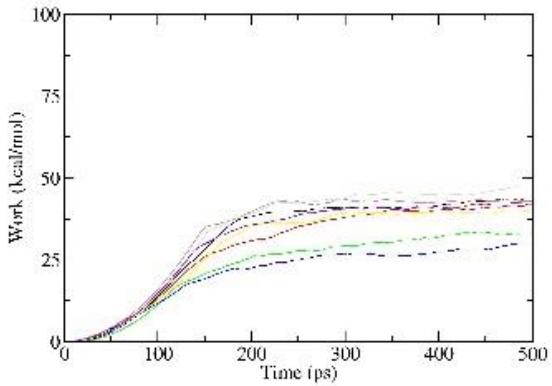
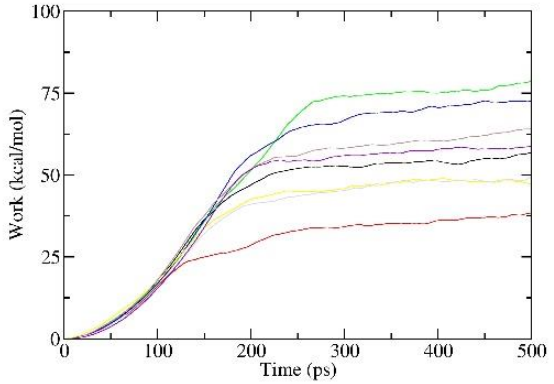
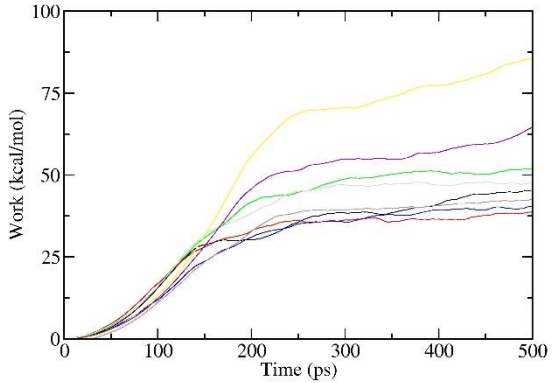
13a	 Work (cal/mol) Time (ps)	 Work (kcal/mol) Time (ps)
13b	 Work (kcal/mol) Time (ps)	 Work (kcal/mol) Time (ps)

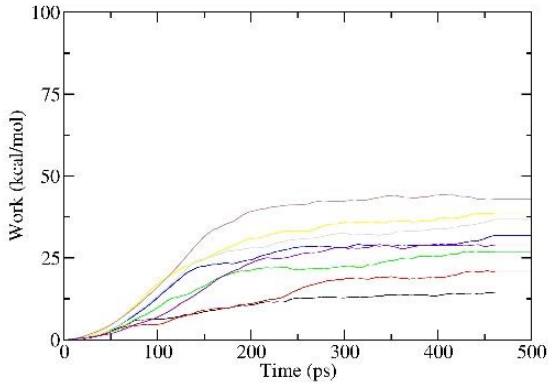
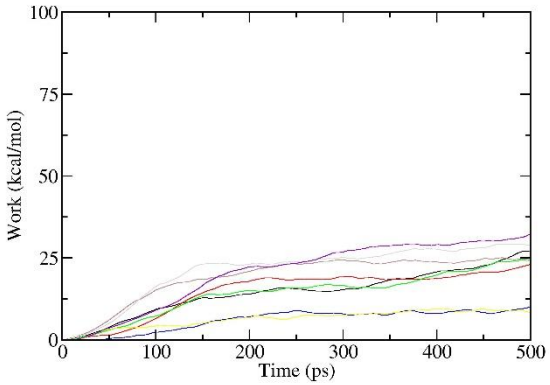
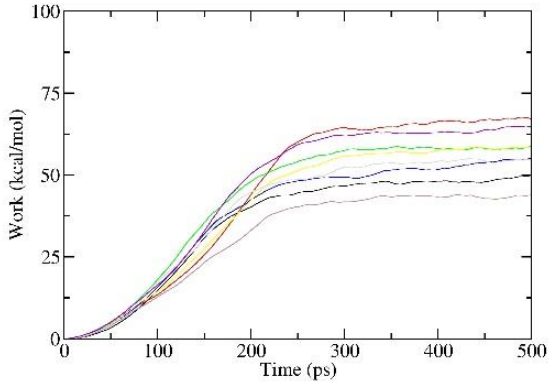
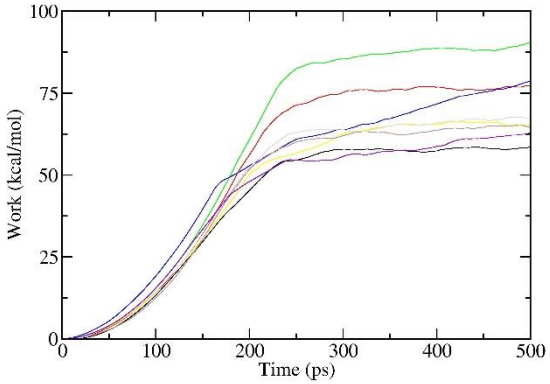
Calpain inhibitor I		
Calpain inhibitor II		

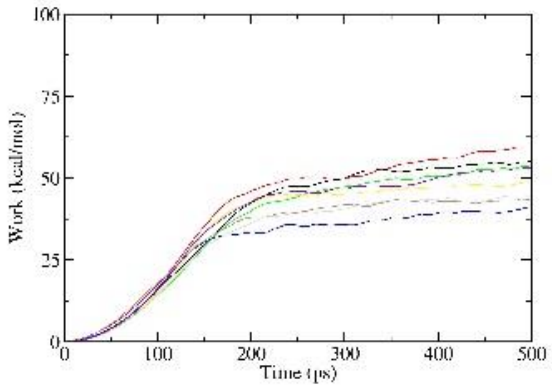
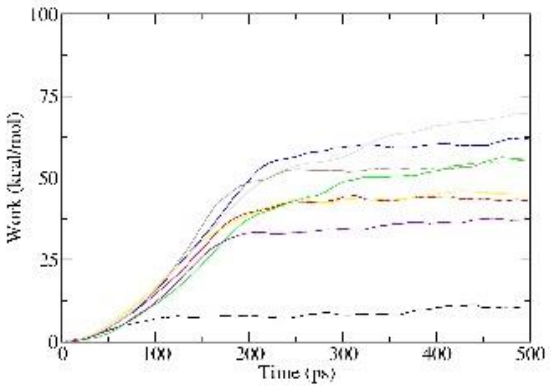
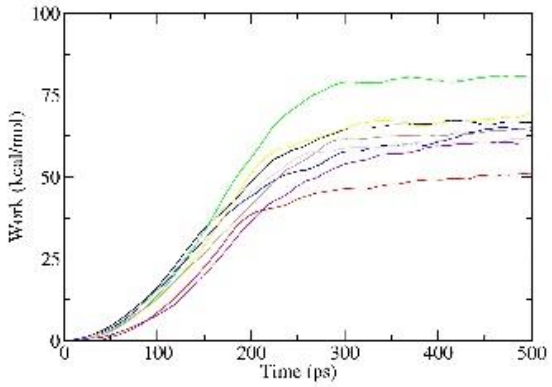
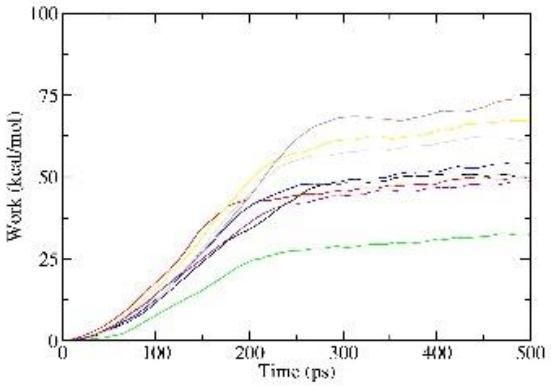
Calpain inhibitor XII		
Calpeptin		

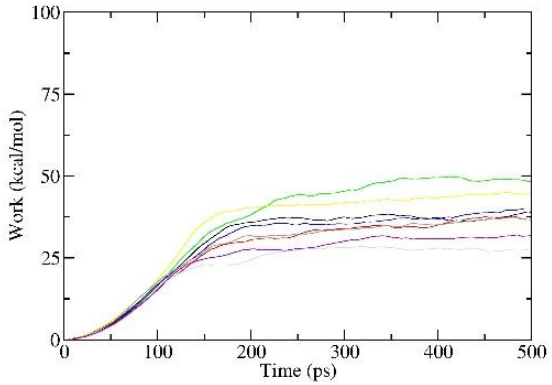
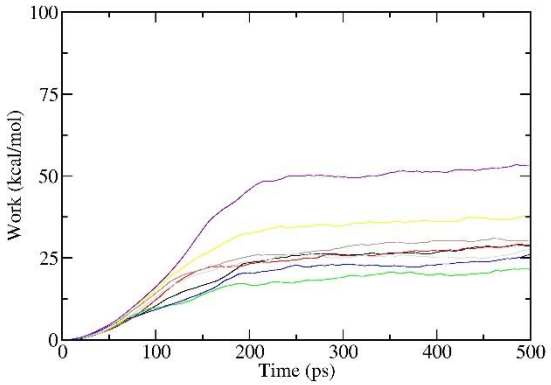
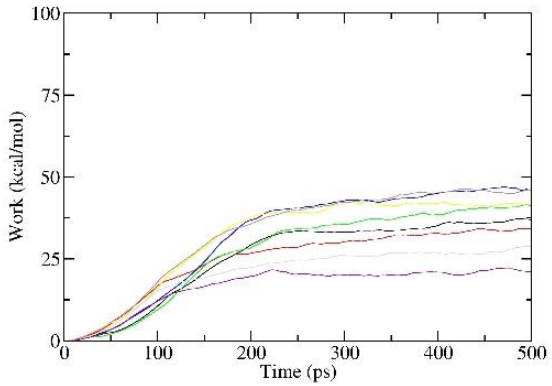
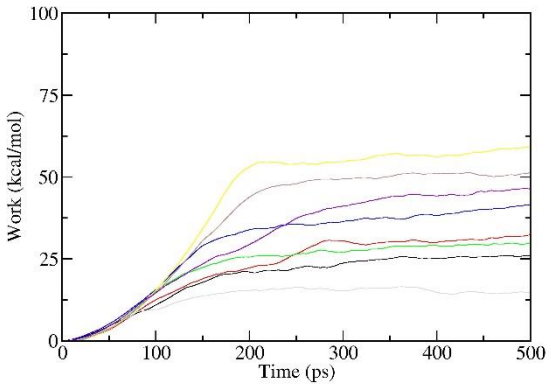
Candesartan cilexetil		
Carmofur		

Chloroquine		
Dipyradimole		

Disulfiram		
GC-373		

Hydroxychloroquine		
MG-115		

MG-132		
Narlaprevir		

Omeprazole		
Oxytetracycline		

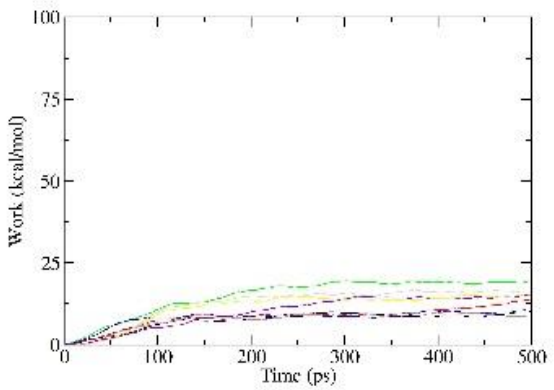
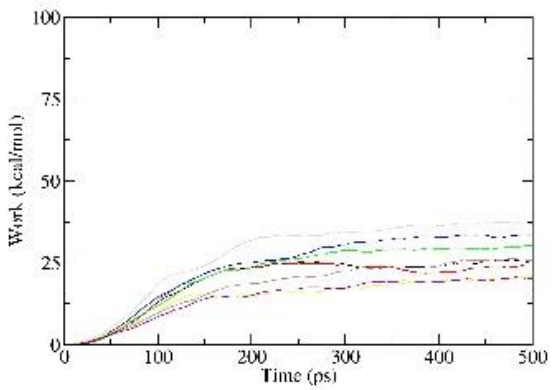
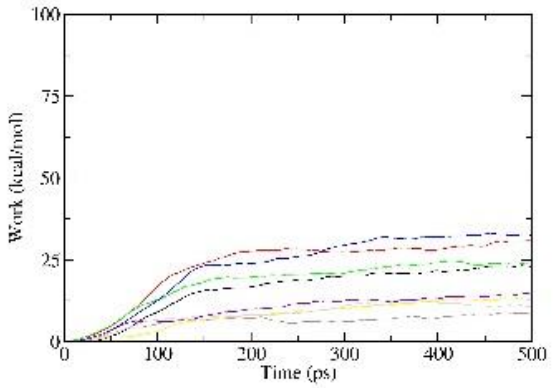
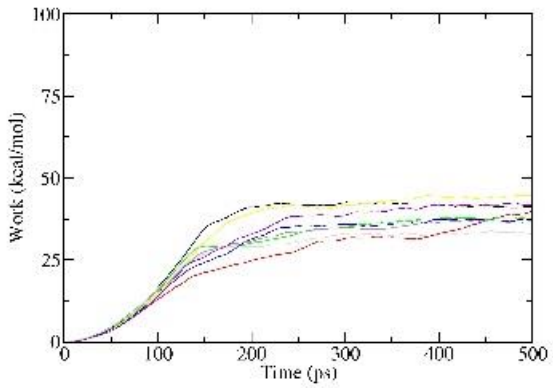
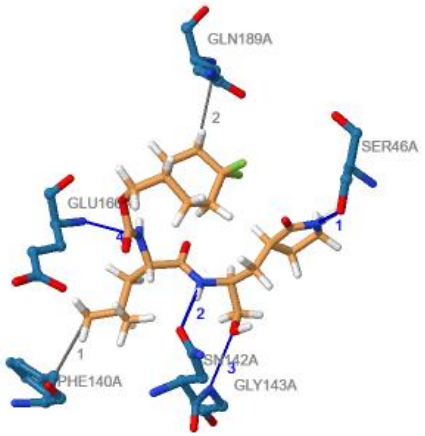
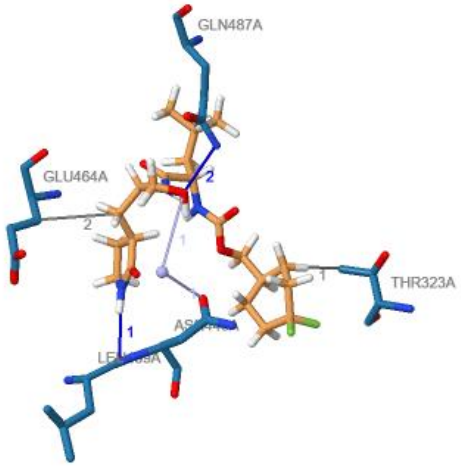
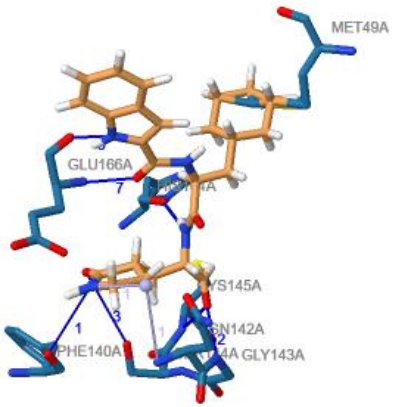
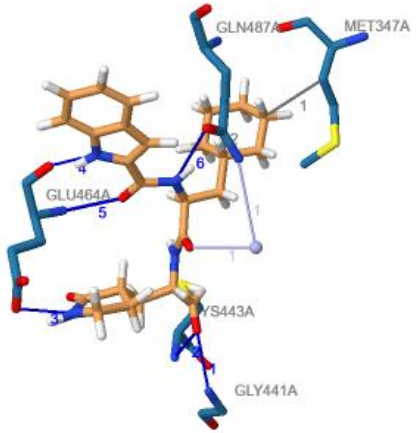
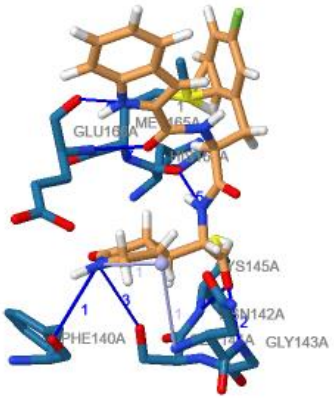
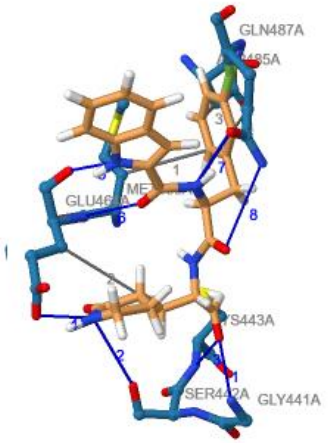
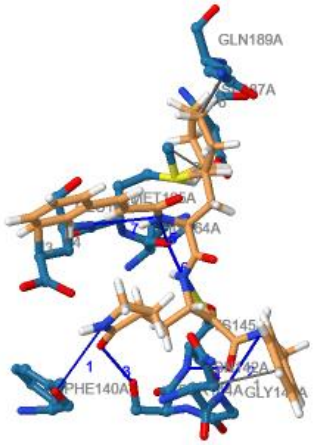
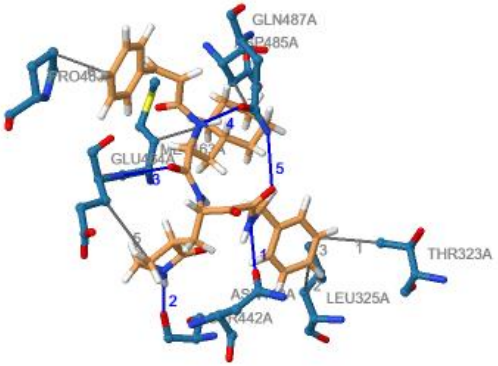
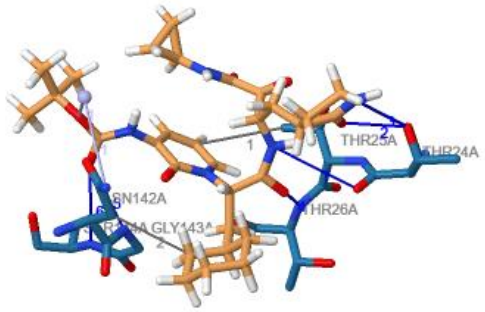
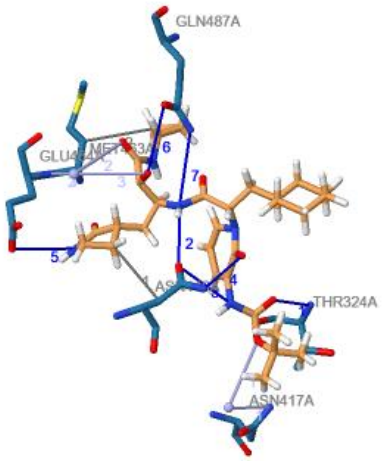
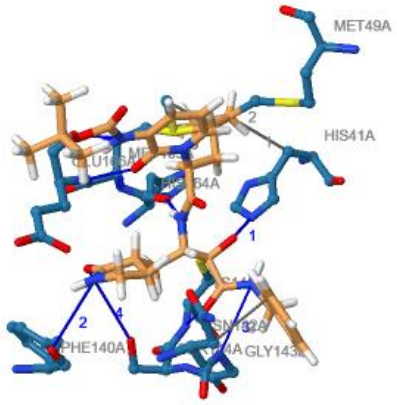
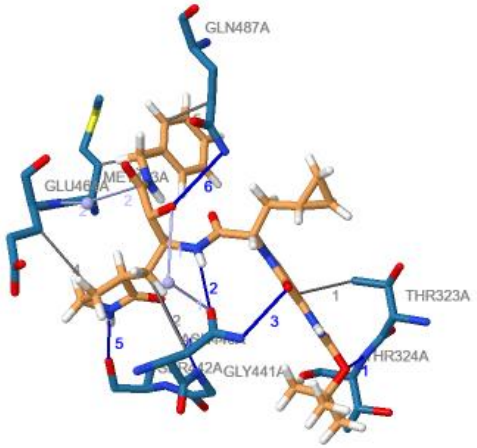
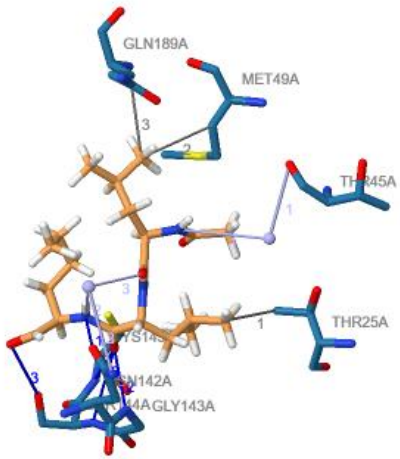
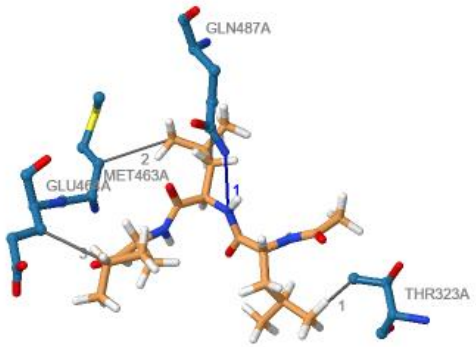
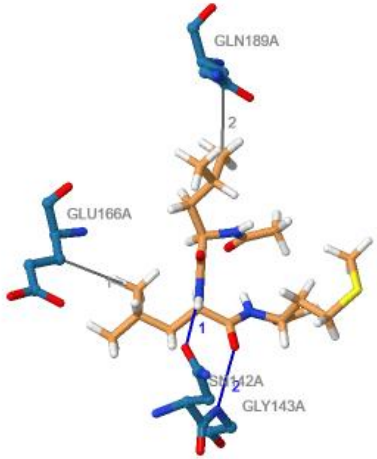
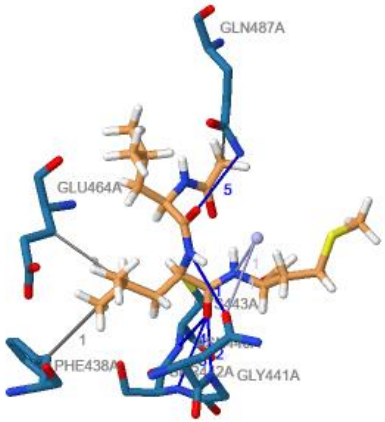
PX-12		
Shikonin		

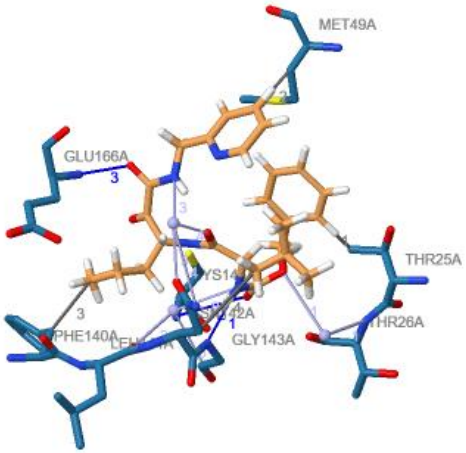
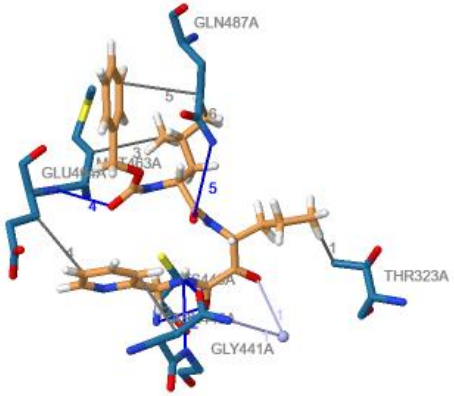
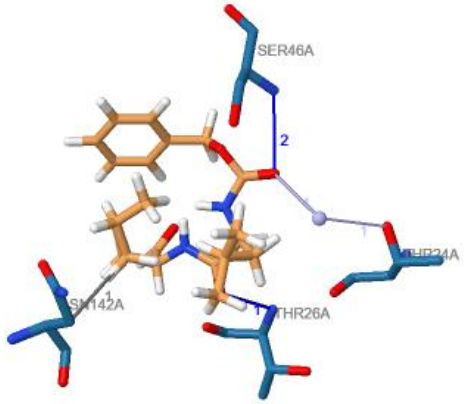
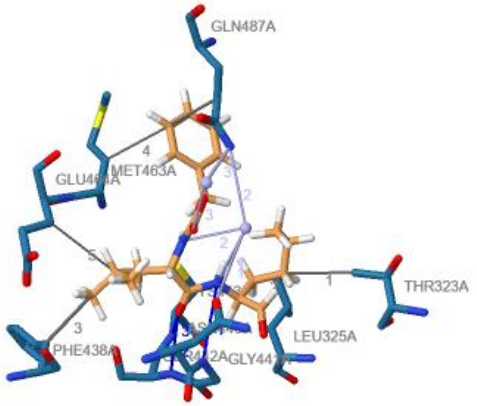
Table S4. Interaction diagram between inhibitors and SARS-CoV-2 Mpro via PLIP protocol.[1]

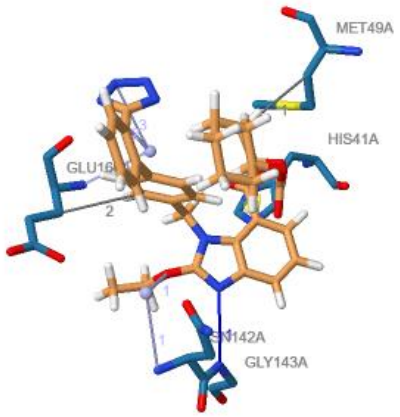
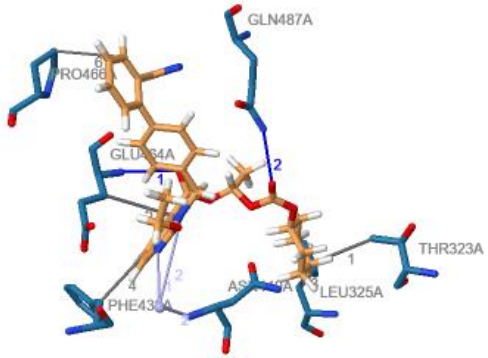
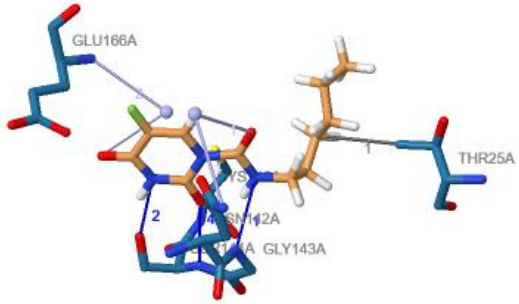
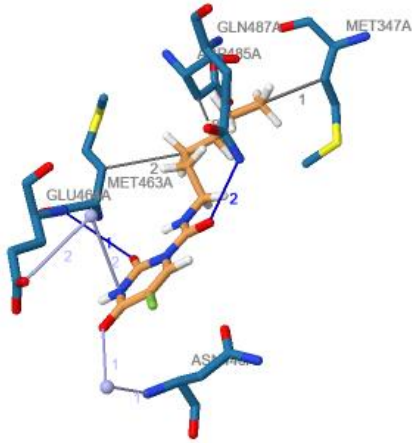
Name	Monomer	Dimer
7J		
11a		

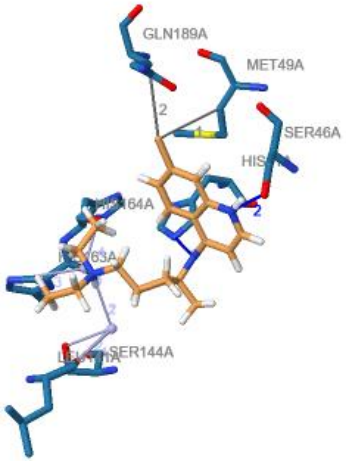
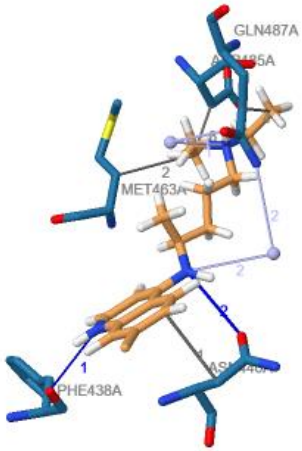
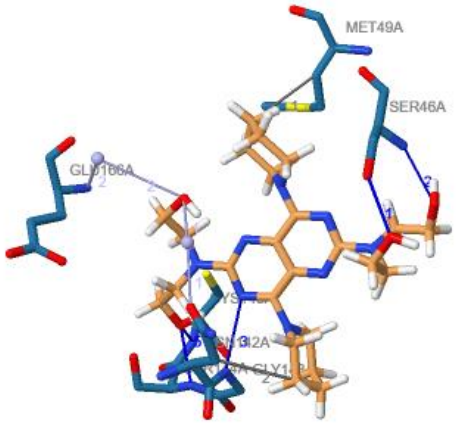
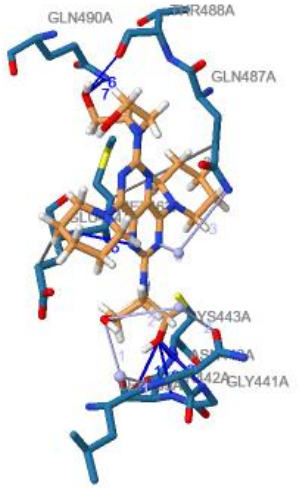
11b		
11r		

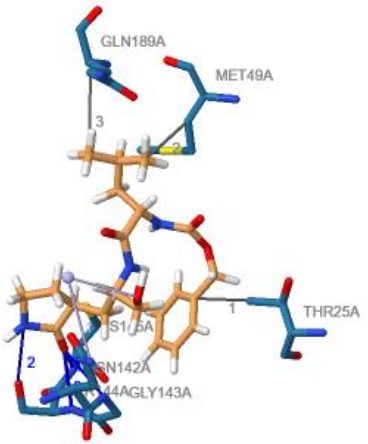
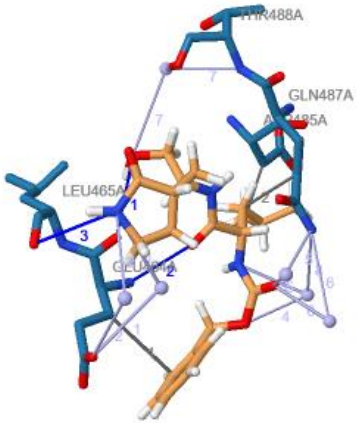
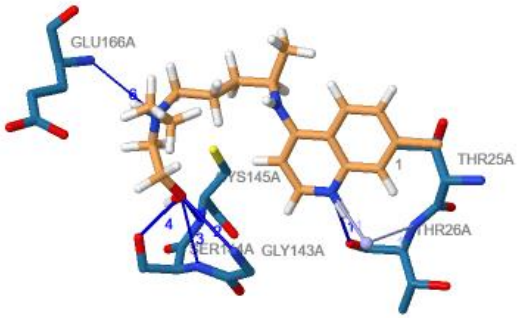
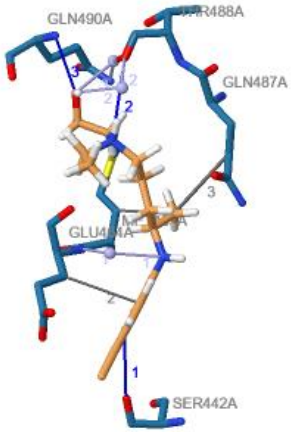
13a	 THR25A THR24A ASN142A THR26A GLY143A	 GLN487A THR324A ASN417A
13b	 MET49A HIS41A PHE140A GLY143A	 GLN487A THR323A THR324A GLY441A

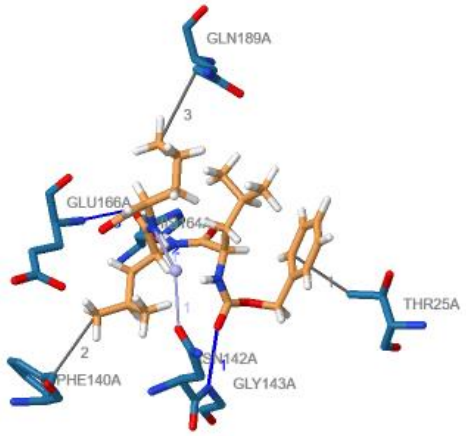
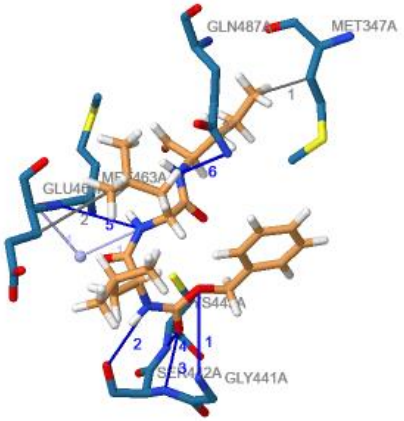
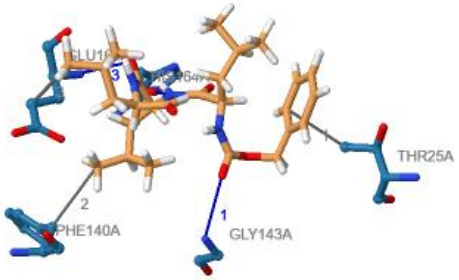
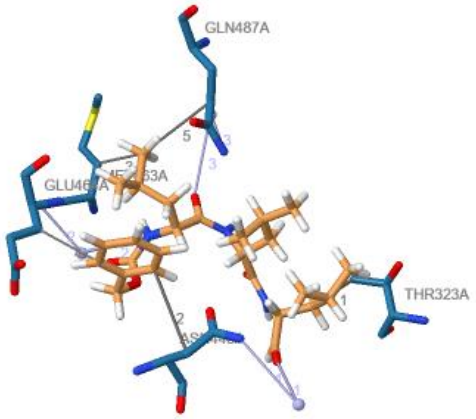
Calpain inhibitor I		
Calpain inhibitor II		

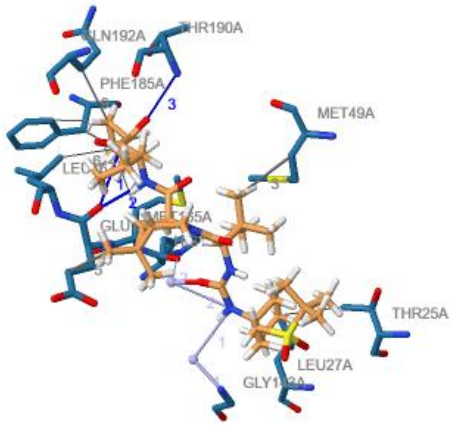
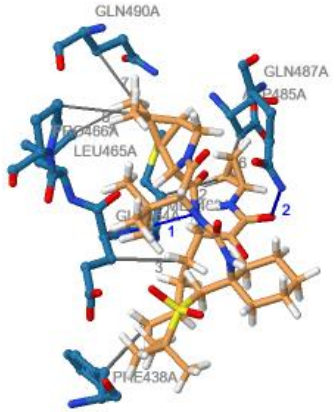
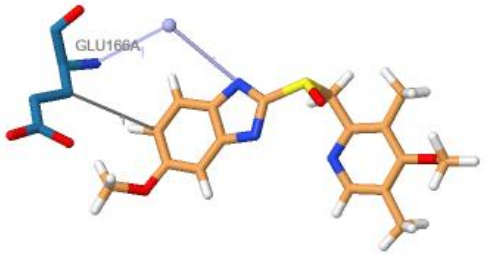
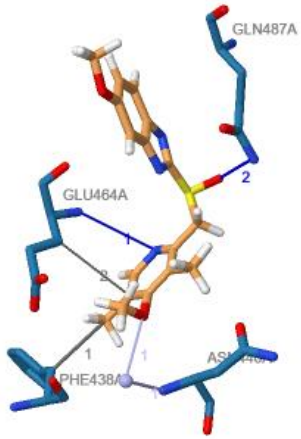
Calpain inhibitor XII		
Calpeptin		

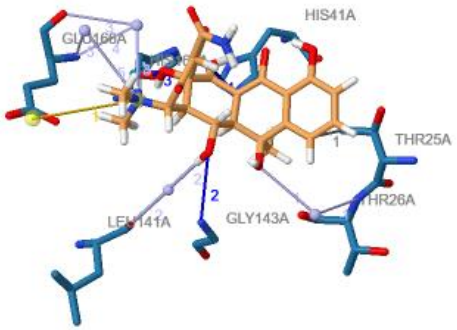
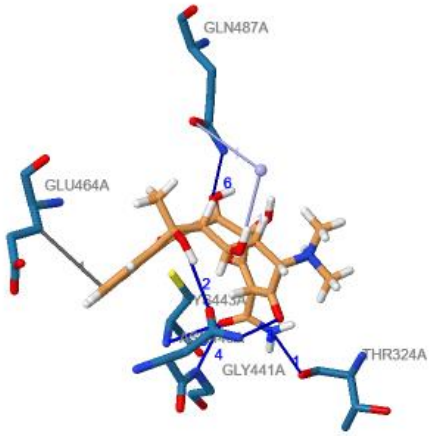
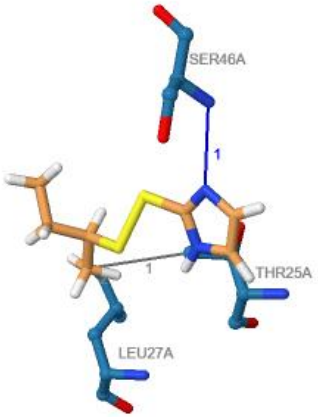
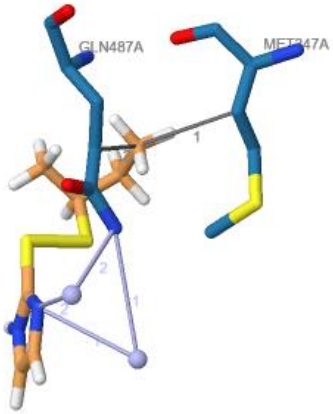
Candesartan cilexetil		
Carmofur		

Chloroquine		
Dipyridamole		
Disulfiram	N/A	N/A

GC-373		
Hydroxychloroquine		

MG-115	 GLN189A GLU166A THR25A PHE140A GLY143A	 GLN487A MET347A GLY441A
MG-132	 THR25A PHE140A GLY143A	 GLN487A THR323A

Narlaprevir		
Omeprazole		

Oxytetracycline		
PX-12		

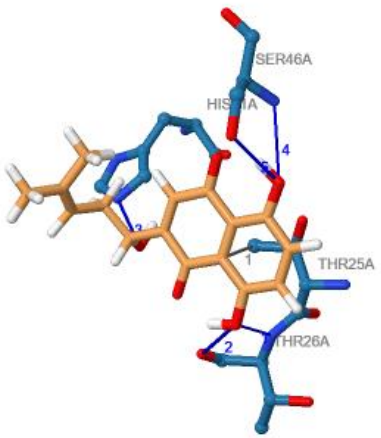
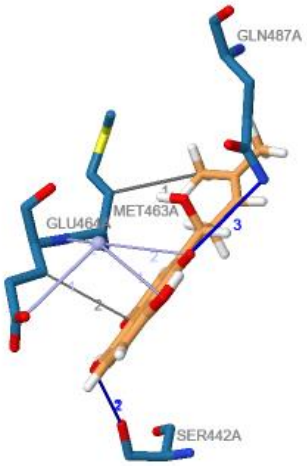
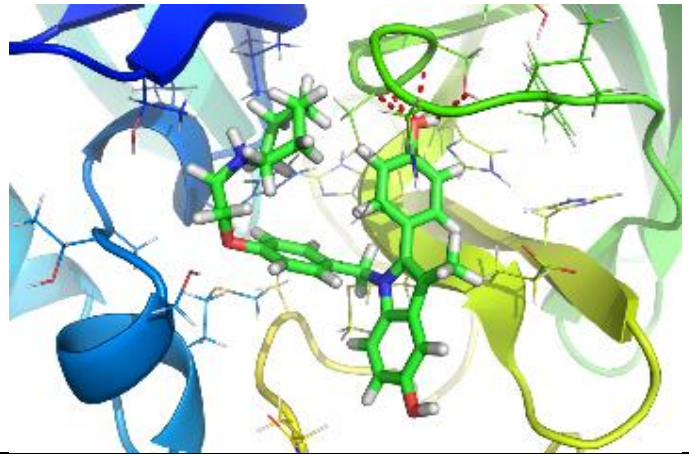
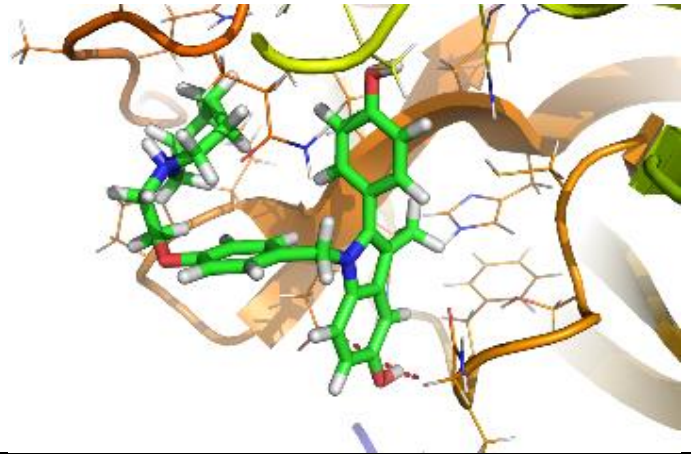
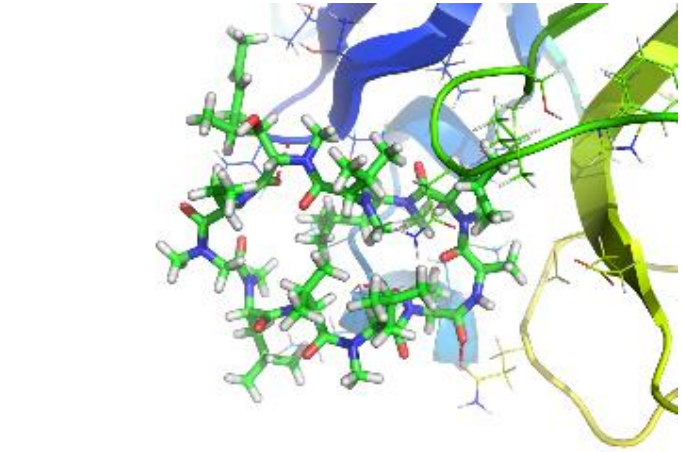
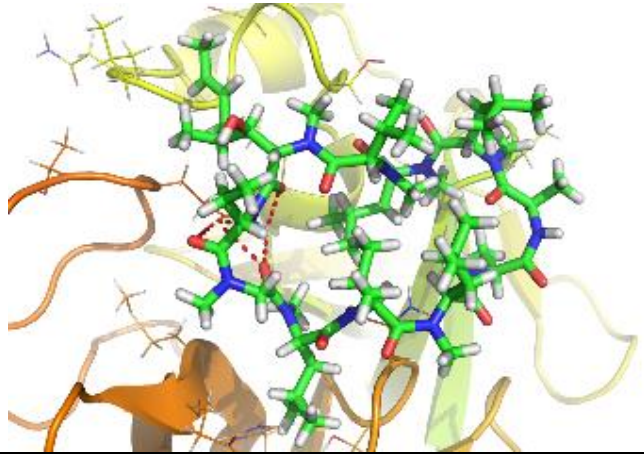
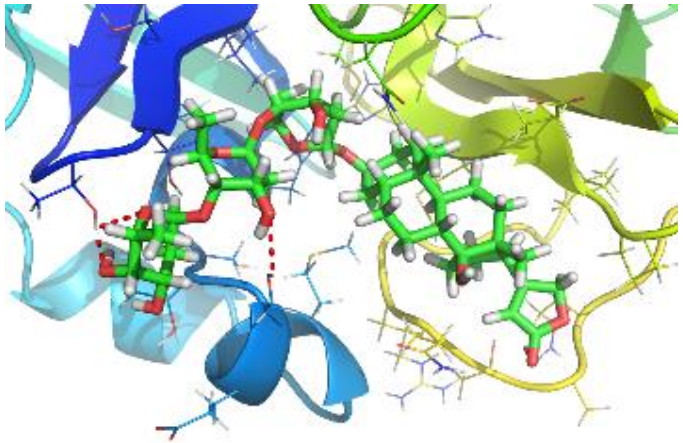
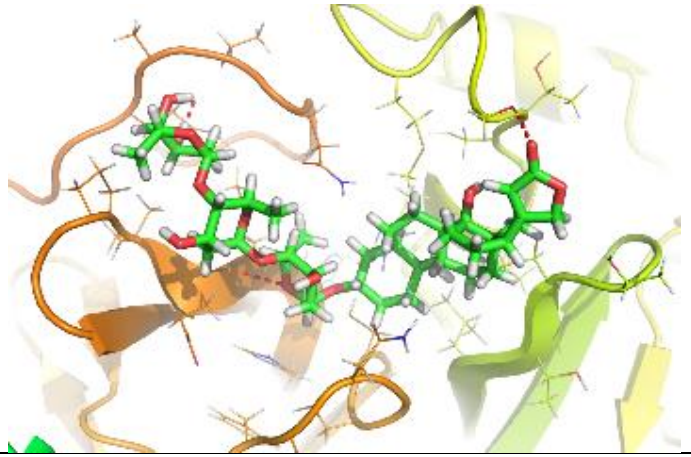
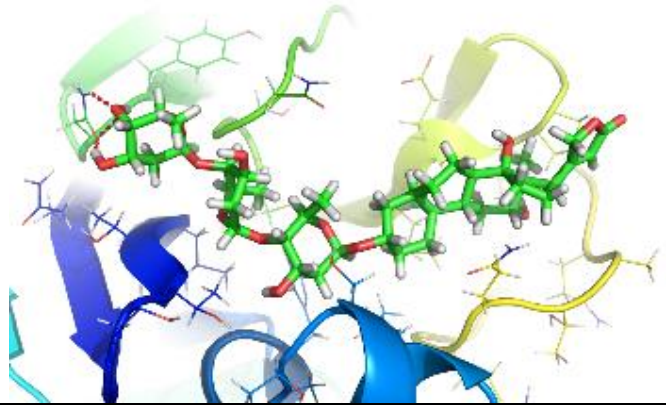
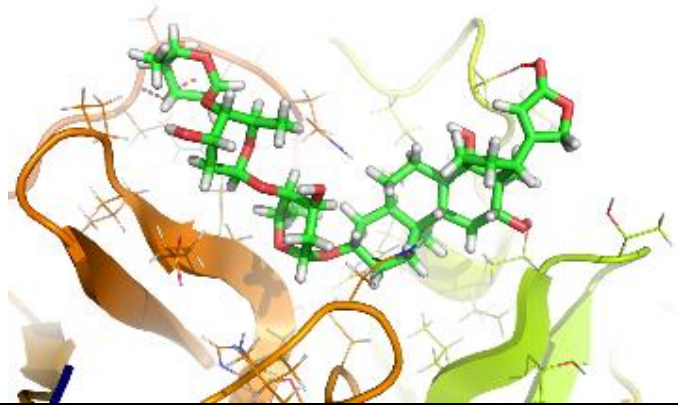
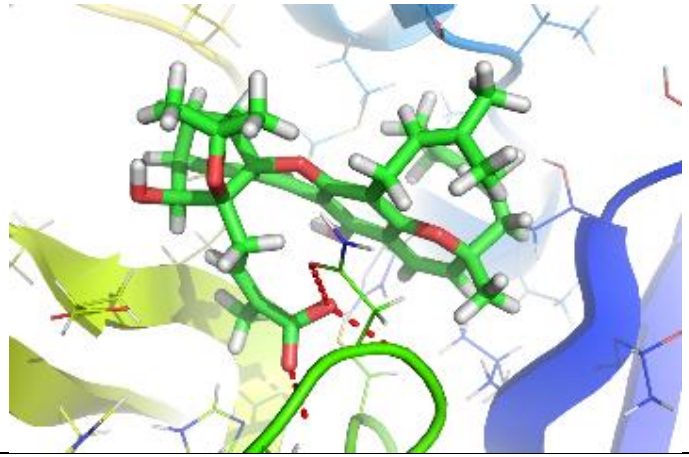
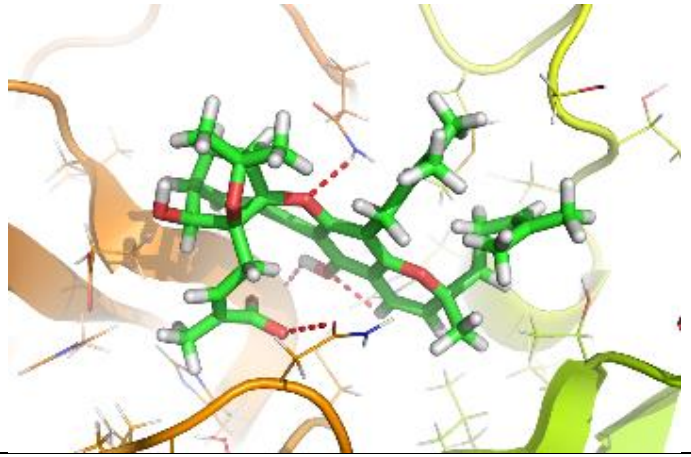
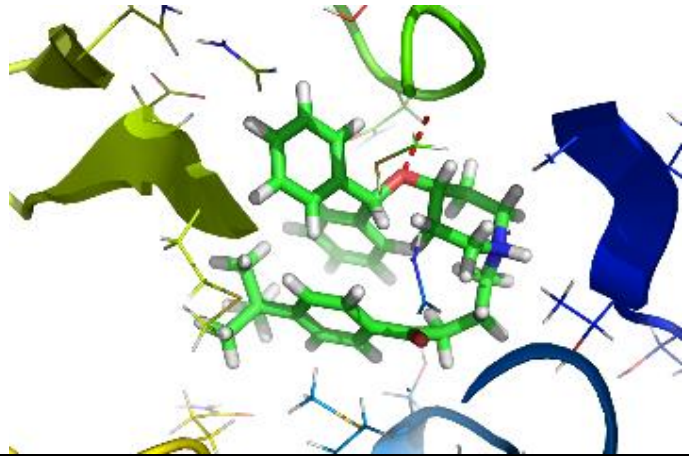
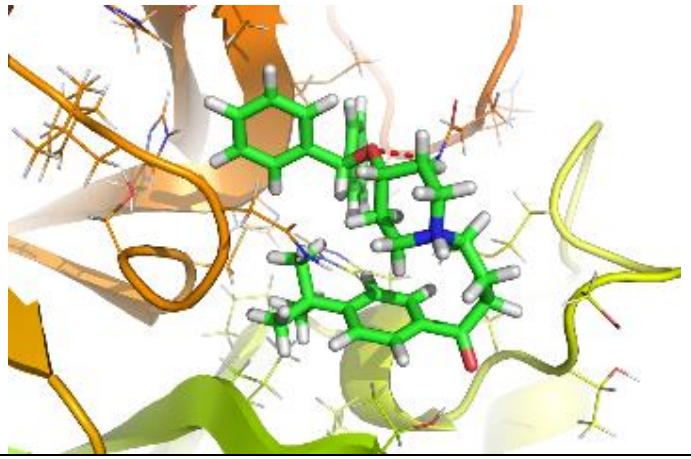
Shikonin		

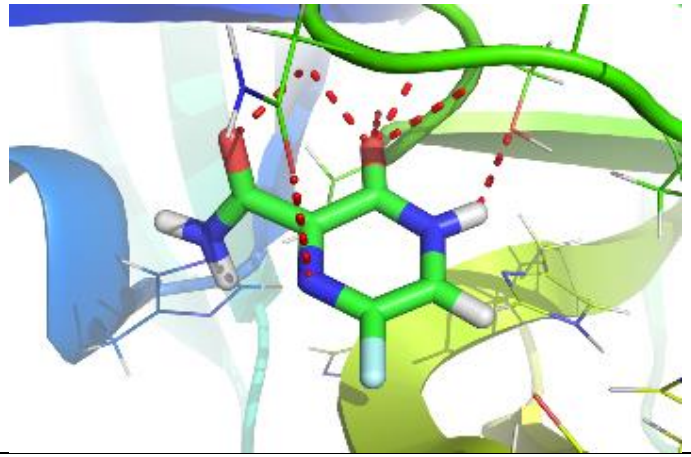
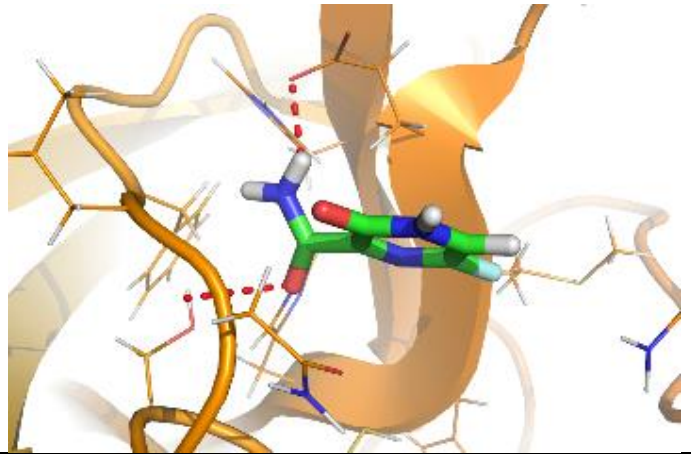
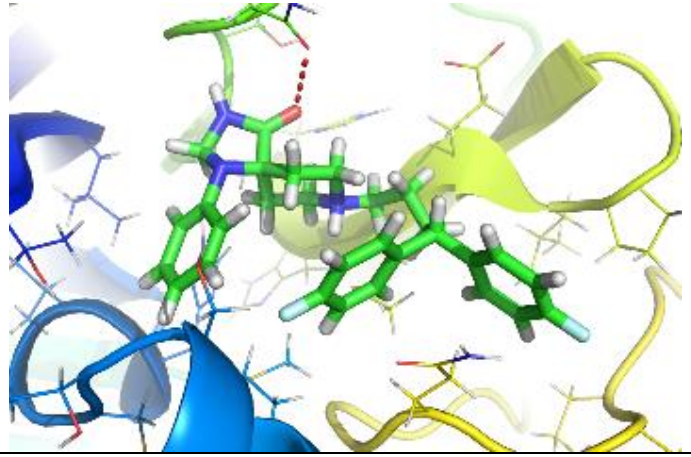
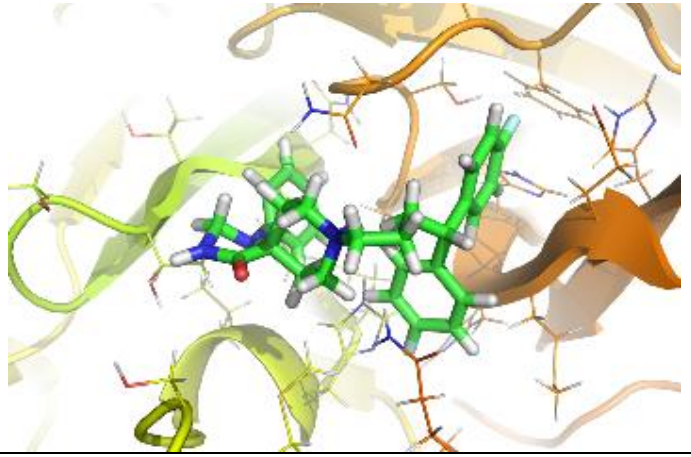
Table S5. The binding pose of other inhibitors to SARS-CoV-2 Mpro.

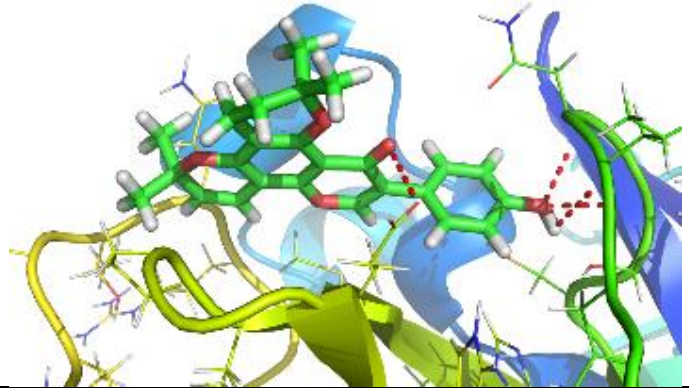
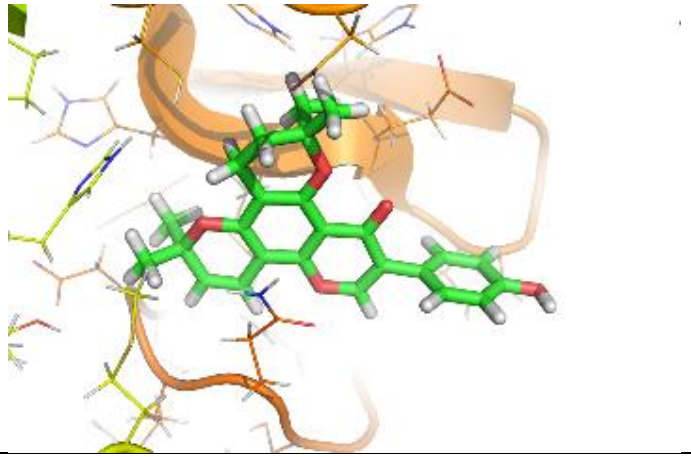
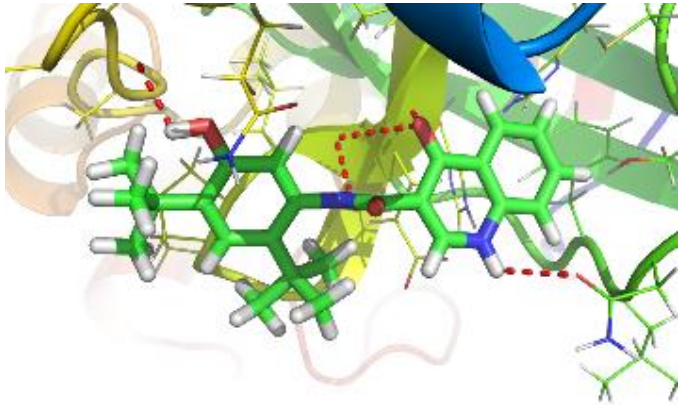
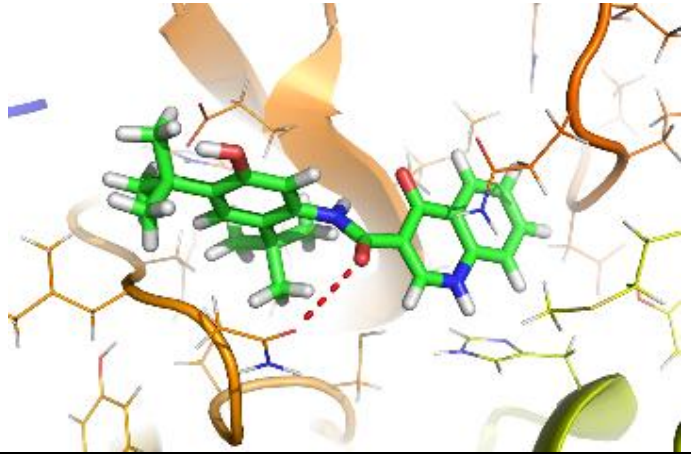
Name	Monomer	Dimer

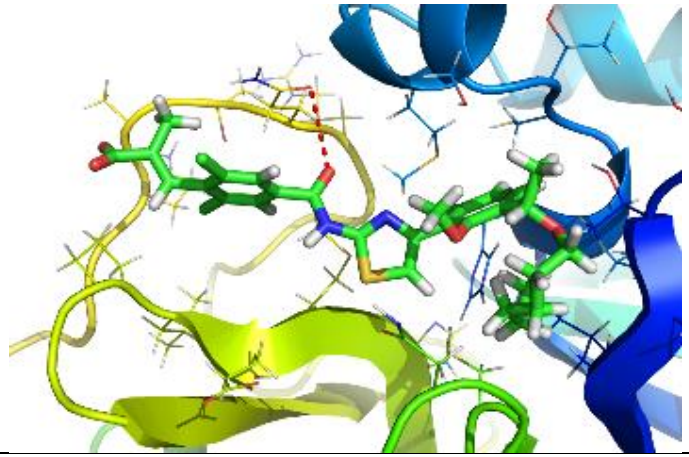
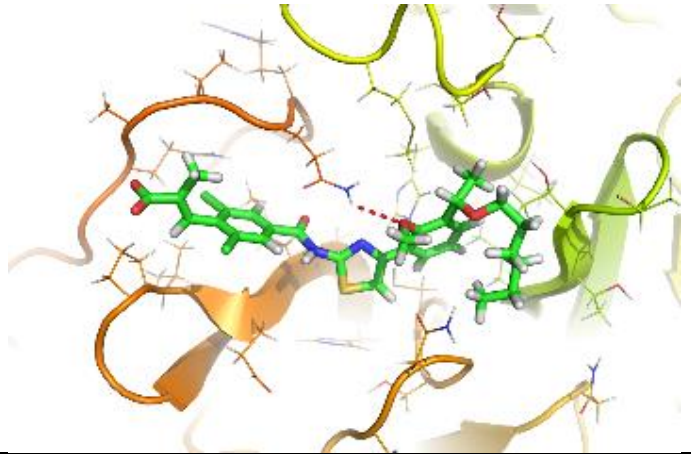
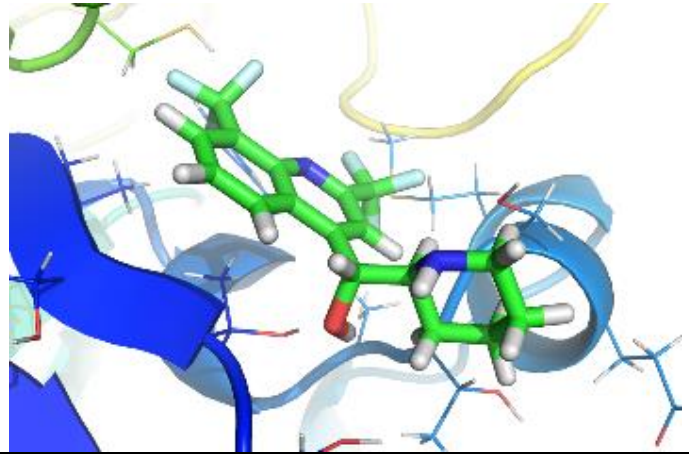
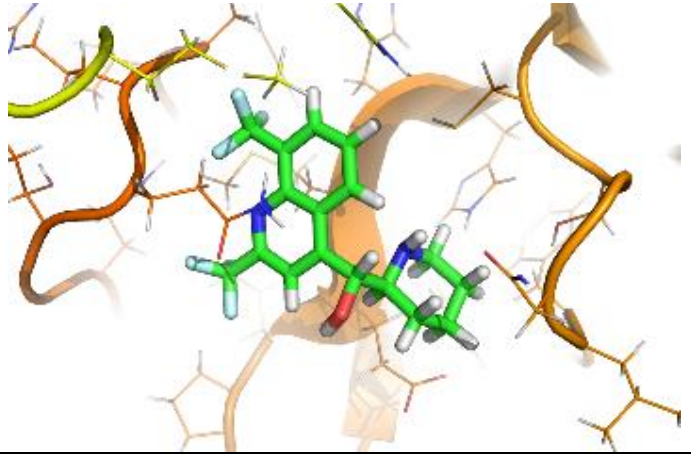
Bazedoxifene		
Cyclosporine		

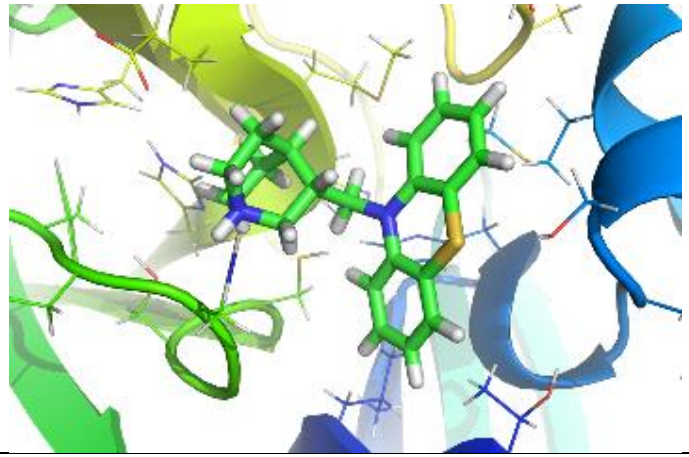
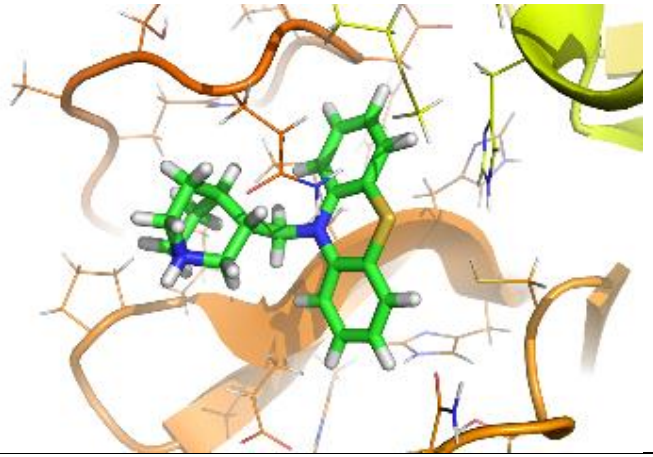
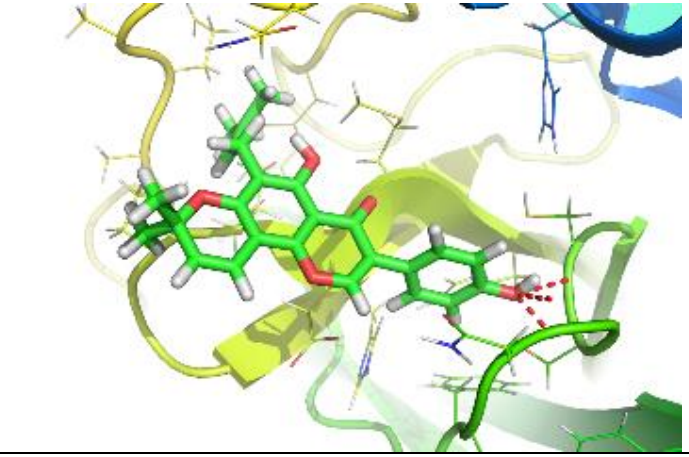
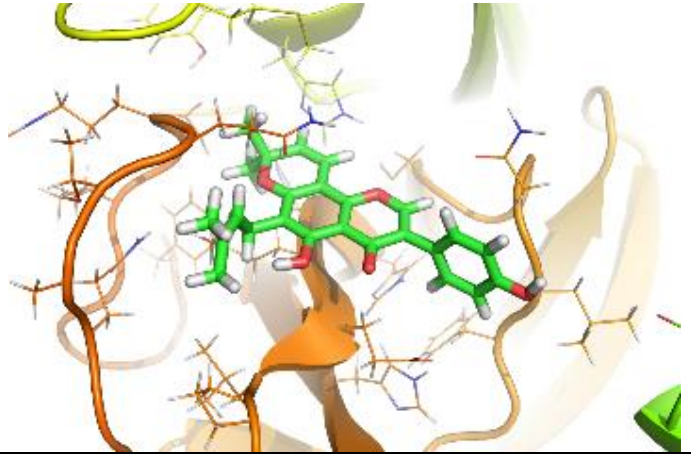
Digitoxin		
Digoxin		

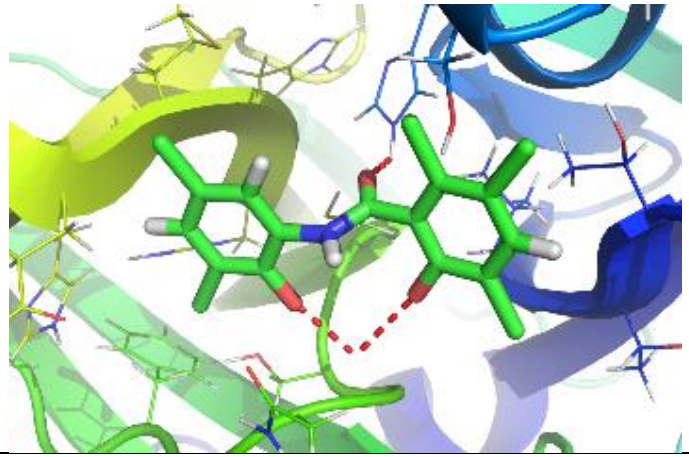
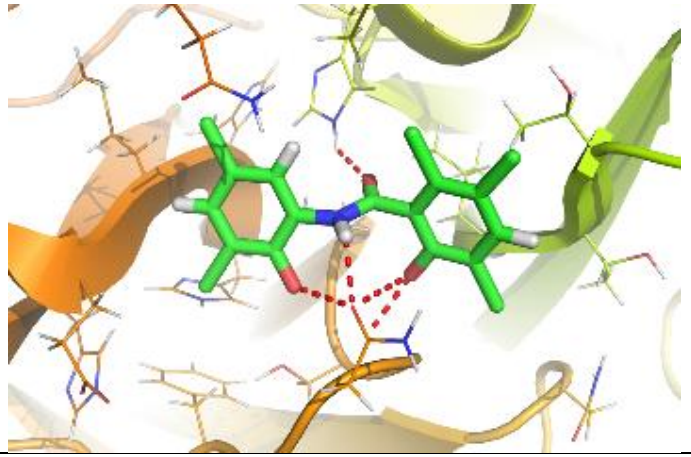
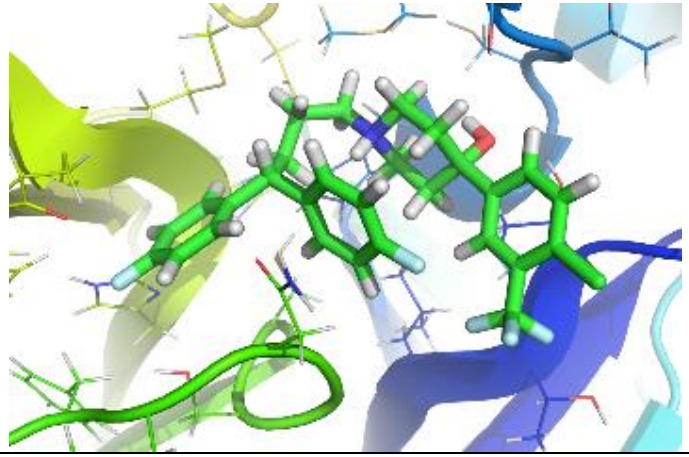
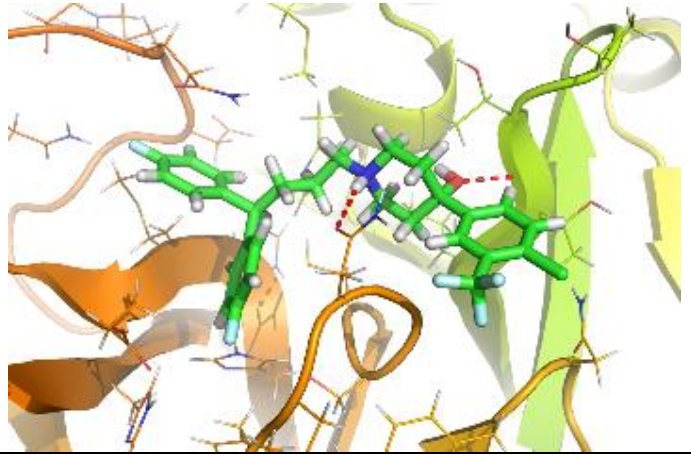
Dihydrogambogic Acid		
Ebastine		

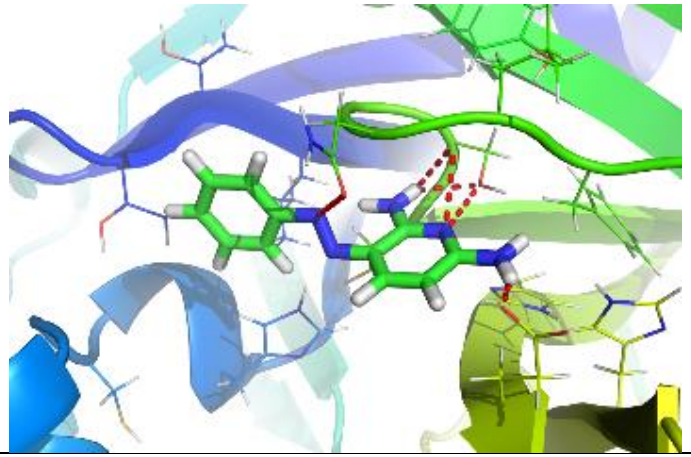
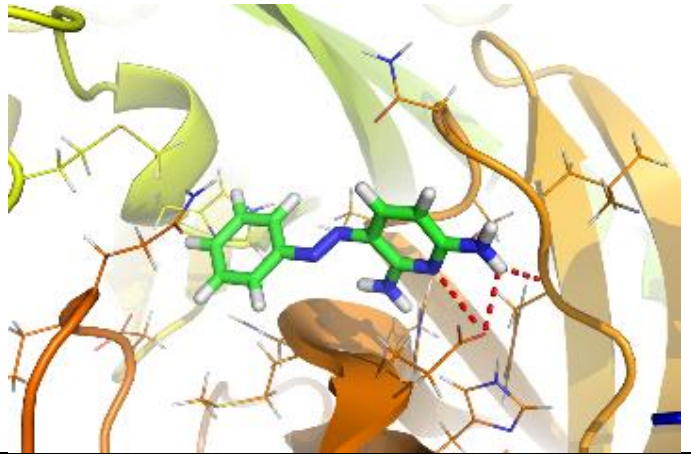
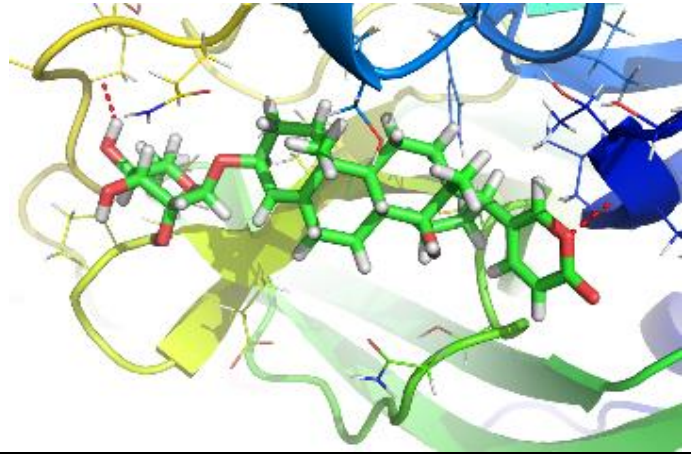
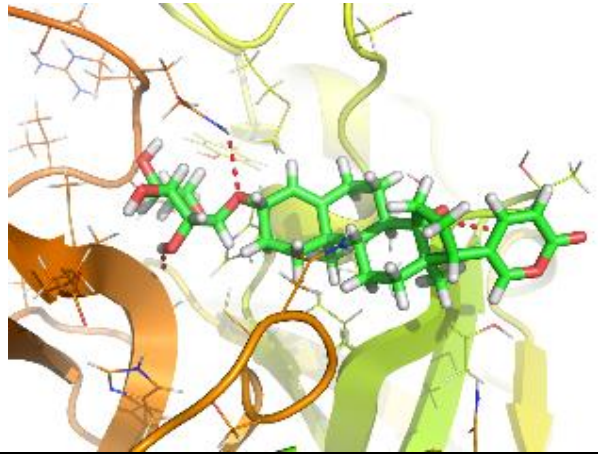
Favipiravir		
Fluspirilene		

Isoosajin		
Ivacaftor		

Lusutrombopag		
Mefloquine		

Mequitazine		
Osajin		

Oxyclozanide		
Penfluridol		

Phenazopyridine		
Proscillaridin		

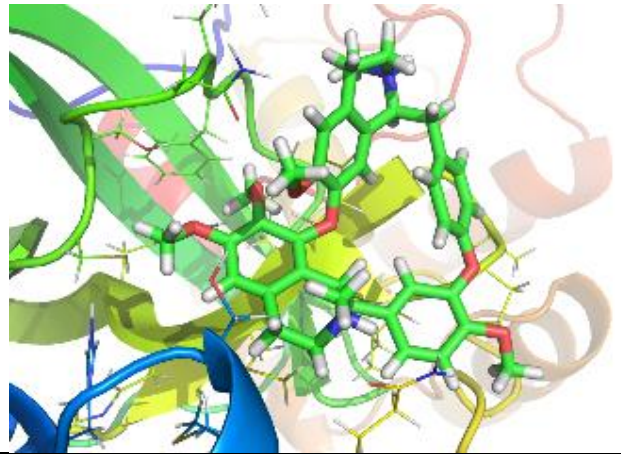
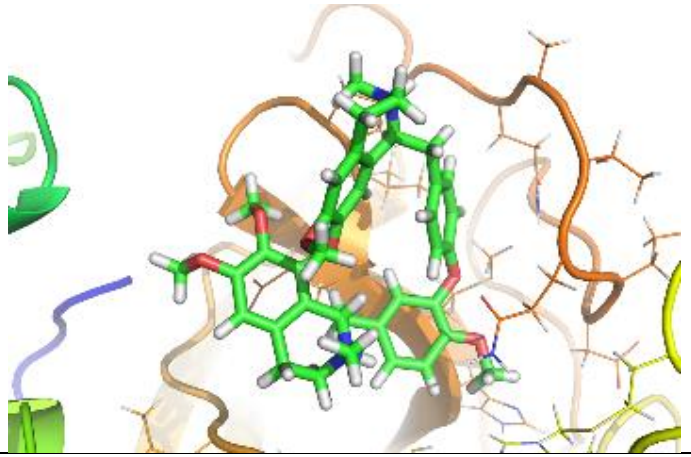
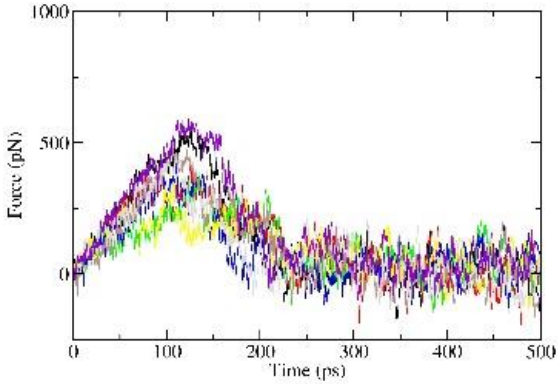
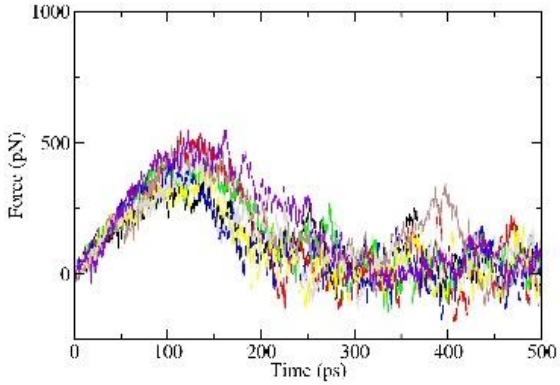
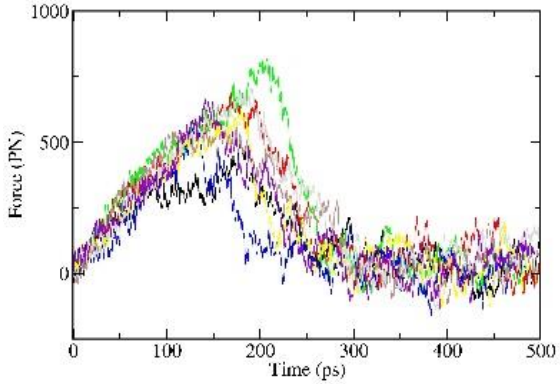
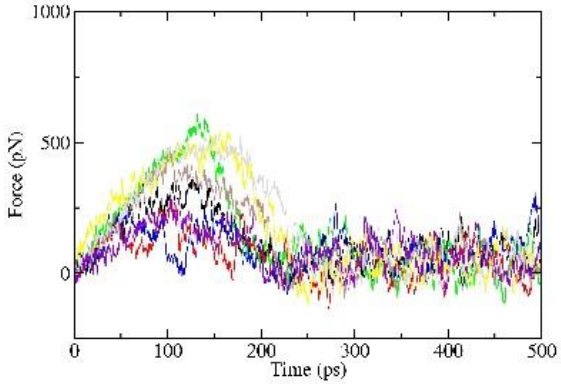
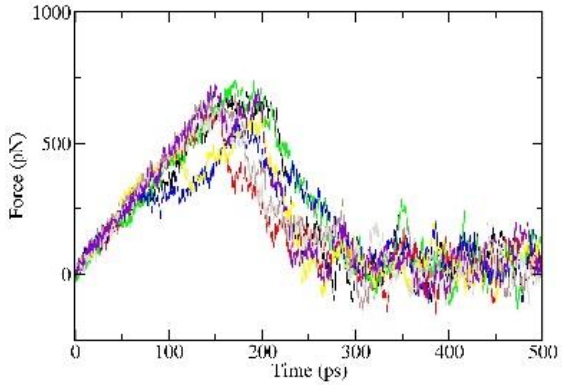
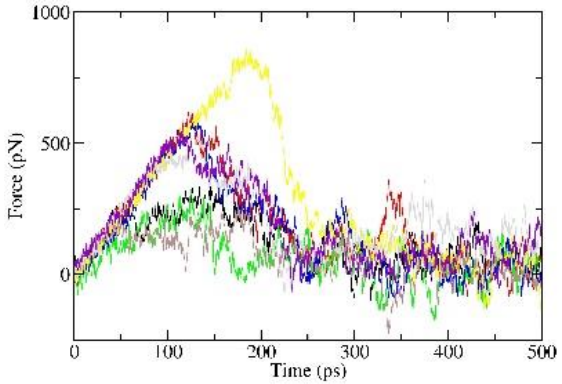
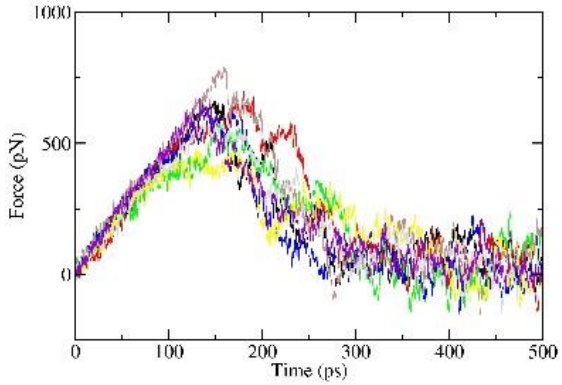
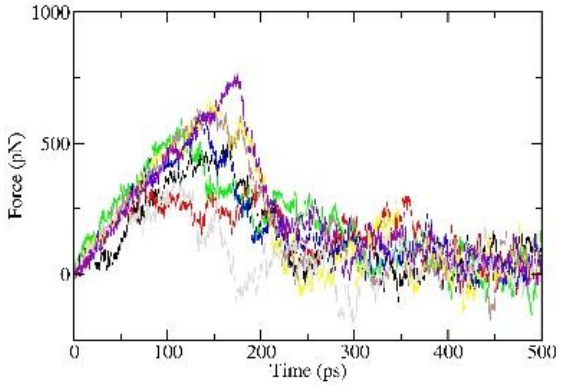
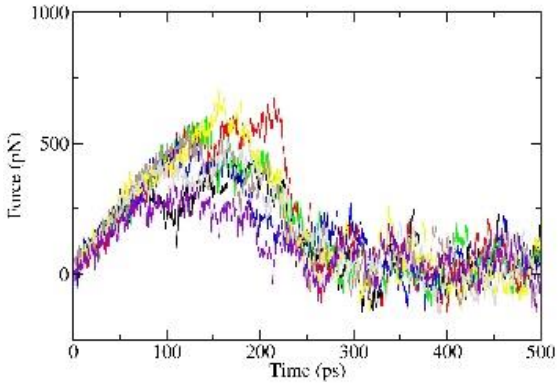
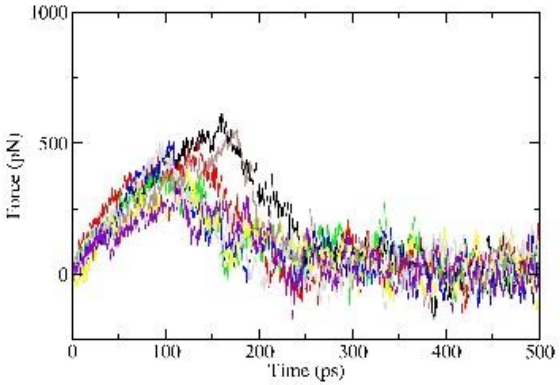
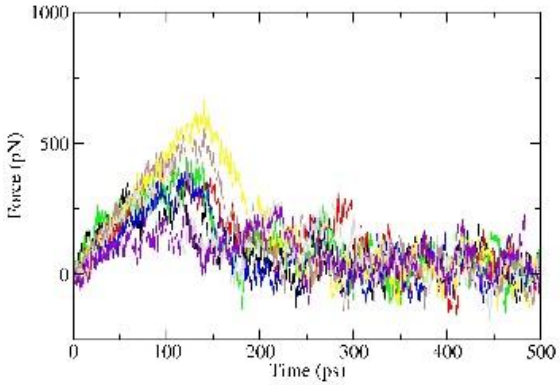
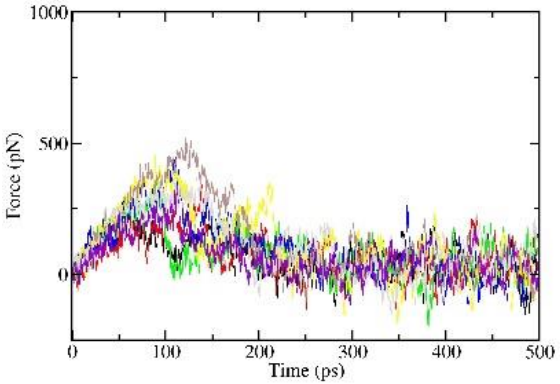
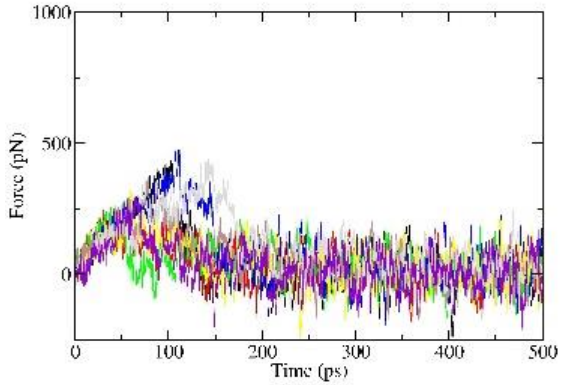
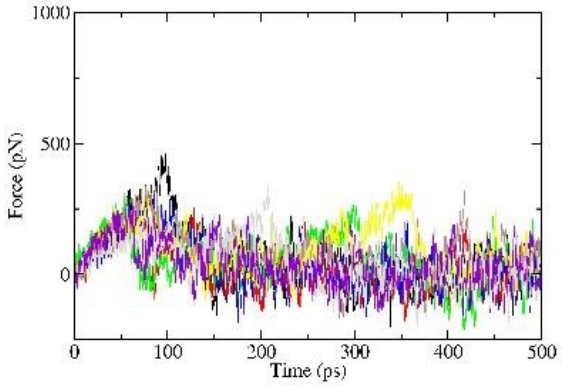
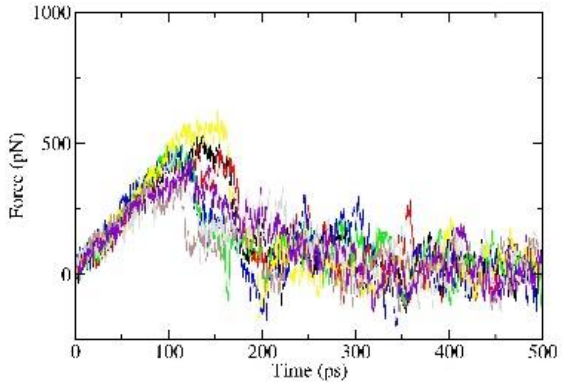
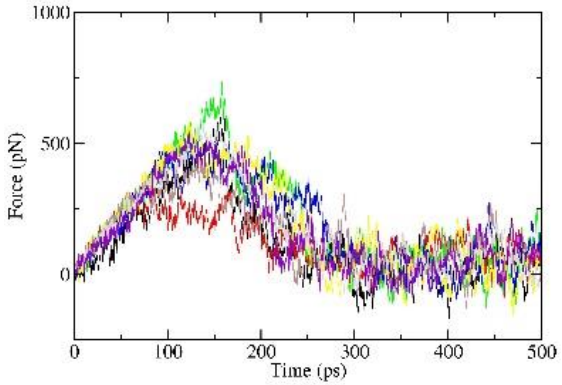
Tetrandrine		

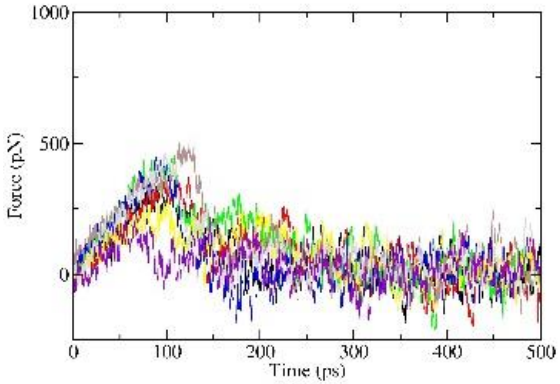
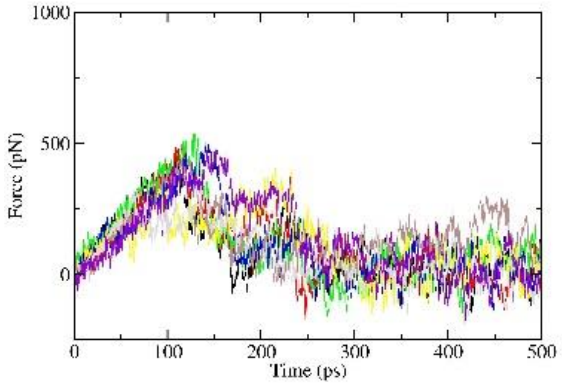
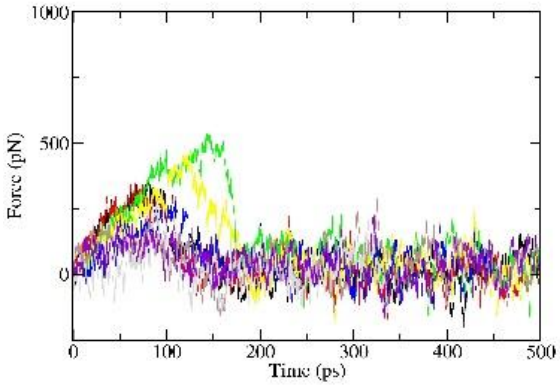
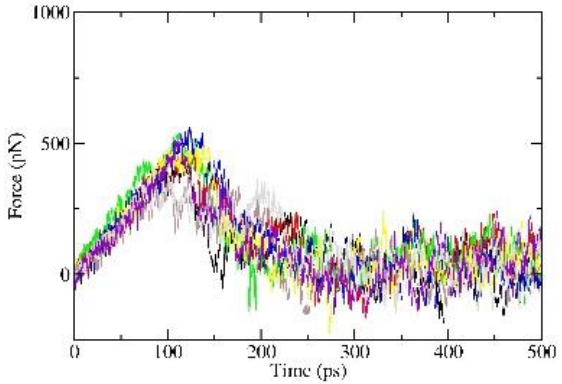
Table S6. The Pulling Force in Time Evolution.

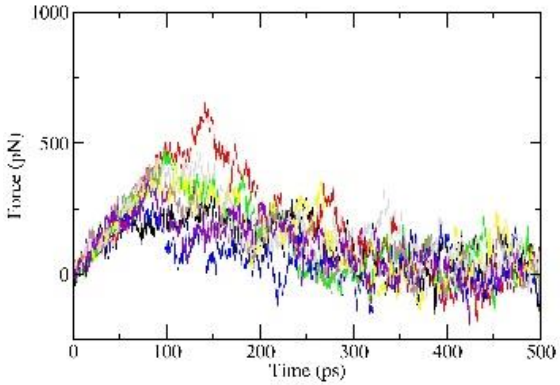
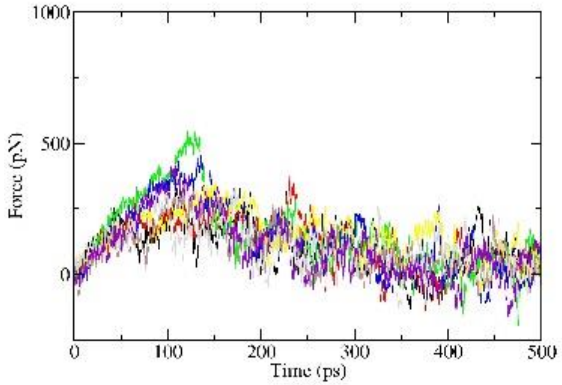
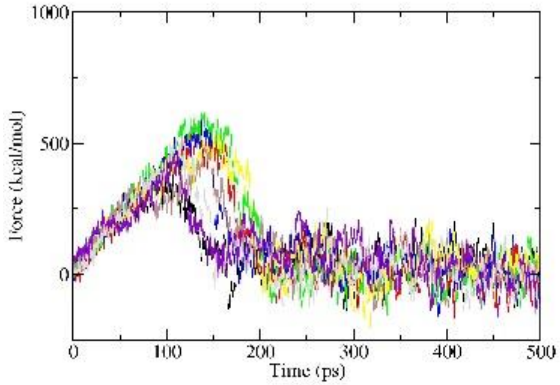
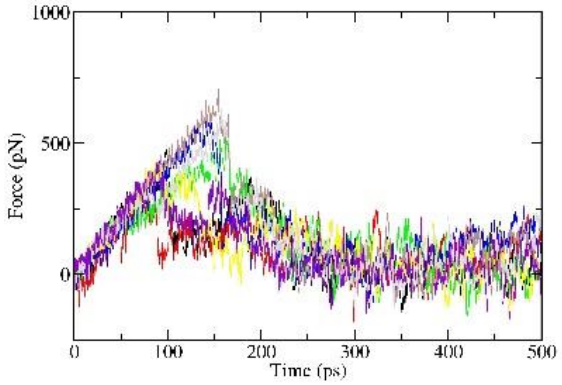
Name	Monomer	Dimer
Bazedoxifene		
Cyclosporine		

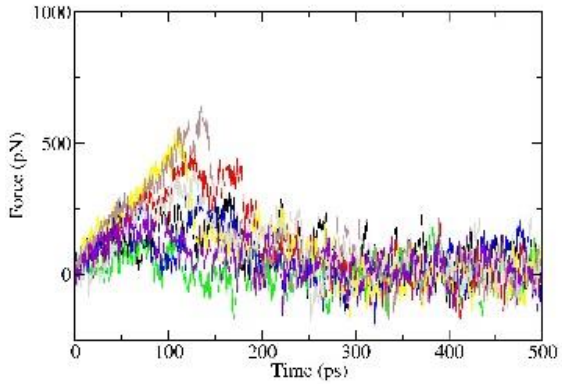
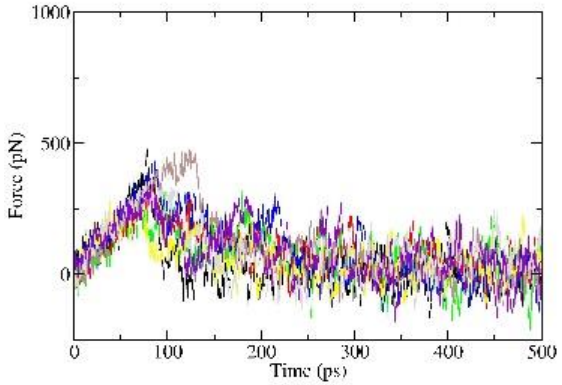
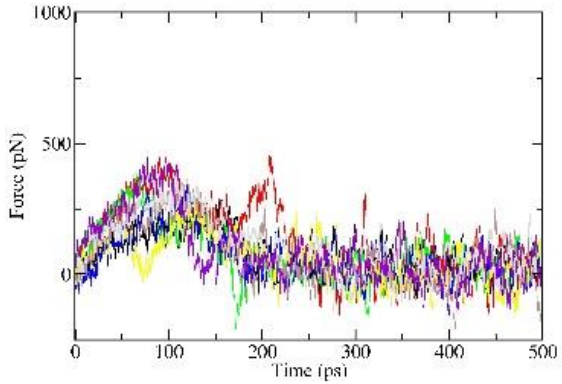
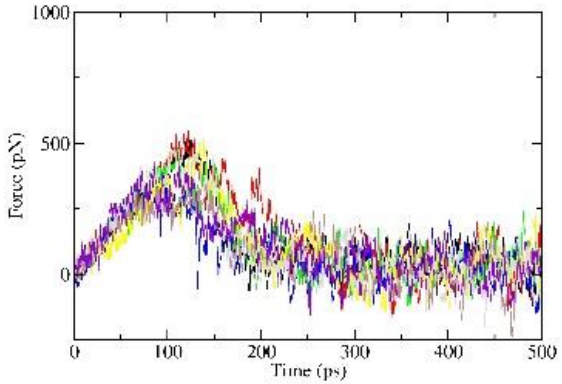
Digitoxin		
Digoxin		

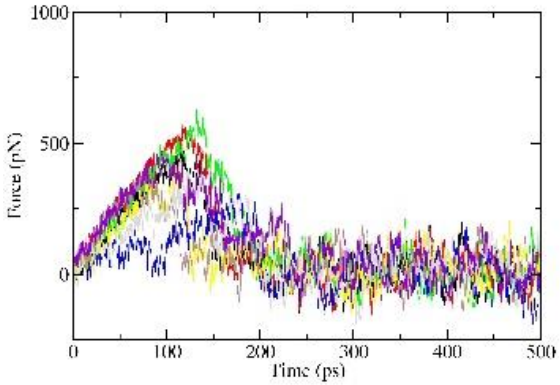
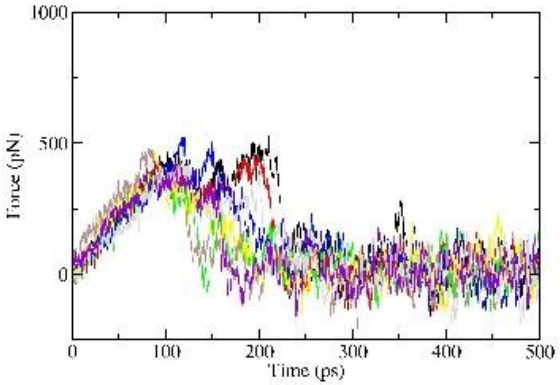
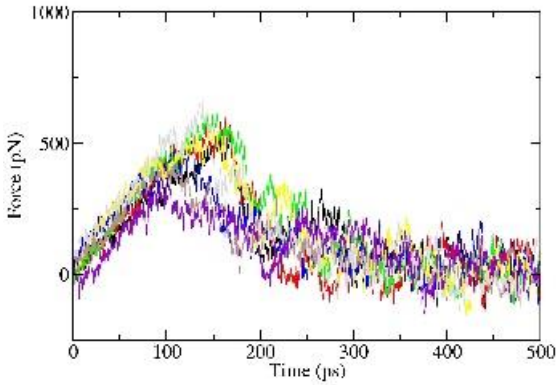
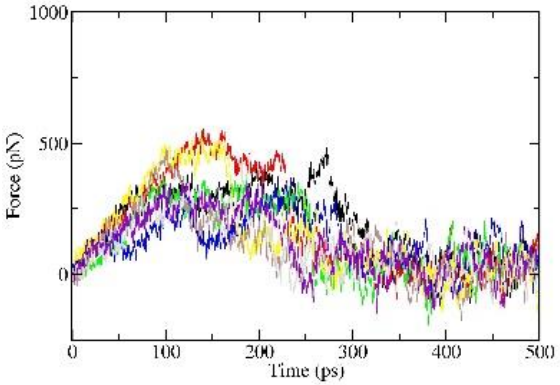
Dihydrogambogic Acid		
Ebastine		

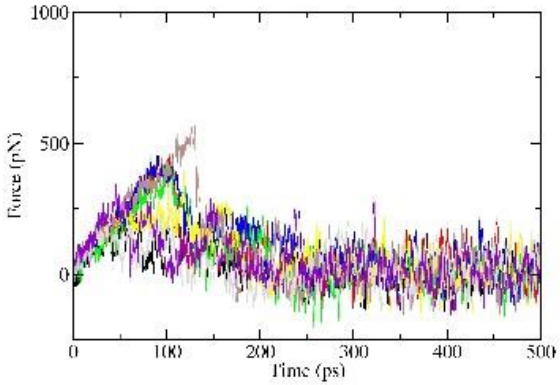
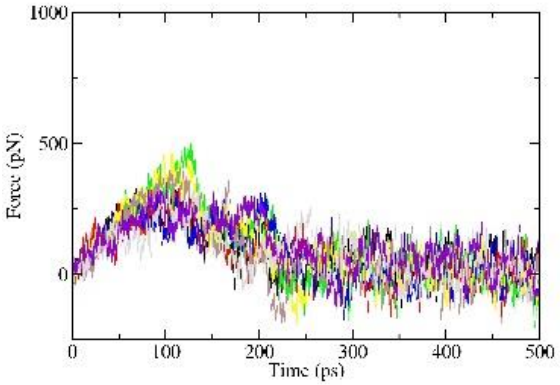
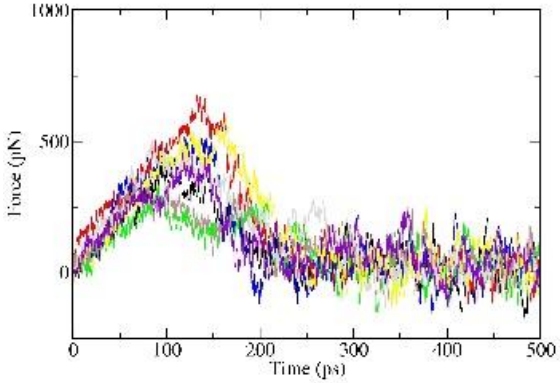
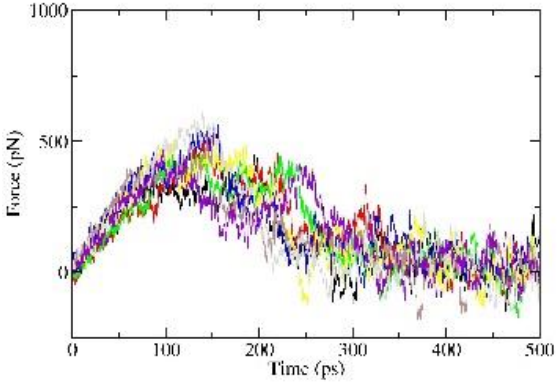
Favipiravir		
Fluspirilene		

Isoosajin		
Ivacaftor		

Lusutrombopag		
Mefloquine		

Mequitazine		
Osajin		

Oxyclozanide		
Penfluridol		

Phenazopyridine		
Proscillaridin		

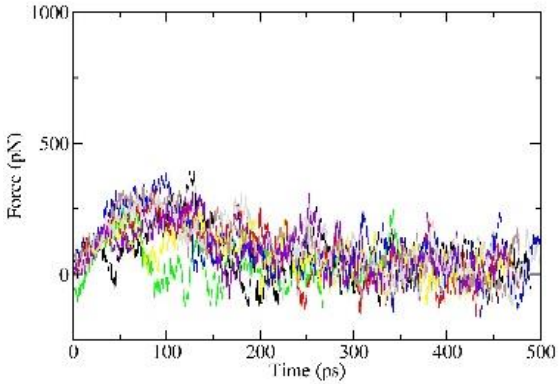
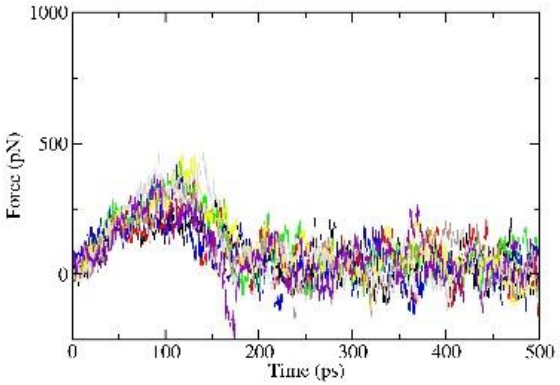
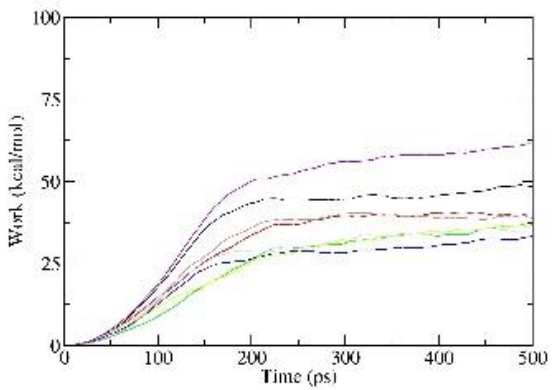
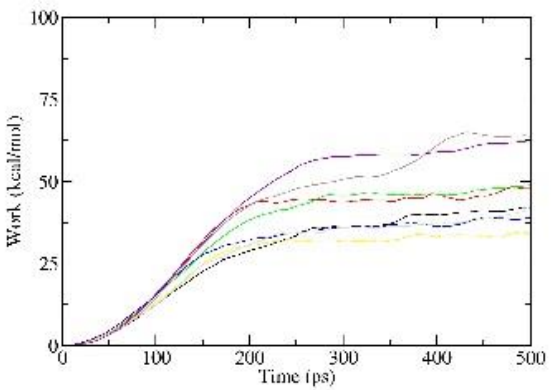
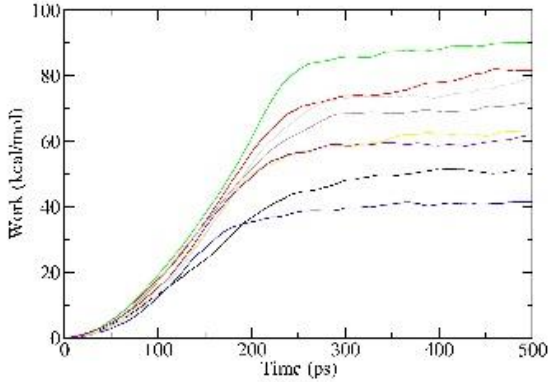
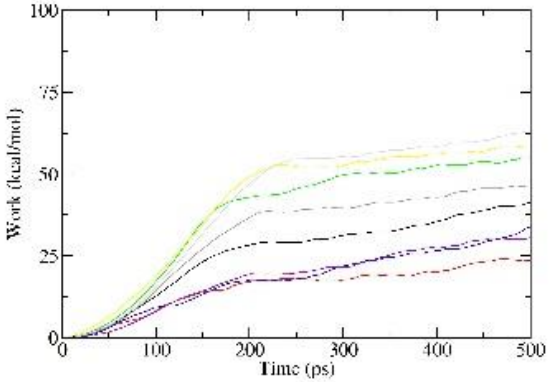
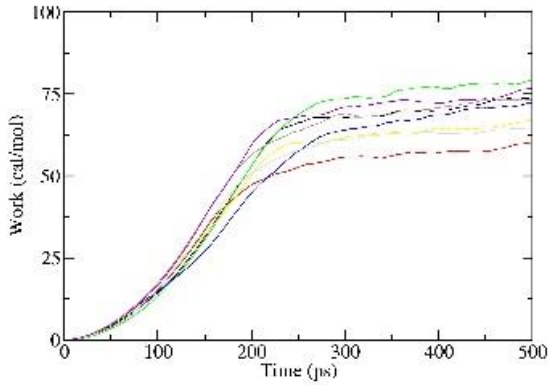
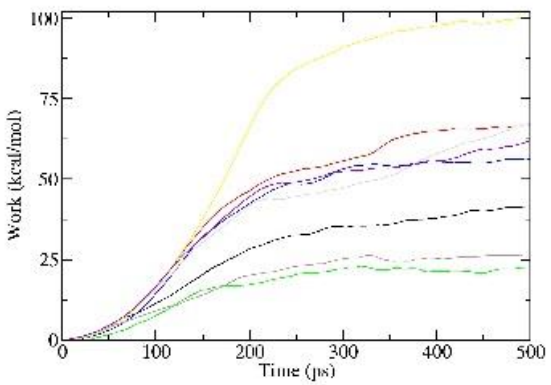
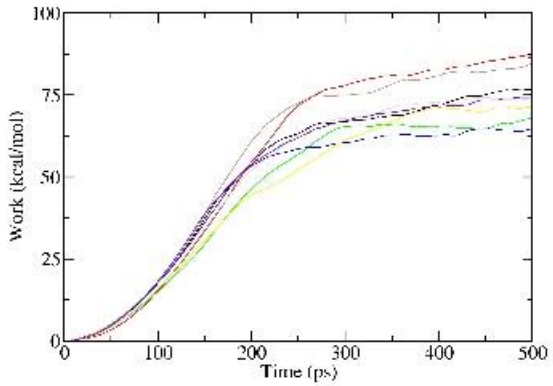
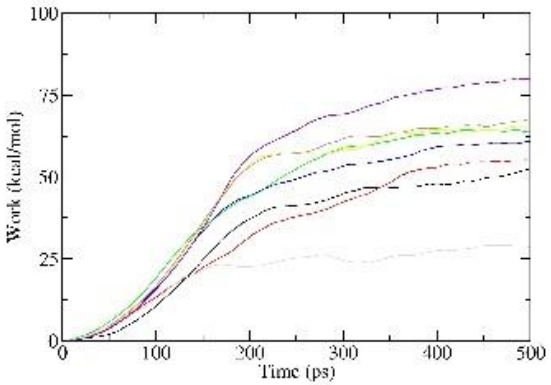
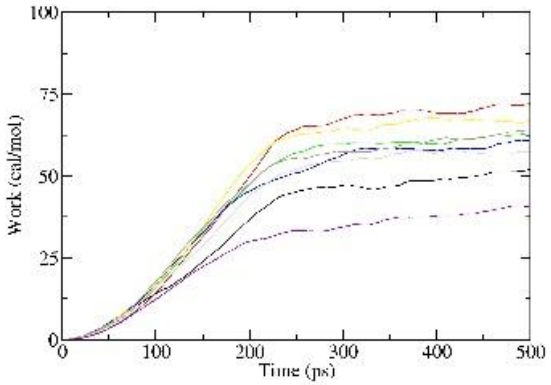
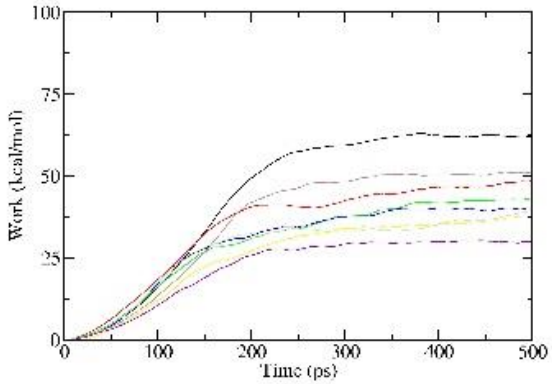
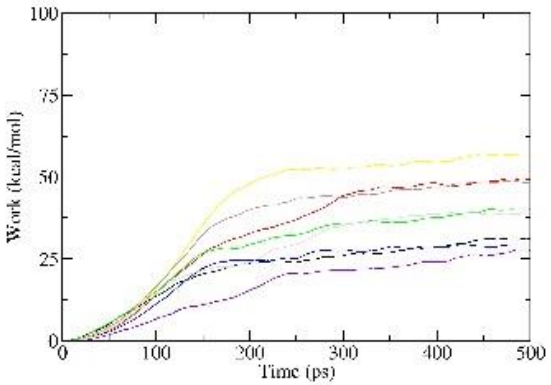
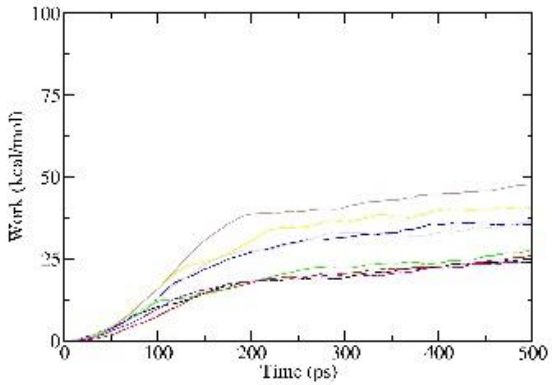
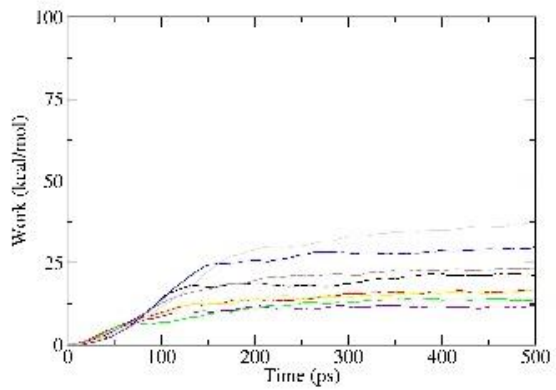
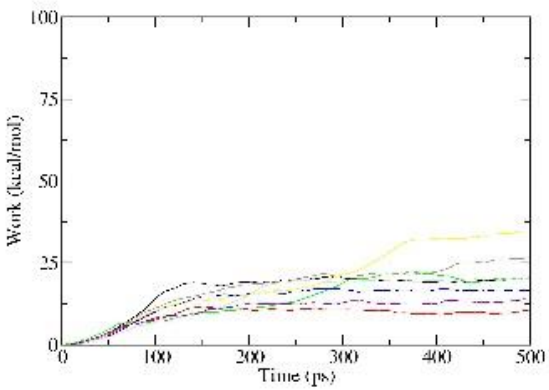
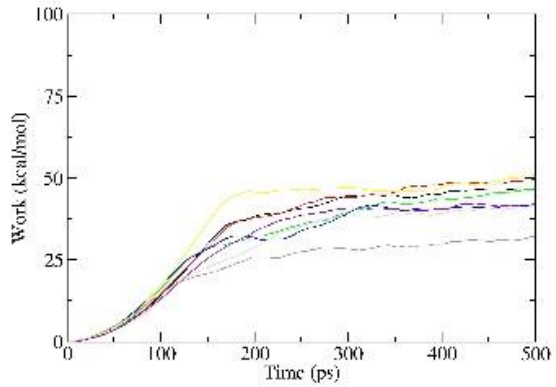
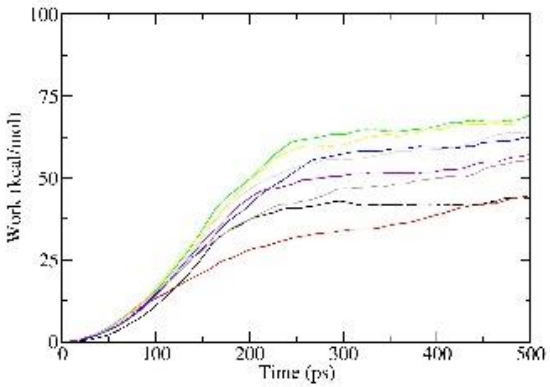
Tetrandrine		

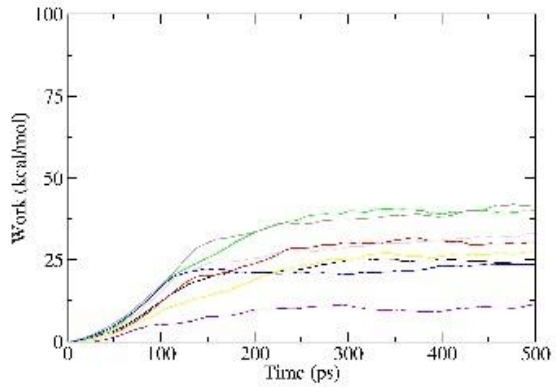
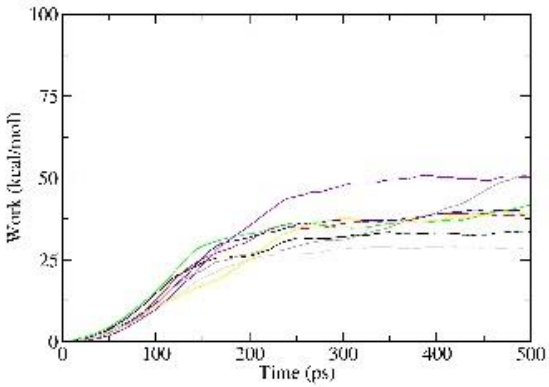
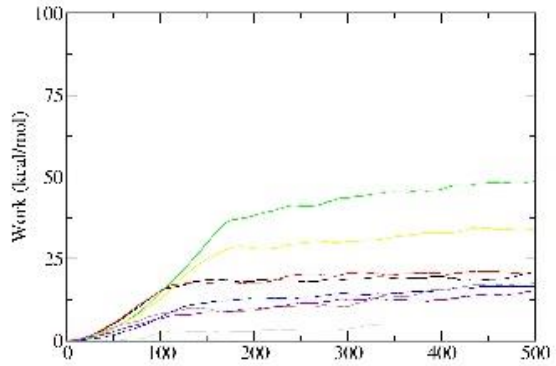
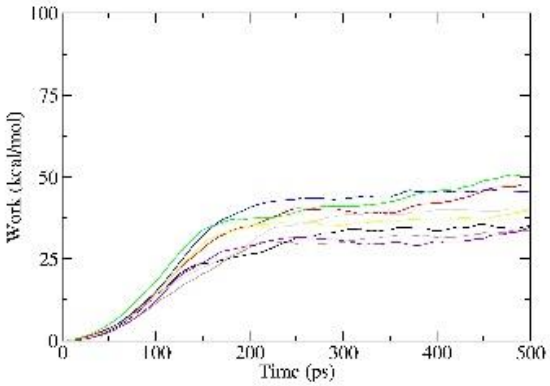
Table S7. The Pulling Work in Time Dependence over 8 Independent SMD Trajectories.

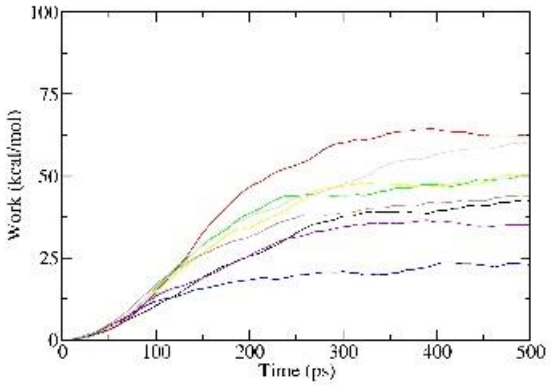
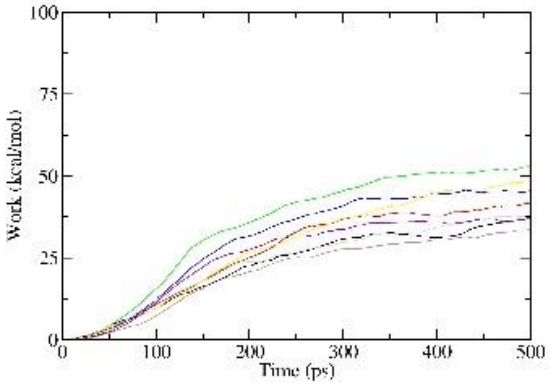
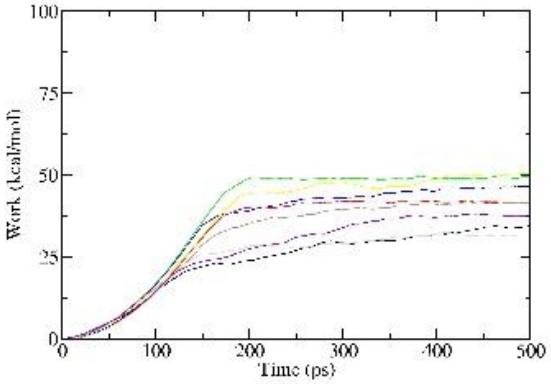
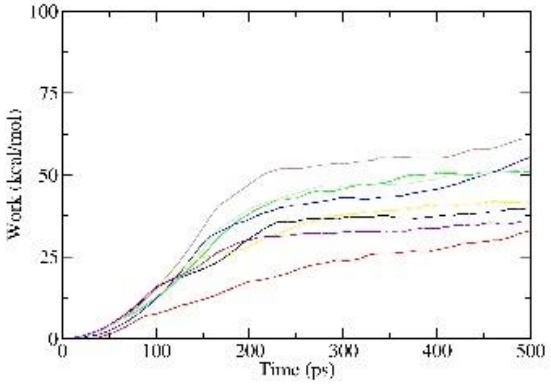
Name	Monomer	Dimer
Bazedoxifene		
Cyclosporine		

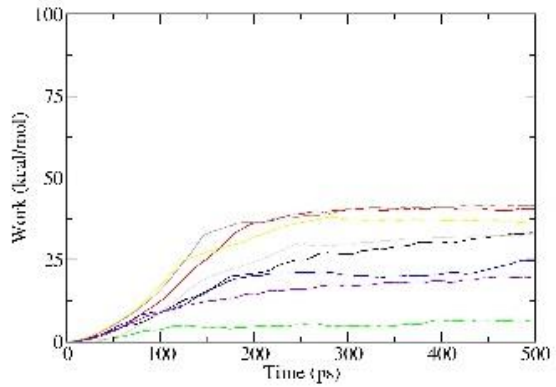
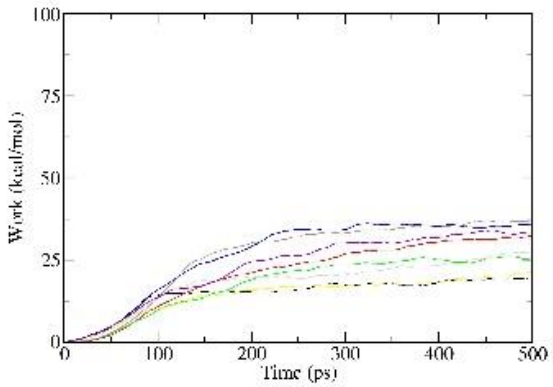
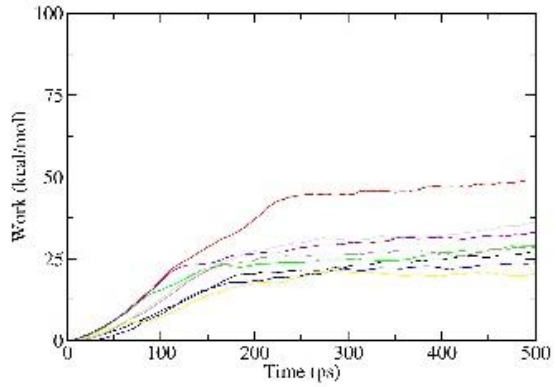
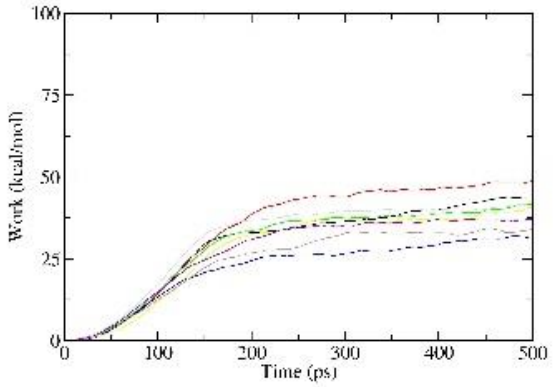
Digitoxin		
Digoxin		

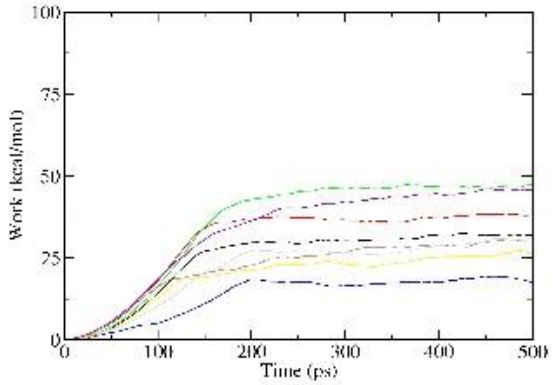
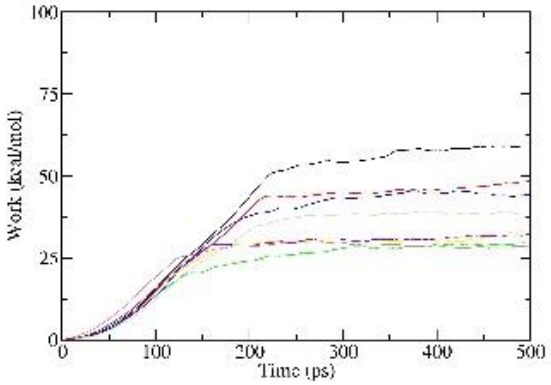
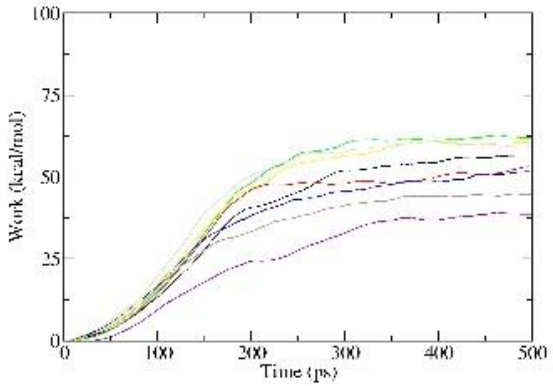
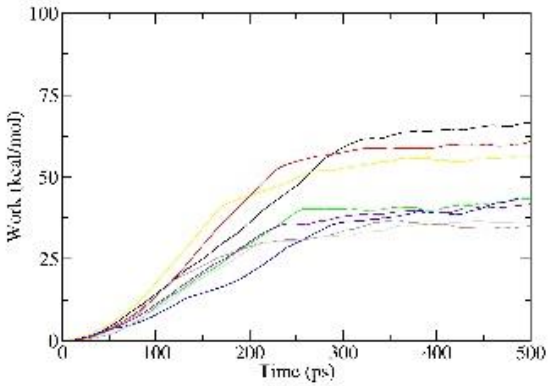
Dihydrogambogic Acid		
Ebastine		

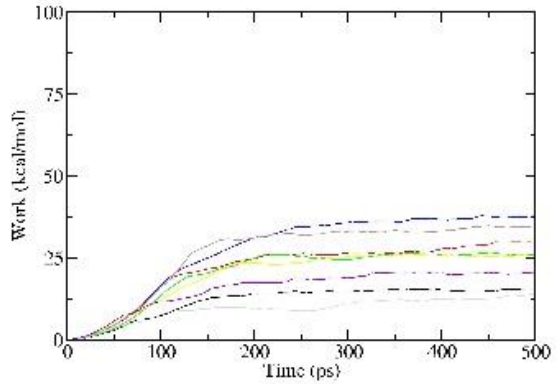
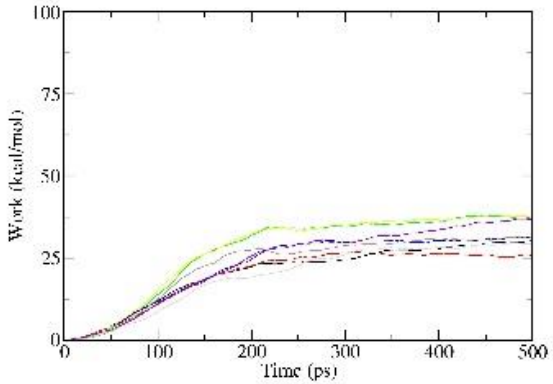
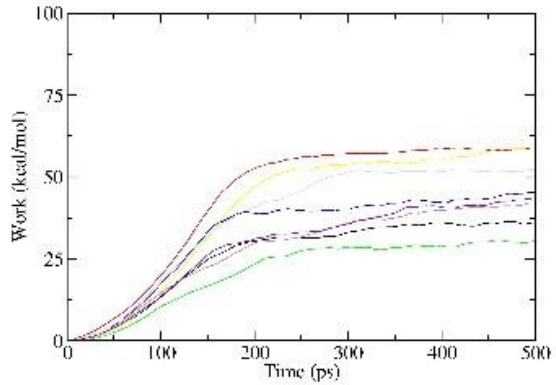
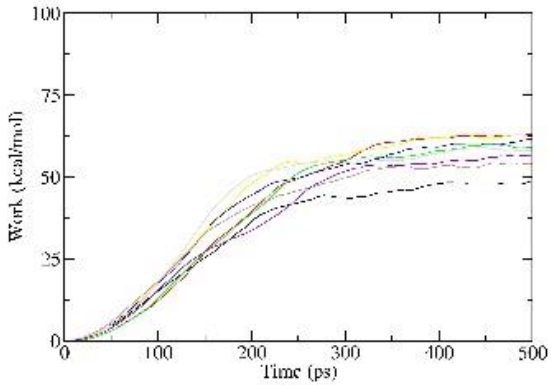
Favipiravir		
Fluspirilene		

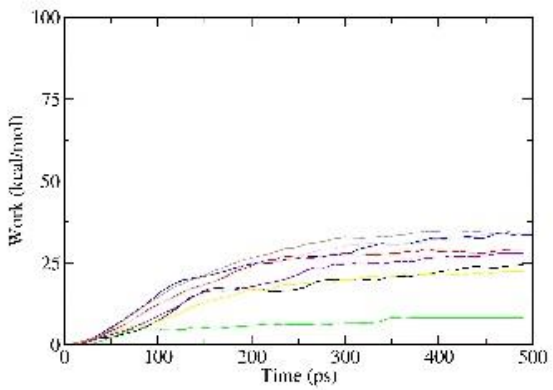
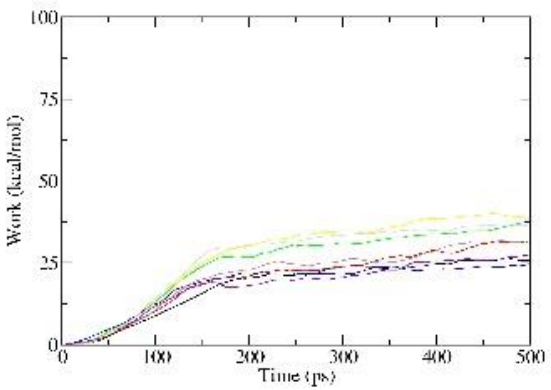
Isoosajin		
Ivacaftor		

Lusutrombopag		
Mefloquine		

Mequitazine		
Osajin		

Oxyclozanide		
Penfluridol		

Phenazopyridine		
Proscillaridin		

Tetrandrine		

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