NS5 expression and purification gels

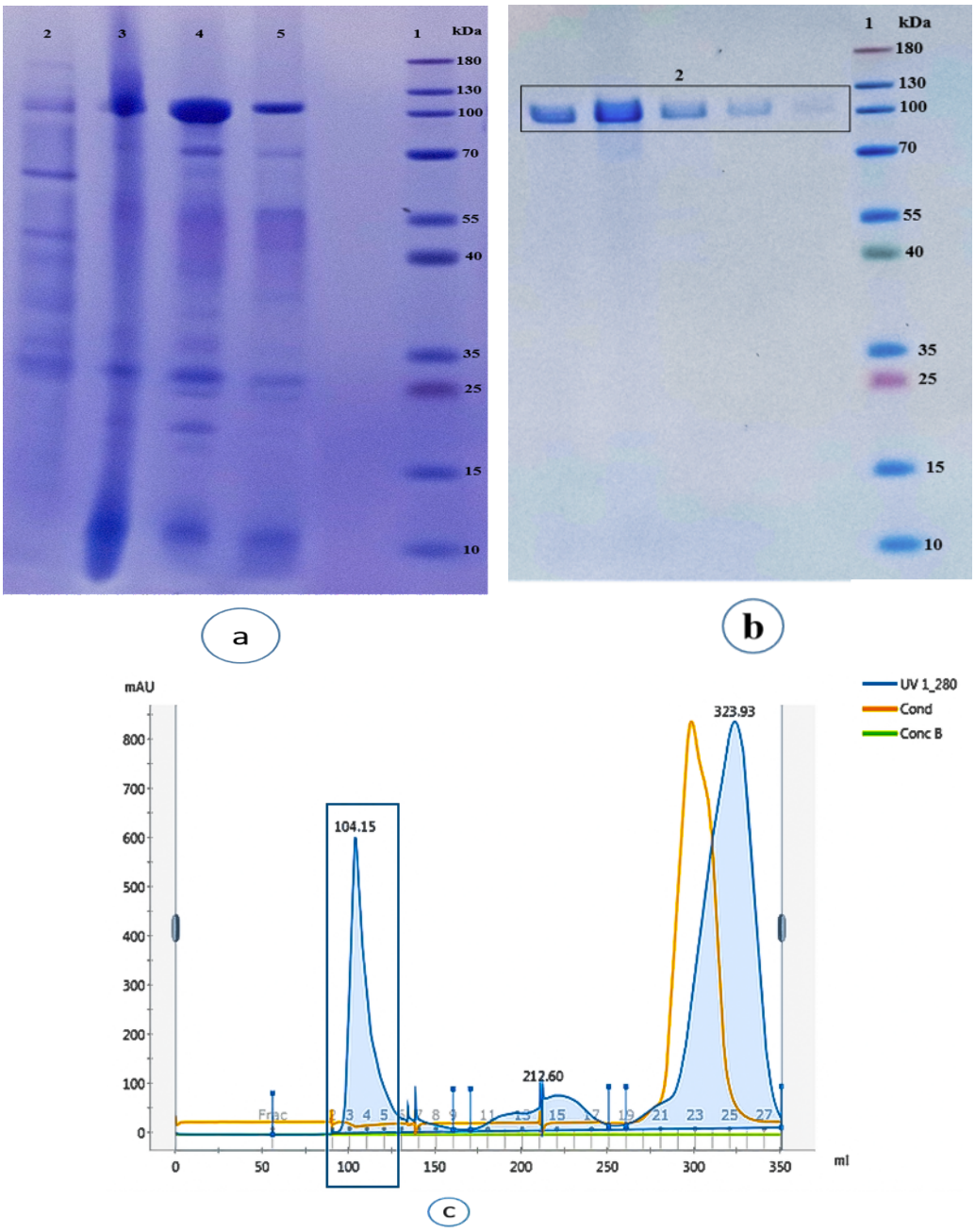


Fig. S1: (a) 4-12% SDS-PAGE analysis of NS5 protein expression Lane 1: Molecular weight ladder; Lane 2: Uninduced; Lane 3: Induce pellet; Lane 4: Soluble; Lane 5: Insoluble. (b) 4-12% SDS-PAGE analysis of NS5 protein purification. Lane 1: Molecular weight ladder; Lane 2: NS5 sample used for STD-NMR. c) Chromatogram of size exclusion chromatography highlighted peak showing the elution region of protein

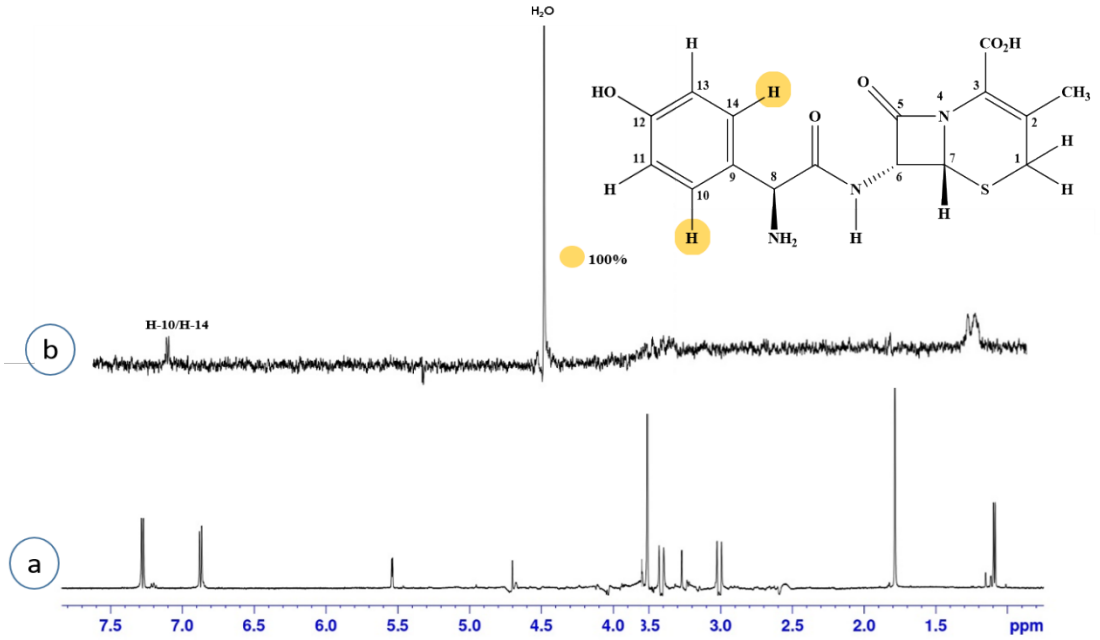


Fig. S2. STD-NMR of drug molecule **5.** a) ^{1}H NMR reference spectrum of compound **5**. b) STD difference spectrum recorded with NS5 protein of 2 µM concentration. Only H-10/H-14 has received the saturation STD integral value, and set to 100% indicated with a color code.

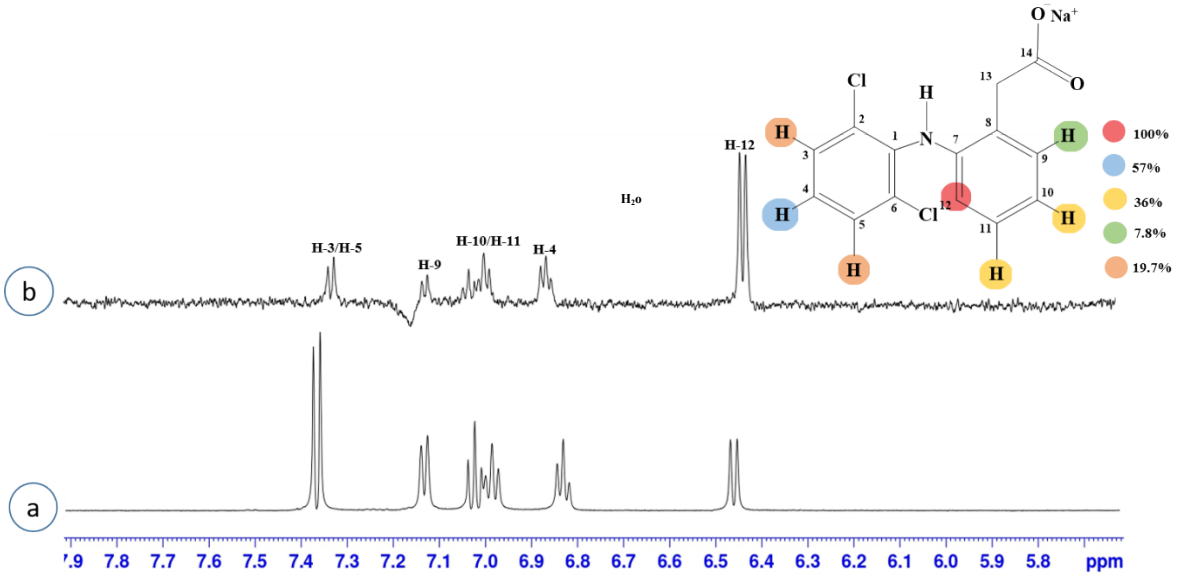


Fig. S3. STD-NMR of drug molecule **6.** a) ^{1}H NMR reference spectrum of compound **6**. b) STD difference spectrum recorded with NS5 protein of 2 µM concentration. H-12 has the largest STD integral value, and set to 100%. All other interacting protons are normalized against H-12 are indicated with a color code.

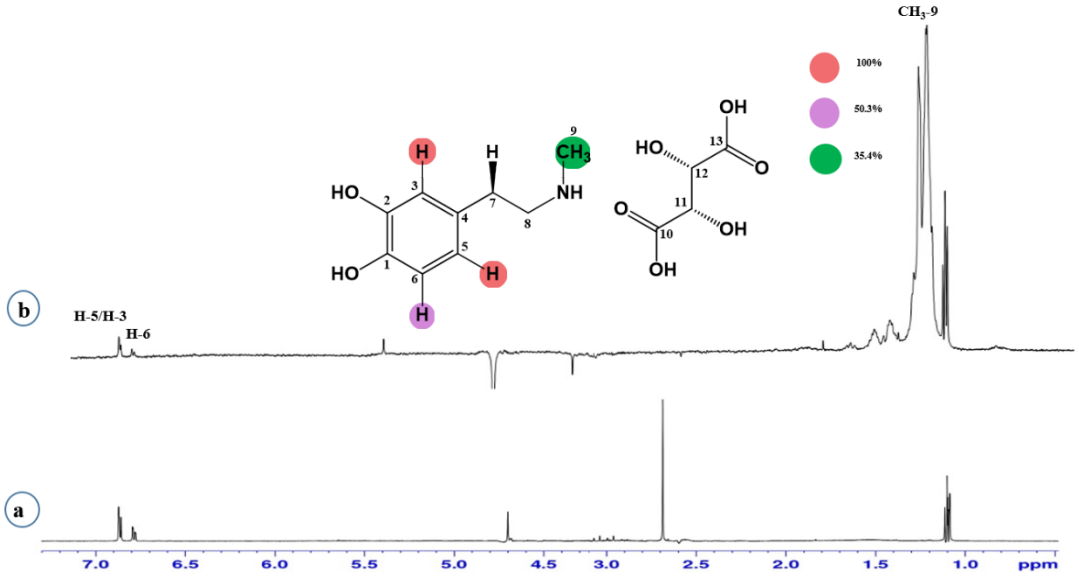


Fig. S4. STD-NMR of drug molecule **7.** a) ^{1}H NMR reference spectrum of compound **7**. b) STD difference spectrum recorded with NS5 protein of 2 μM concentration. H-3/H-5 has the largest STD integral value, and set to 100%. All other interacting protons are normalized against H-3/H-5 are indicated with a color code.

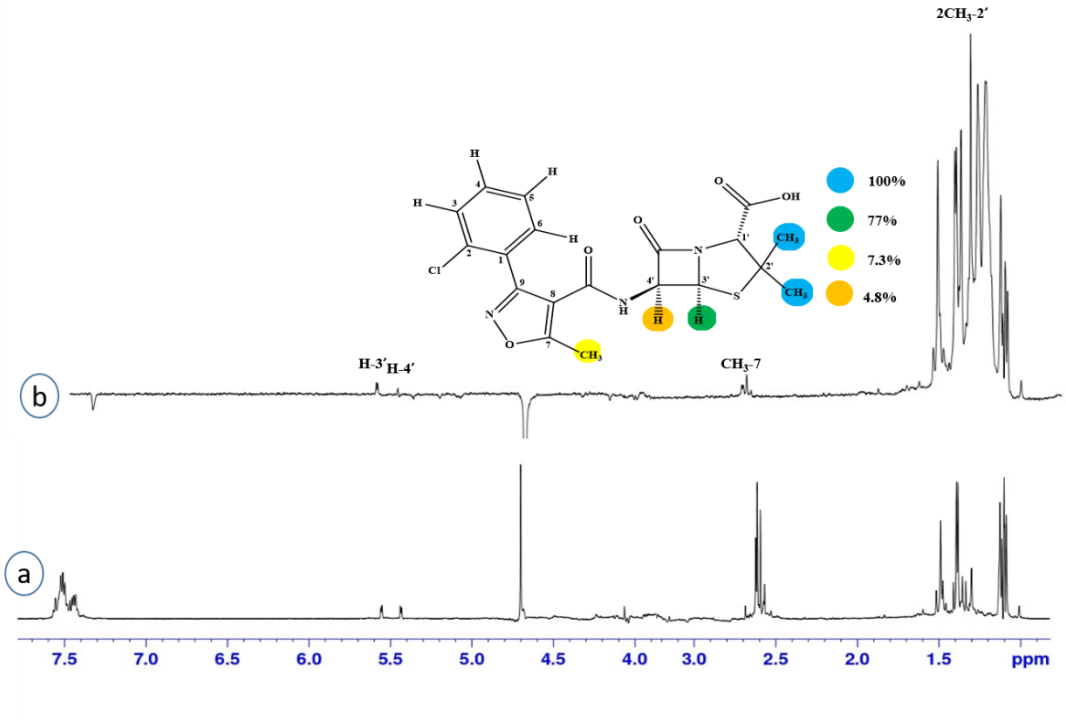


Fig. S5. STD-NMR of drug molecule **8.** a) ^{1}H NMR reference spectrum of compound **8**. b) STD difference spectrum recorded with NS5 protein of 2 μM concentration. $2CH_3$ at C-2′ has the largest STD integral value, and set to 100%. All other interacting protons are normalized against

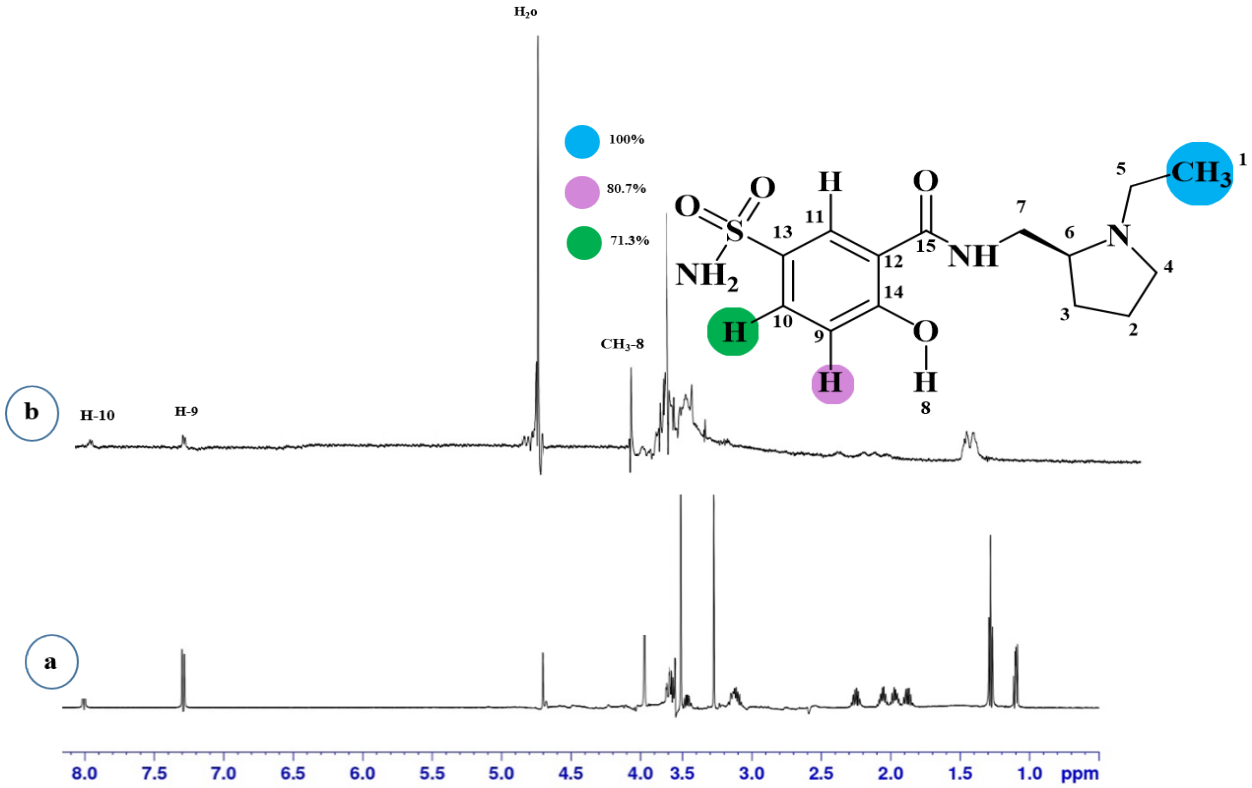


Fig. S6. STD-NMR of drug molecule **9.** a) ^{1}H NMR reference spectrum of compound **9**. b) STD difference spectrum recorded with NS5 protein of 2 µM concentration. Methoxy at position 8 has the largest STD integral value, and set to 100%. All other interacting protons are normalized against CH_3-8 are indicated with a color code.

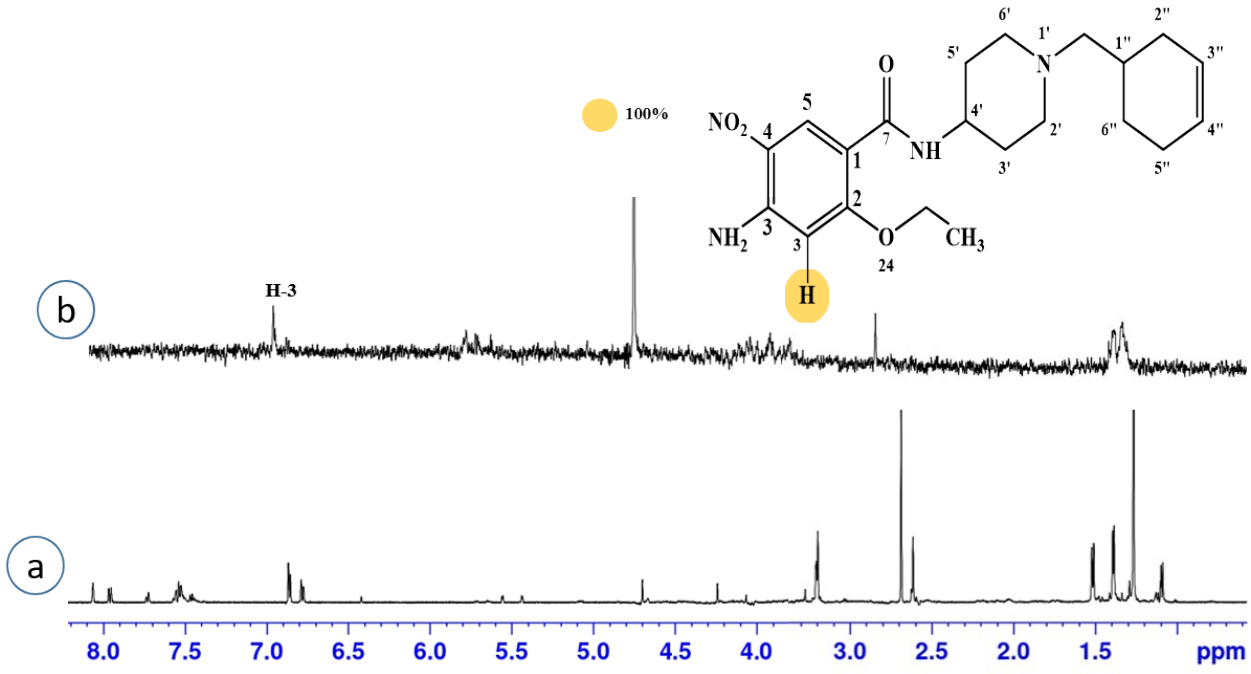


Fig. S7. STD-NMR of drug molecule **10.** a) ^{1}H NMR reference spectrum of compound **10**. b) STD difference spectrum recorded with NS5 protein of 2 µM concentration. H-3 has the largest STD integral value, and set to 100% indicated with a color code.

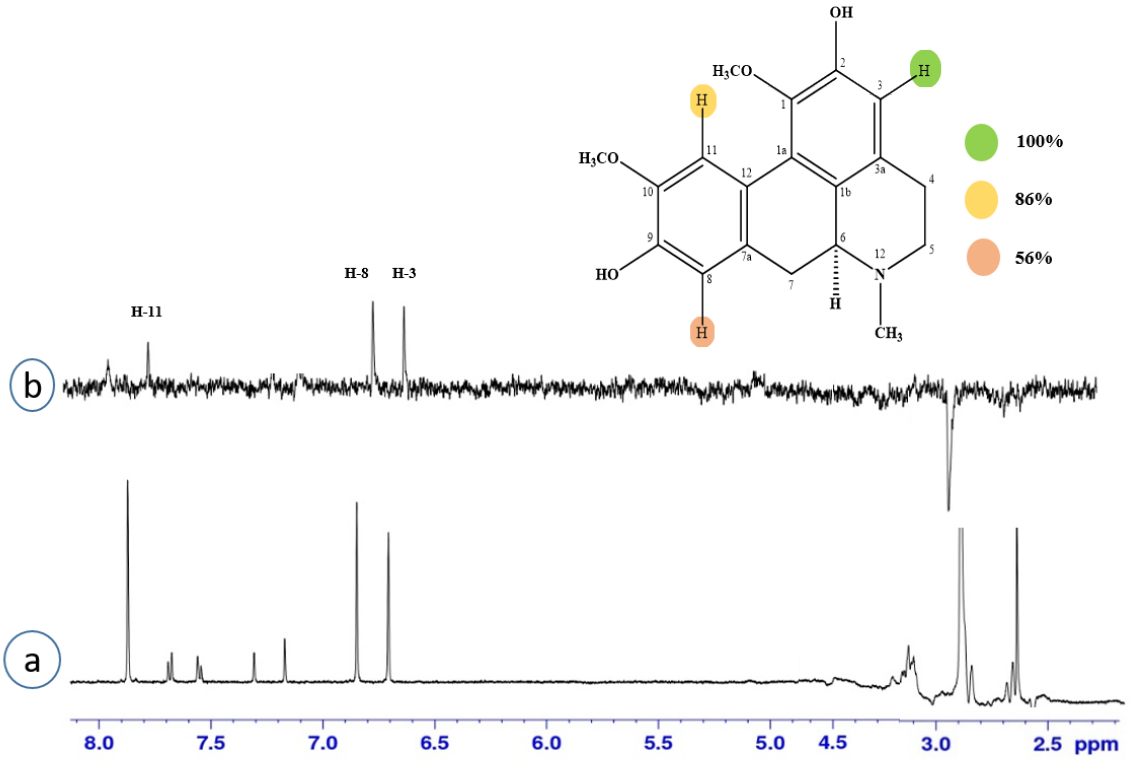


Fig. S8. STD-NMR of drug molecule **11.** a) ^{1}H NMR reference spectrum of compound **11**. b) STD difference spectrum recorded with NS5 protein of 2 µM concentration. H-3 has the largest STD integral value, and set to 100%. All other interacting protons are normalized against H-5 are indicated with a color code.

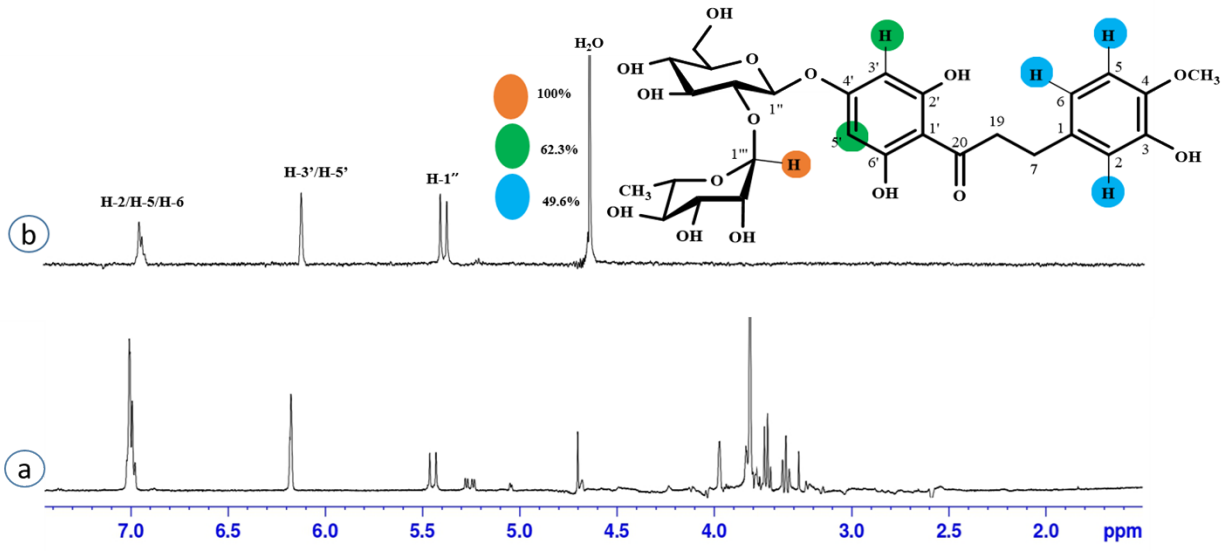
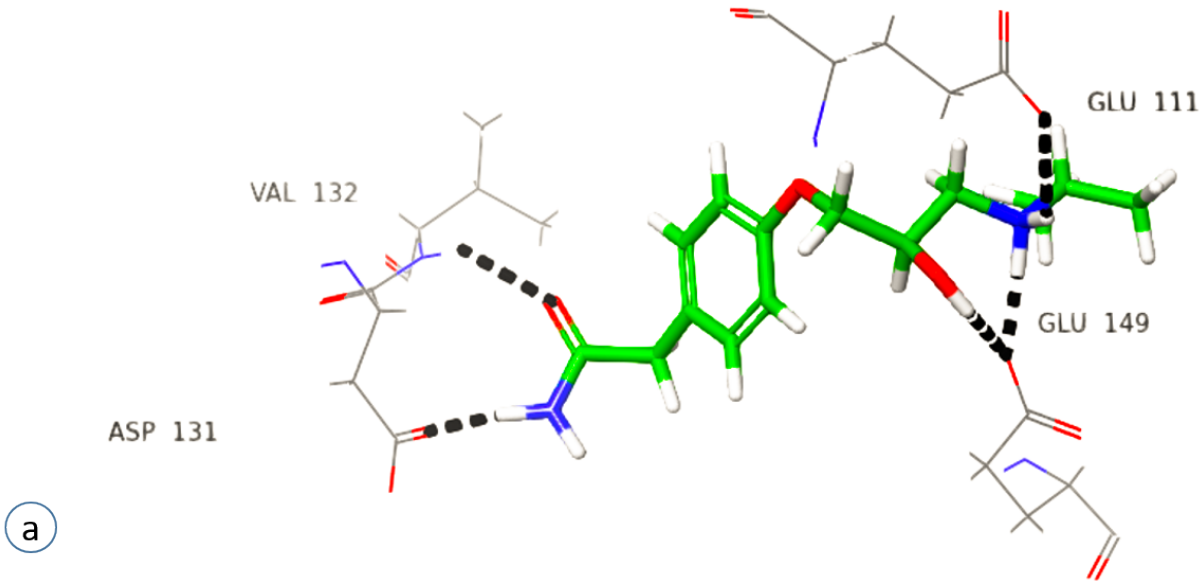


Fig. S9. STD-NMR of drug molecule **12.** a) ^{1}H NMR reference spectrum of compound **12**. b) STD difference spectrum recorded with NS5 protein of 2 µM concentration. H-1″ has the largest STD integral value, and set to 100% indicated with a color code. All other interacting protons are normalized against H-1″ are indicated with a color code.



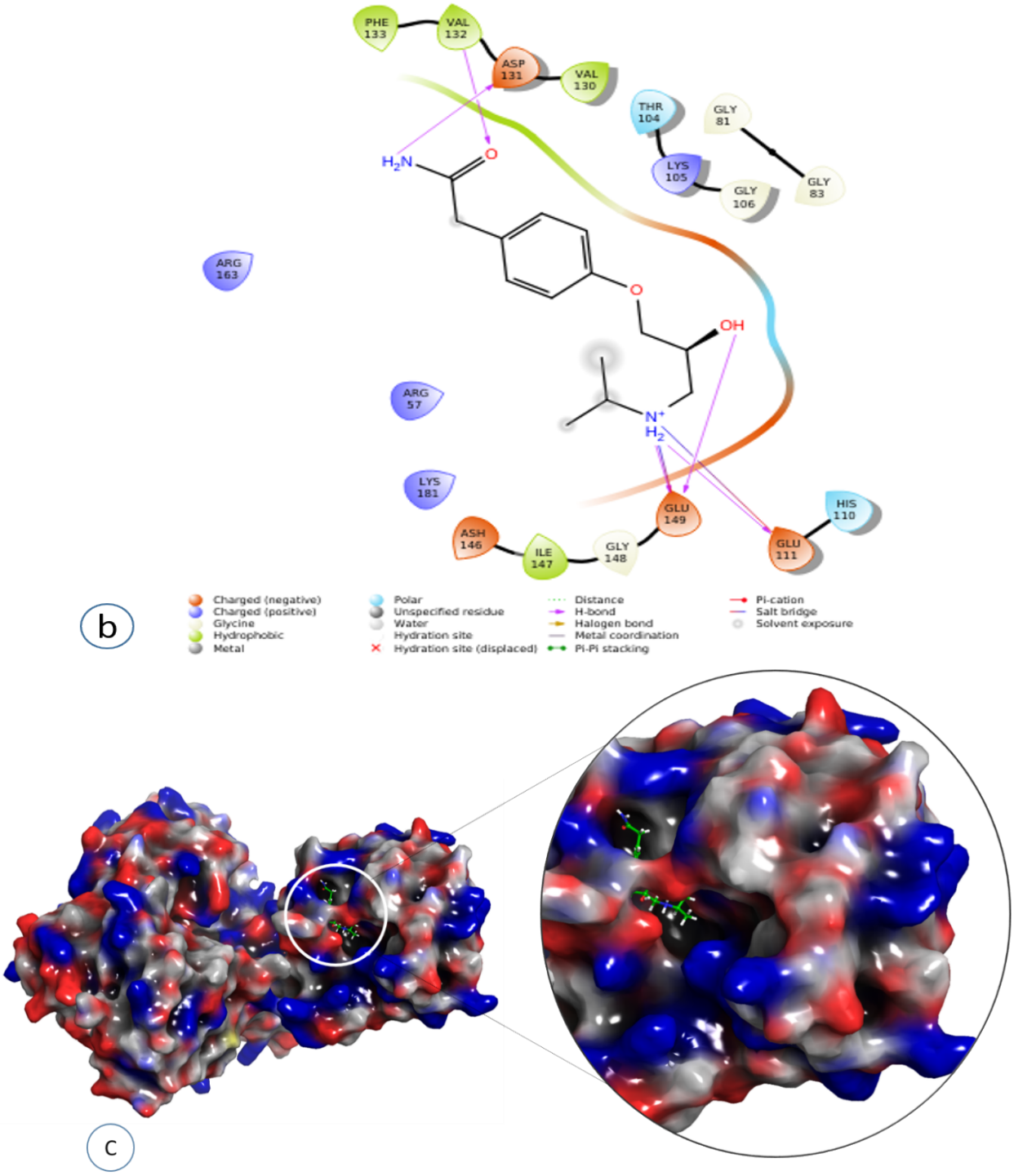
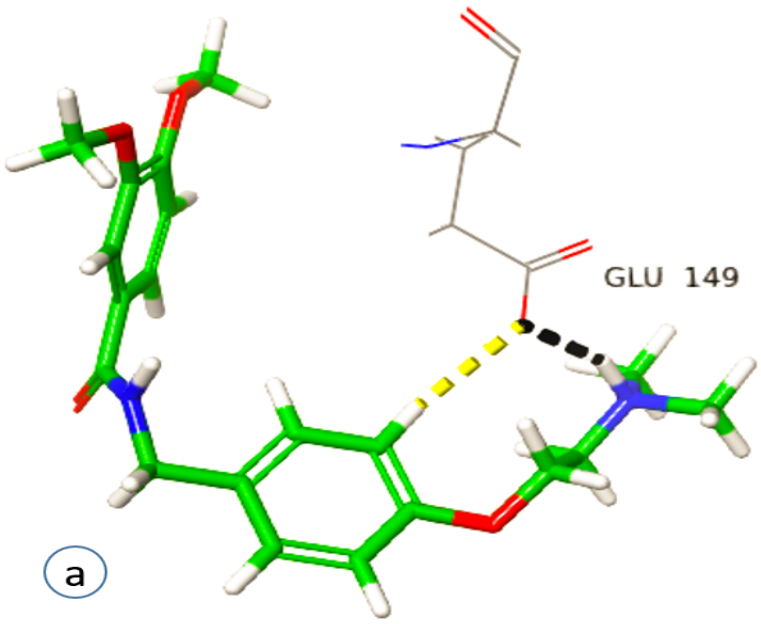
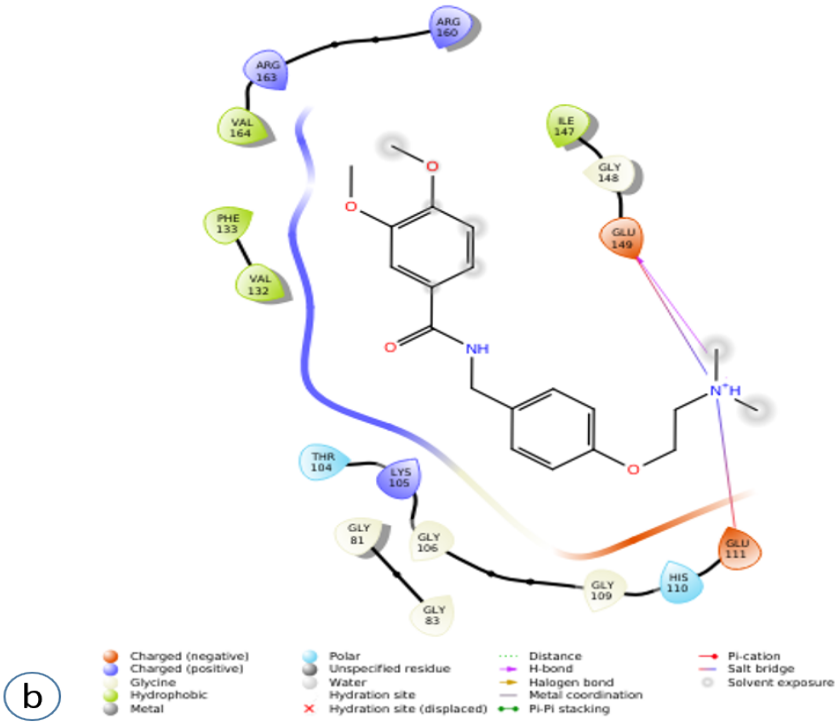


Fig. S10. Docked pose of compound **1** (Atenolol): a) 3D representation of ligand-protein interaction in dotted lines indicating hydrogen bond (black). b) 2D representation of ligand protein profile. c) Solid surface representation of ligand protein profile, depicting the electrostatic potential distribution over the surface (red, negative regions; blue, positive regions.


GLU 149
a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ARG 163
VAL 164
PHE 133
VAL 132
ILE 147
GLY 148
GLU 149
THR 104
LYS 105
GLY 81
GLY 106
GLY 109
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GLU 111
GLY 83
NH
N+H
b
Charged (negative)
Charged (positive)
Glycine
Hydrophobic
Metal
Polar
Unspecified residue
Water
Hydration site
Hydration site (displaced)
Distance
H-bond
Halogen bond
Metal coordination
Pi-Pi stacking
Pi-cation
Salt bridge
Solvent exposure

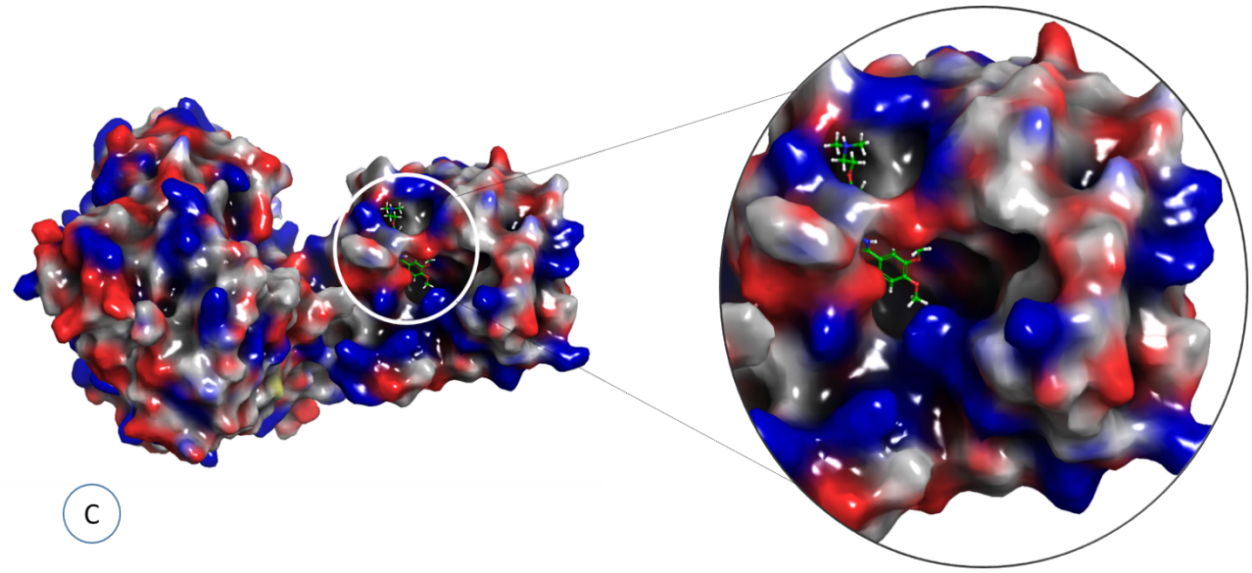
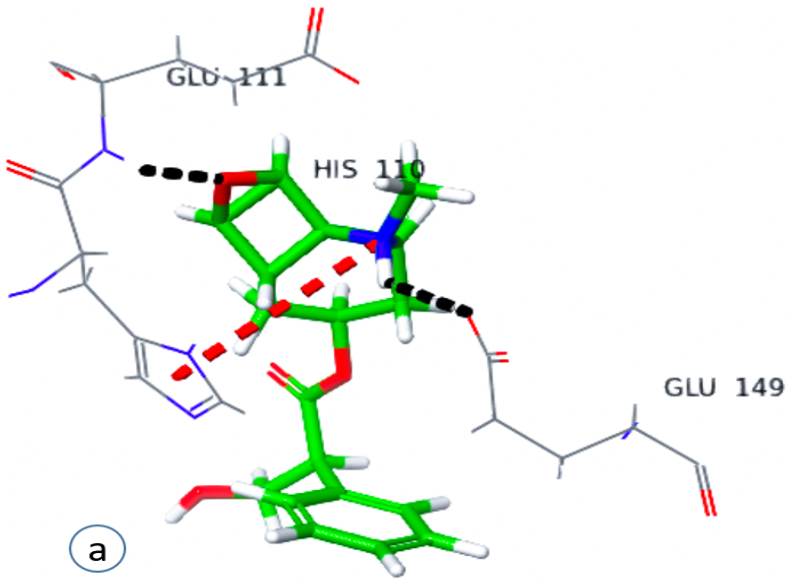


Fig. S11. Docked pose of compound **2** (Itopride hydrochloride): a) 3D representation of ligand-protein interaction in dotted lines indicating hydrogen bond (black) and aromatic hydrogen bond (yellow). b) 2D representation of ligand-protein profile. c) Solid surface representation of ligand protein profile, depicting the electrostatic potential distribution over the surface (red, negative regions; blue, positive regions.



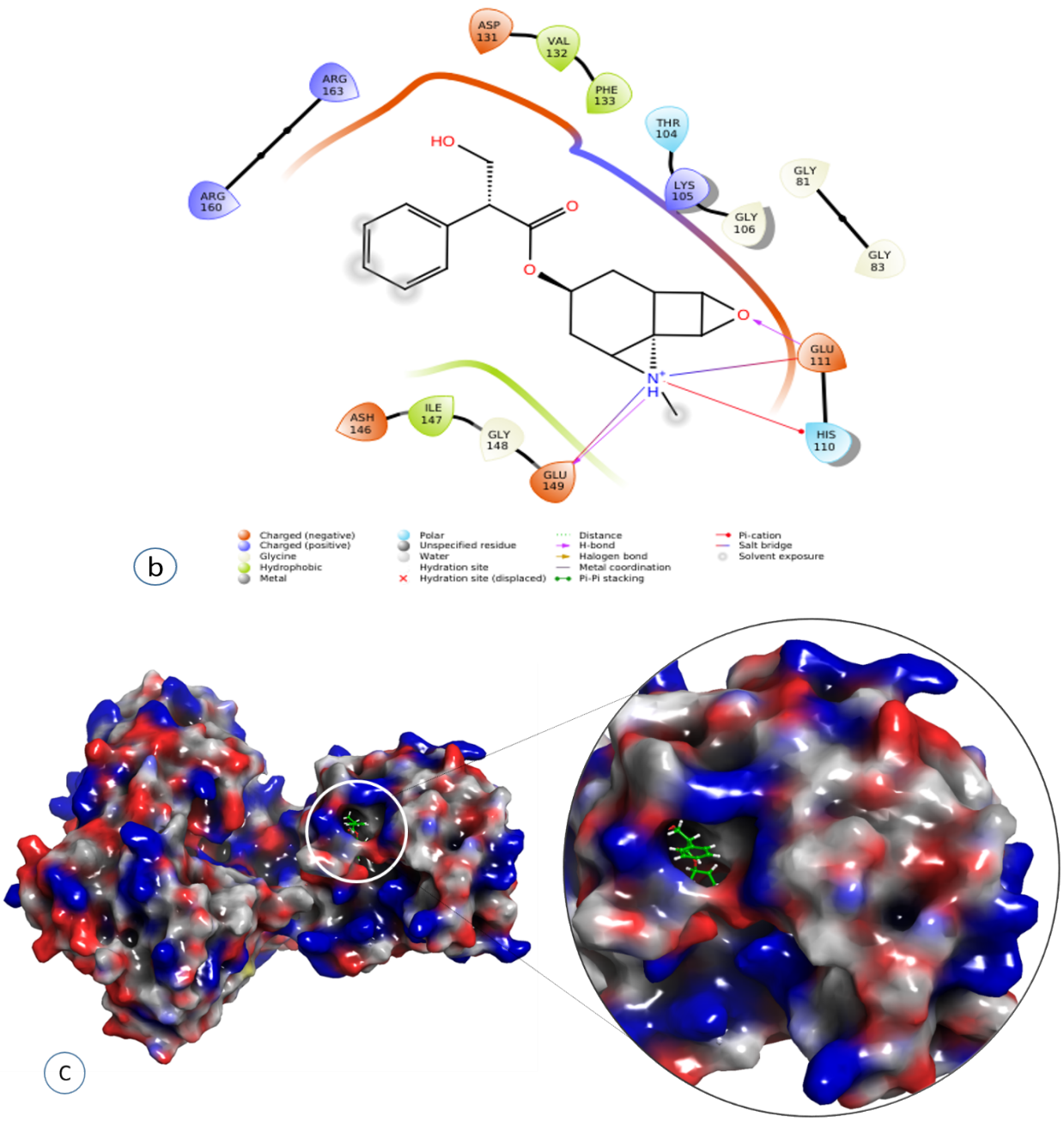
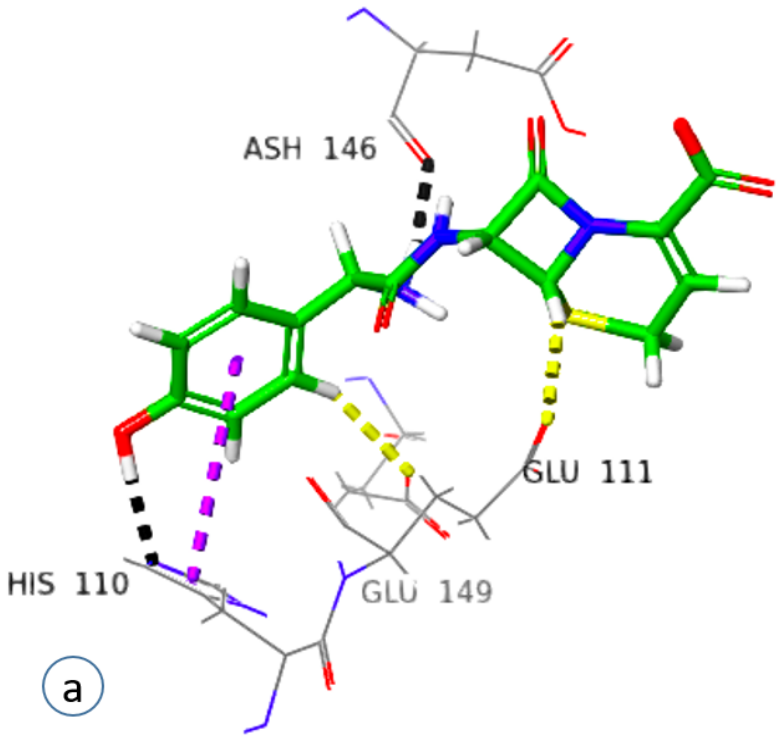


Fig. S12. Docked pose of compound **3** (Scopolamine hydrobromide trihydrate): a) 3D representation of ligand-protein interaction in dotted lines indicating hydrogen bond (black) and π cation interaction (red). b) 2D representation of ligand-protein profile. c) Solid surface representation of ligand protein profile, depicting the electrostatic potential distribution over the surface (red, negative regions; blue, positive regions.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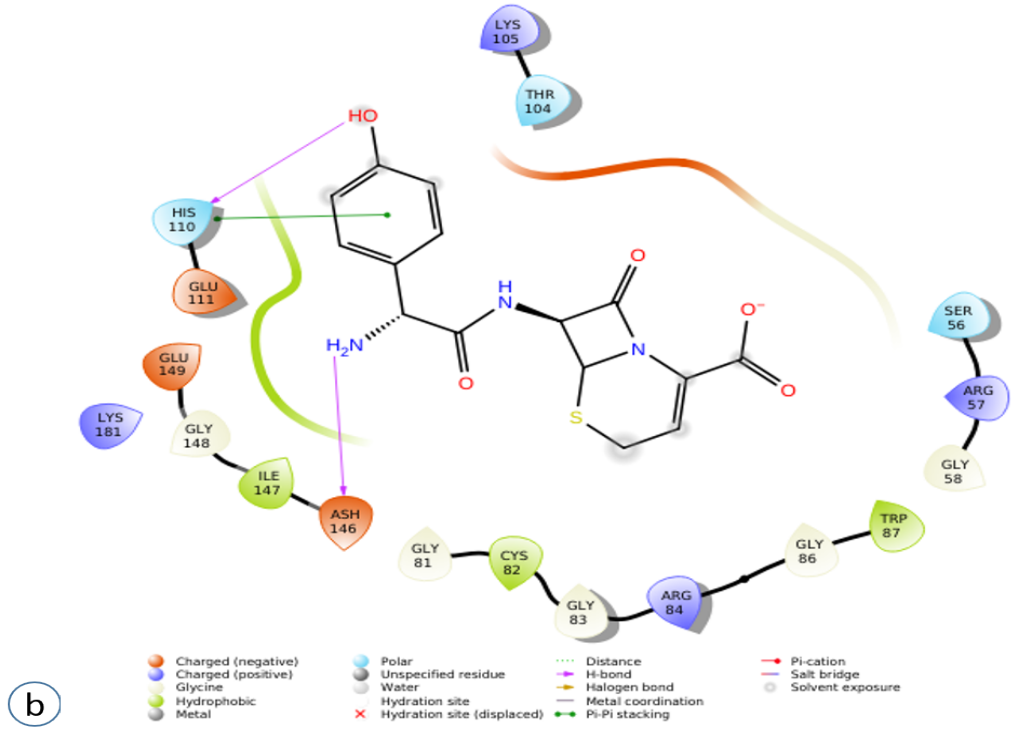
GLU 111
HIS 110
GLU 149
a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THR 104
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HIS 110
GLU 111
GLU 149
LYS 181
GLY 148
ILE 147
ASH 146
GLY 81
CYS 82
GLY 83
ARG 84
GLY 86
TRP 87
SER 56
ARG 57
GLY 58
H2N
H
N
O
O⁻
N
S
O
Charged (negative)
Charged (positive)
Glycine
Hydrophobic
Metal
Polar
Unspecified residue
Water
Hydration site
Hydration site (displaced)
Distance
H-bond
Halogen bond
Metal coordination
Pi-Pi stacking
Pi-cation
Salt bridge
Solvent exposure
b

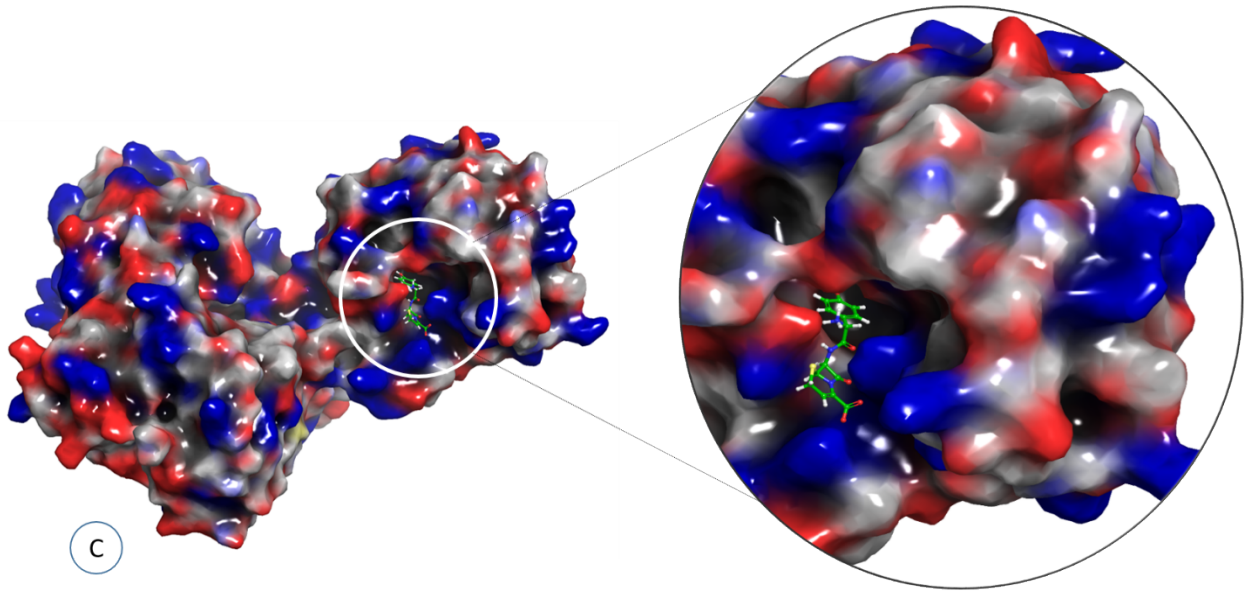
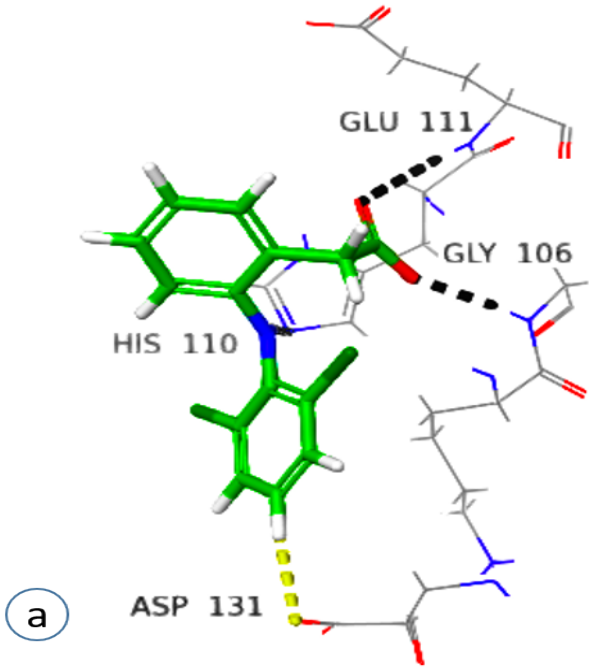


Fig. S13. Docked pose of compound **5** (Cefadroxil monohydrate): a) 3D representation of ligand-protein interaction in dotted lines indicating hydrogen bond (black), aromatic hydrogen bond (yellow) and pi pi stacking (magenta). b) 2D representation of ligand-protein profile. c) Solid surface representation of ligand protein profile, depicting the electrostatic potential distribution over the surface (red, negative regions; blue, positive regions.



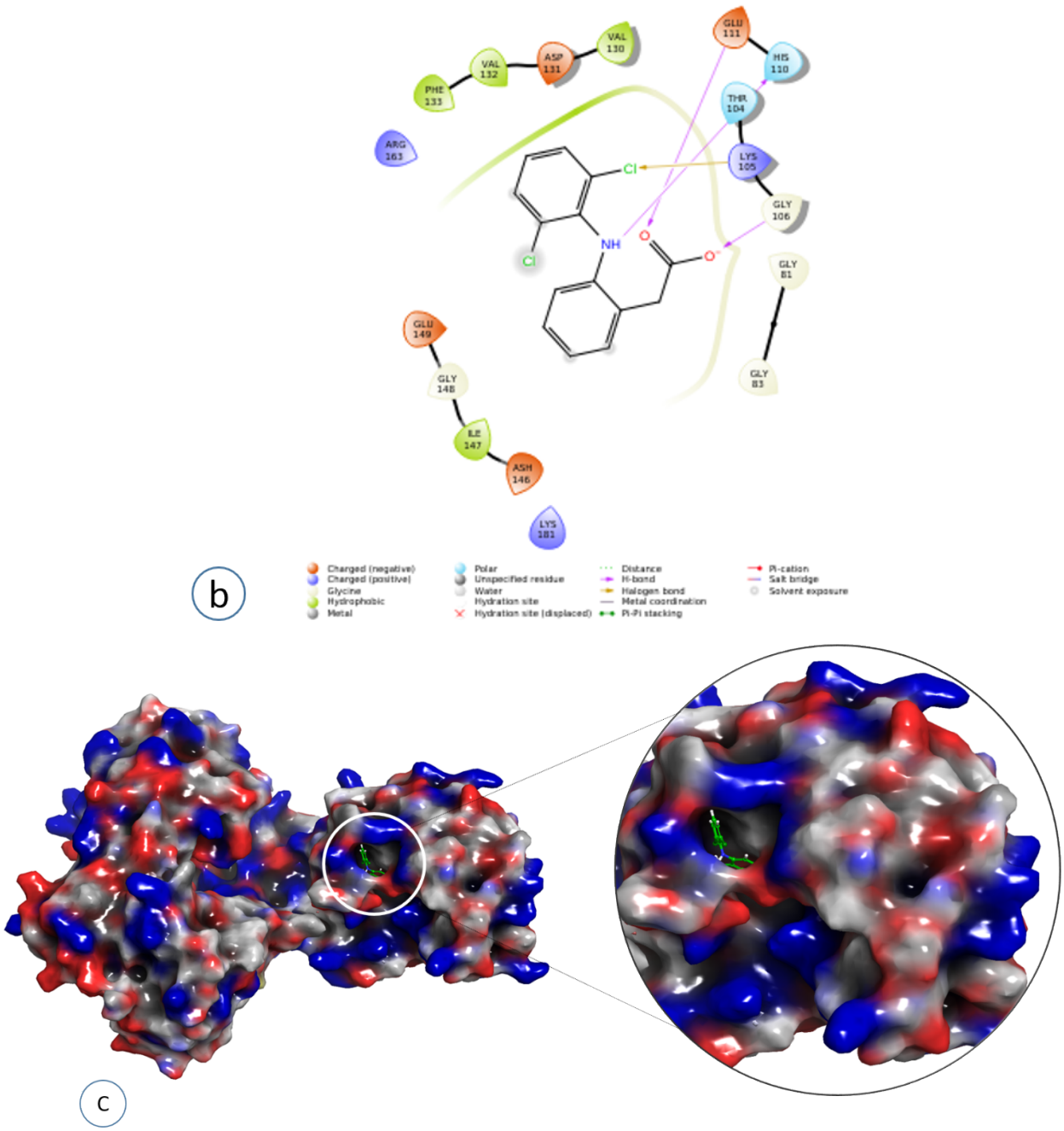
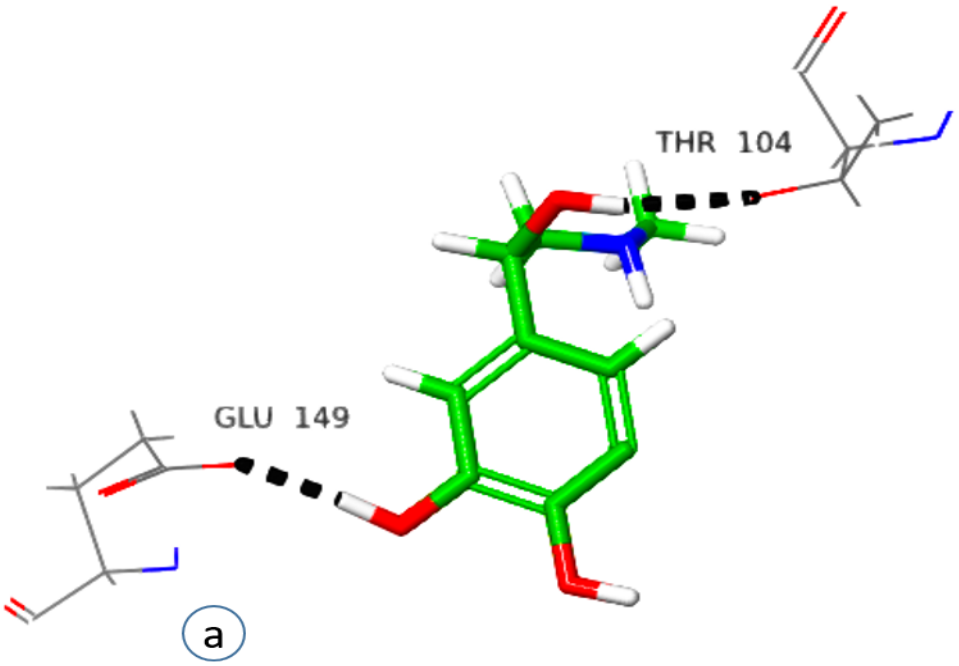
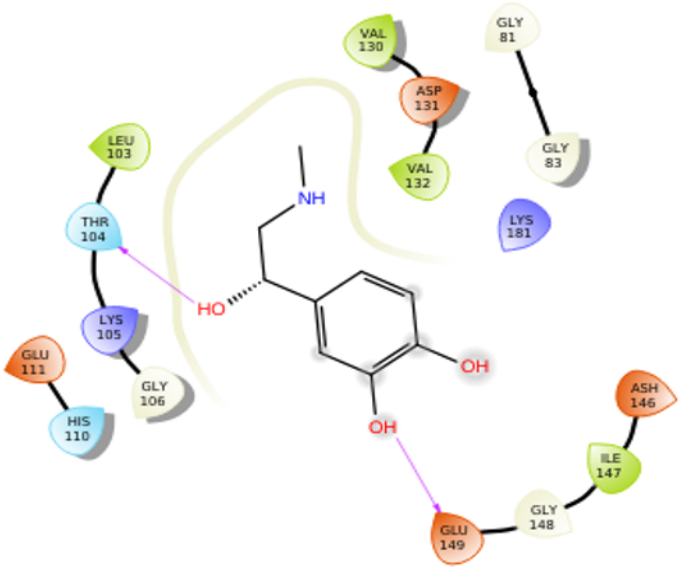


Fig. S14. Docked pose of compound **6** (Diclofenac sodium): a) 3D representation of ligand-protein interaction in dotted lines indicating hydrogen bond (black) and aromatic hydrogen bond (yellow). b) 2D representation of ligand-protein profile. c) Solid surface representation of ligand protein profile, depicting the electrostatic potential distribution over the surface (red, negative regions; blue, positive regions.


THR 104
GLU 149

a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GLY 81
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GLY 83
VAL 132
LYS 181
LEU 103
THR 104
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HO
LYS 105
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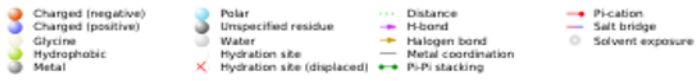
OH
OH
ASH 146
ILE 147
GLY 148
GLU 149

b


Charged (negative)
Charged (positive)
Glycine
Hydrophobic
Metal
Polar
Unspecified residue
Water
Hydration site
Hydration site (displaced)
Distance
H-bond
Halogen bond
Metal coordination
Pi-Pi stacking
Pi-cation
Salt bridge
Solvent exposure

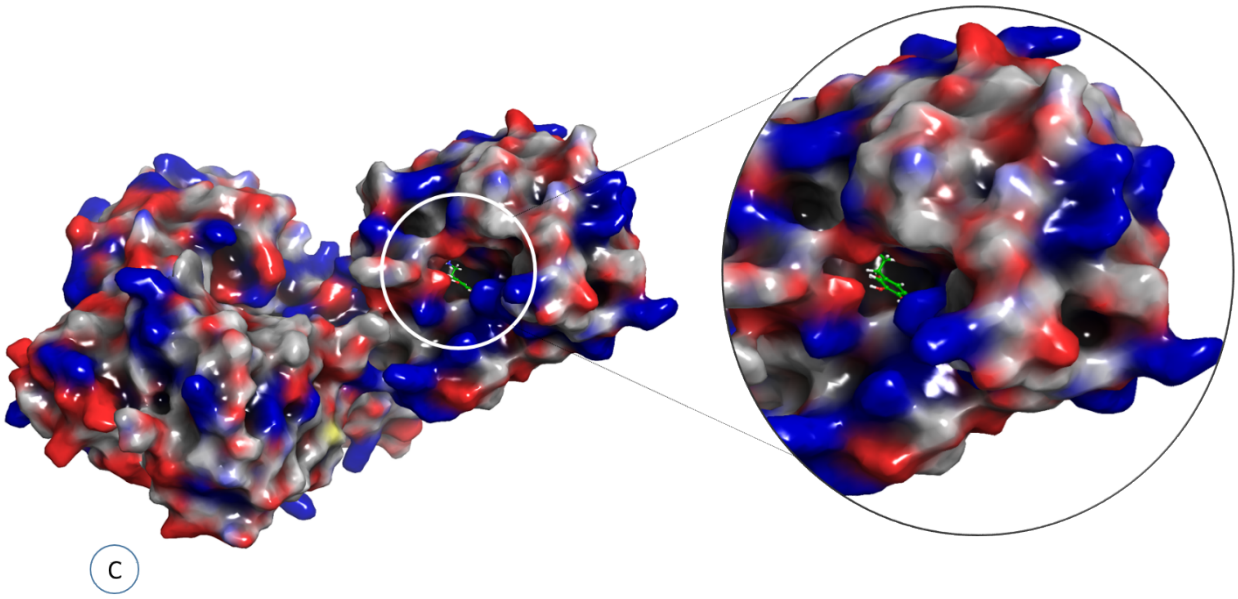
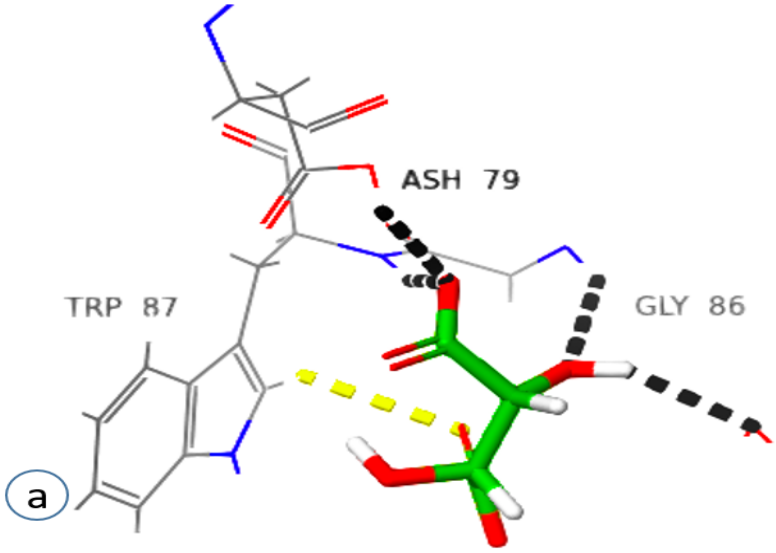


Fig. S15. Docked pose of compound **7a** (Epinephrine Bitartrate): a) 3D representation of ligand-protein (Epinephrine Bitartrate) in dotted lines indicating hydrogen bond (black). b) 2D representation of ligand protein profile. c) Solid surface representation of ligand protein profile, depicting the electrostatic potential distribution over the surface (red, negative regions; blue, positive regions



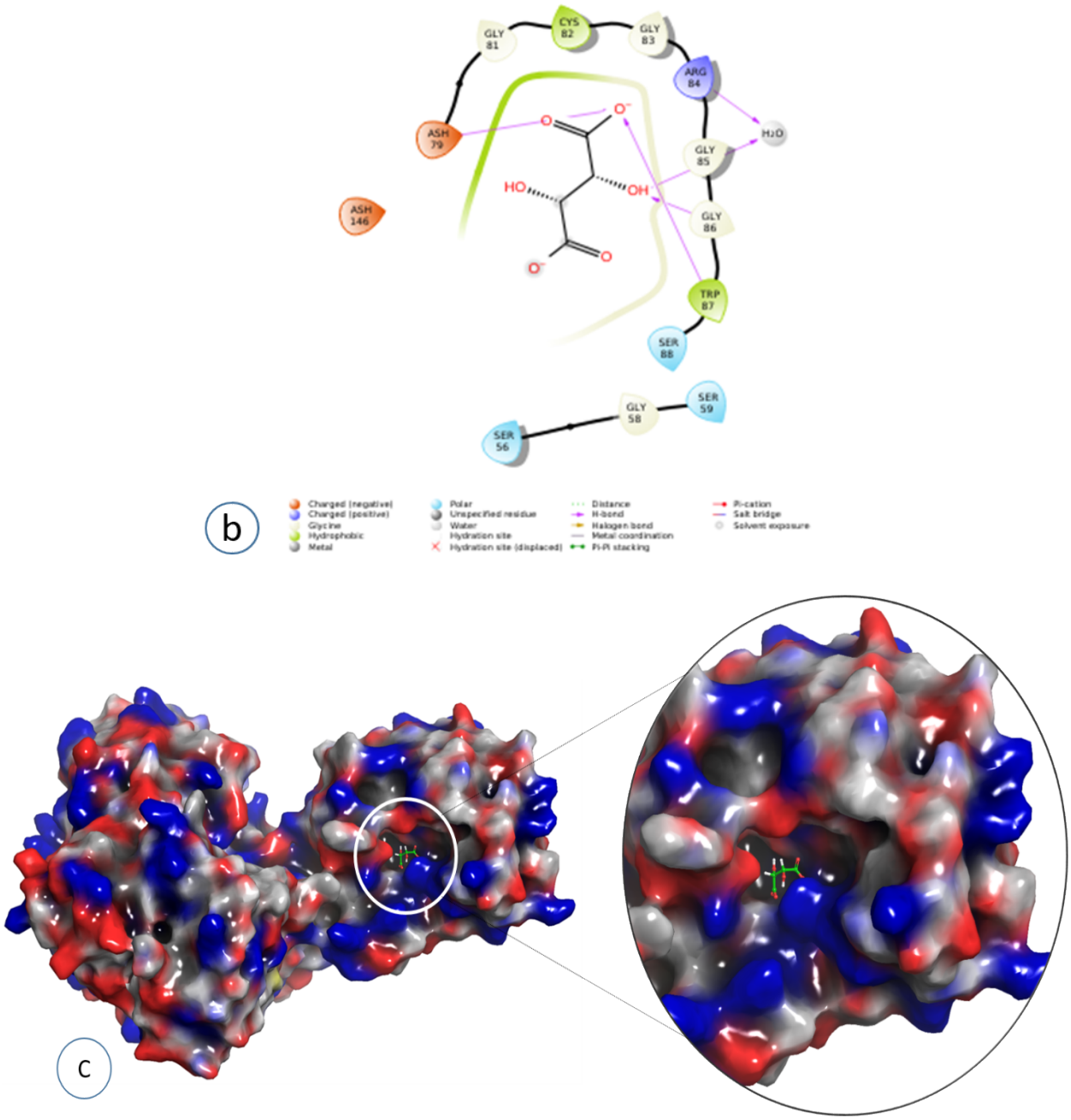
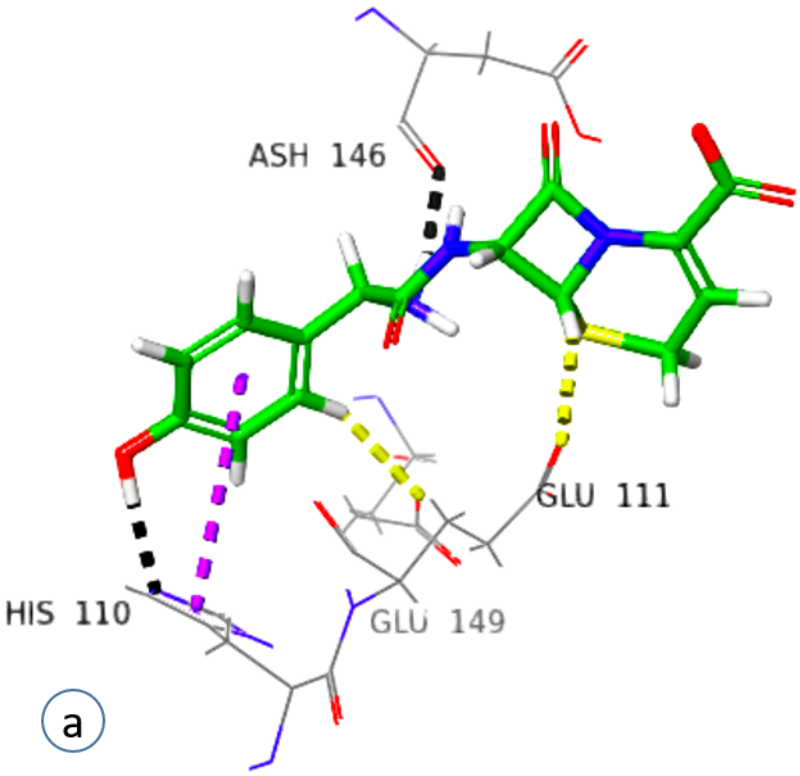


Fig. S16. Docked pose of compound **7b** (Adrenaline Bitartrate): a) 3D representation of ligand-protein (Adrenaline Bitartrate) in dotted lines indicating hydrogen bond (black) and aromatic interaction (yellow). b) 2D representation of ligand protein profile, depicting the electrostatic potential distribution over the surface (red, negative regions; blue, positive regions.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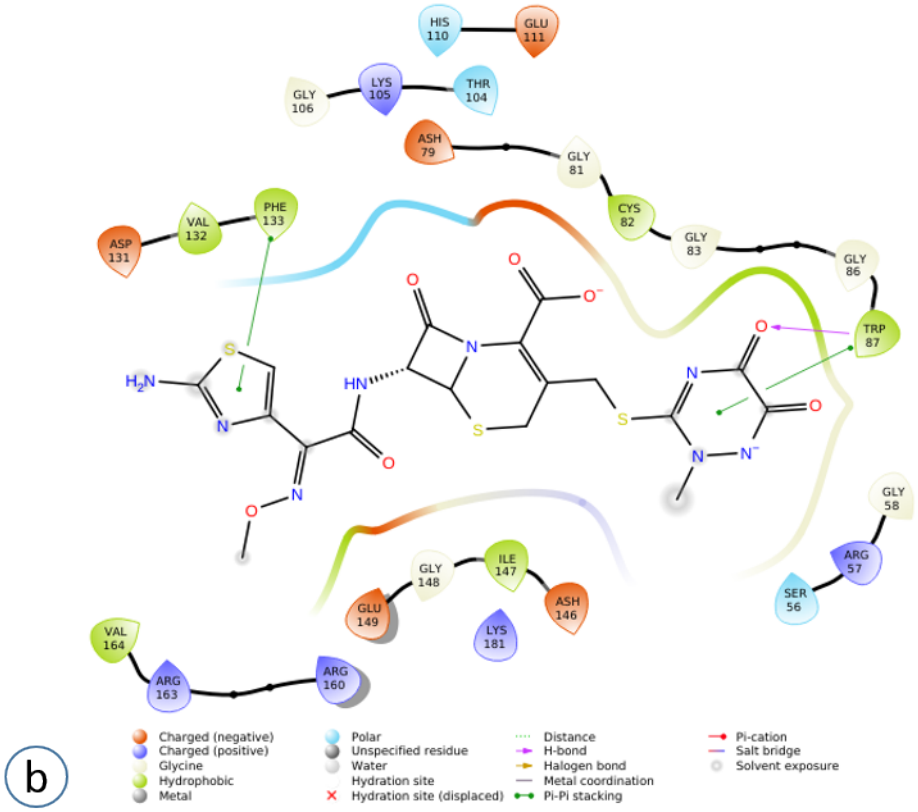
GLU 111
HIS 110
GLU 149
a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THR 104
ASH 79
GLY 81
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GLY 86
TRP 87
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PHE 133
GLY 58
ARG 57
SER 56
GLY 148
ILE 147
GLU 149
ASH 146
LYS 181
VAL 164
ARG 163
ARG 160
Charged (negative)
Charged (positive)
Glycine
Hydrophobic
Metal
Polar
Unspecified residue
Water
Hydration site
Hydration site (displaced)
Distance
H-bond
Halogen bond
Metal coordination
Pi-Pi stacking
Pi-cation
Salt bridge
Solvent exposure
b

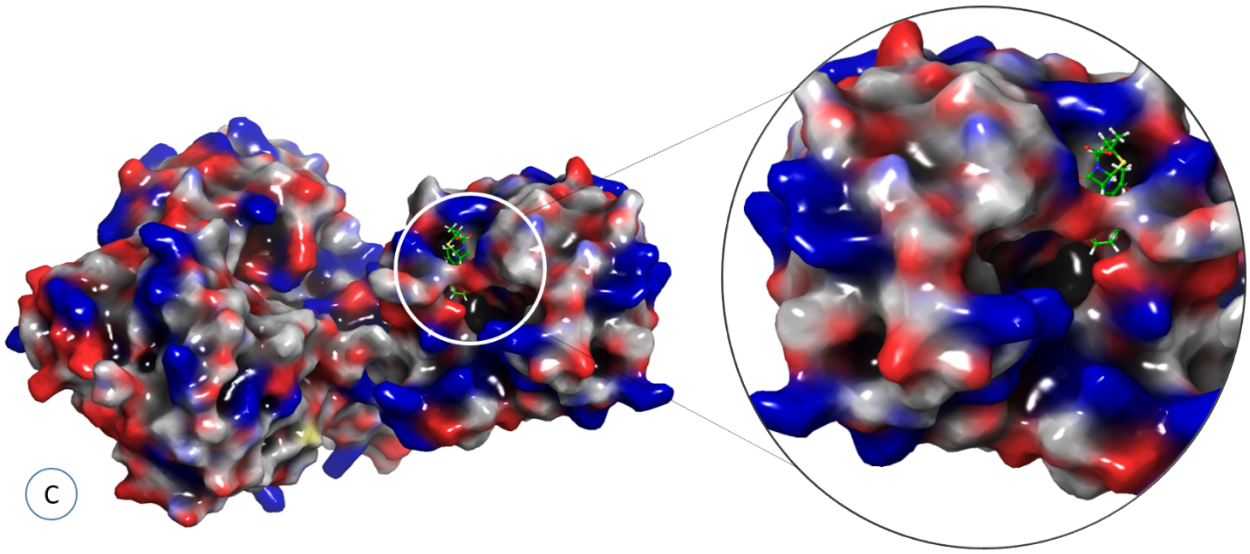
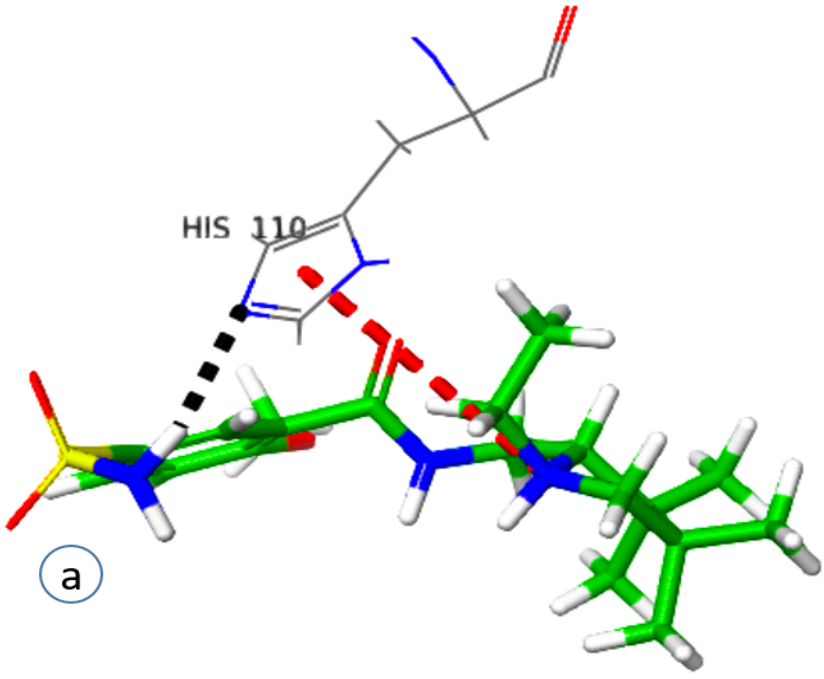


Fig. S17. Docked pose of compound **8** (Cloxacillin): a) 3D representation of ligand-protein interaction in dotted lines lines indicating hydrogen bond (black). b) 2D representation of ligand protein profile. c) Solid surface representation of ligand protein profile, depicting the electrostatic potential distribution over the surface (red, negative regions; blue, positive regions



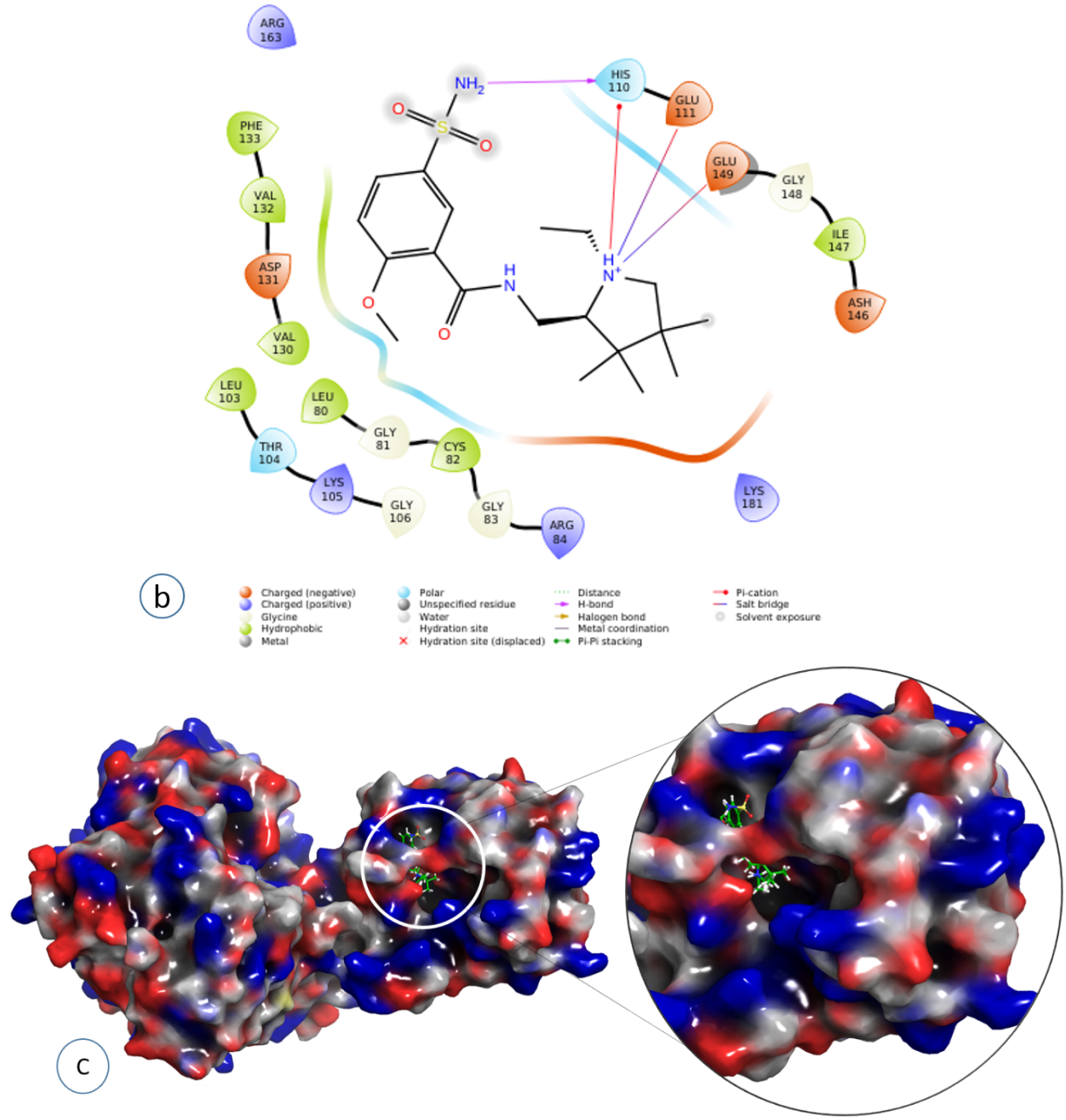
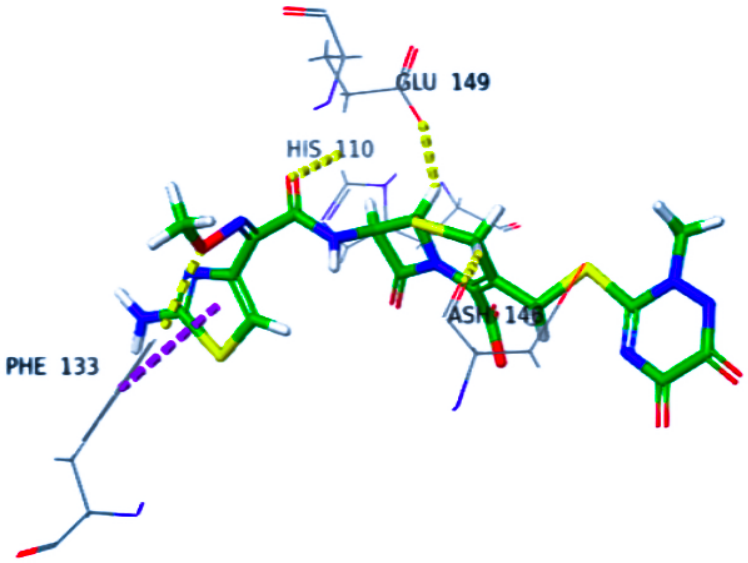


Fig. S18. Docked pose of compound **9** (Levosulpiride): a) 3D representation of ligand-protein interaction in dotted lines indicating hydrogen bond (black) and π cation interaction (red). b) 2D representation of ligand-protein profile. c) Solid surface representation of ligand protein profile, depicting the electrostatic potential distribution over the surface (red, negative regions; blue, positive regions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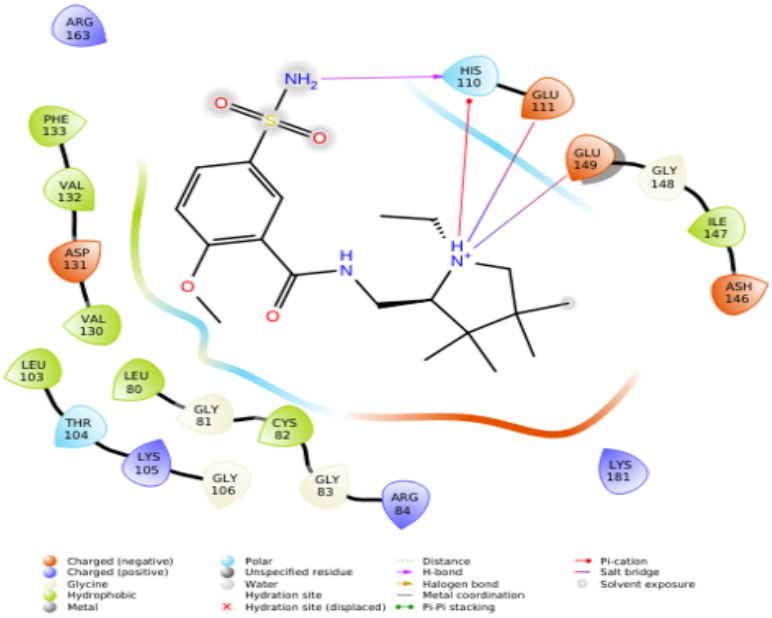
HIS 110
ASN 143
PHE 133

a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PHE 133
VAL 132
ASP 131
VAL 130
LEU 103
THR 104
LYS 105
GLY 106
LEU 80
GLY 81
CYS 82
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LYS 181
ASH 146
ILE 147
GLY 148
GLU 149
GLU 111
HIS 110
Charged (negative)
Charged (positive)
Glycine
Hydrophobic
Metal
Polar
Unspecified residue
Water
Hydration site
Hydration site (displaced)
Distance
H-bond
Halogen bond
Metal coordination
Pi-Pi stacking
Pi-cation
Salt bridge
Solvent exposure

b

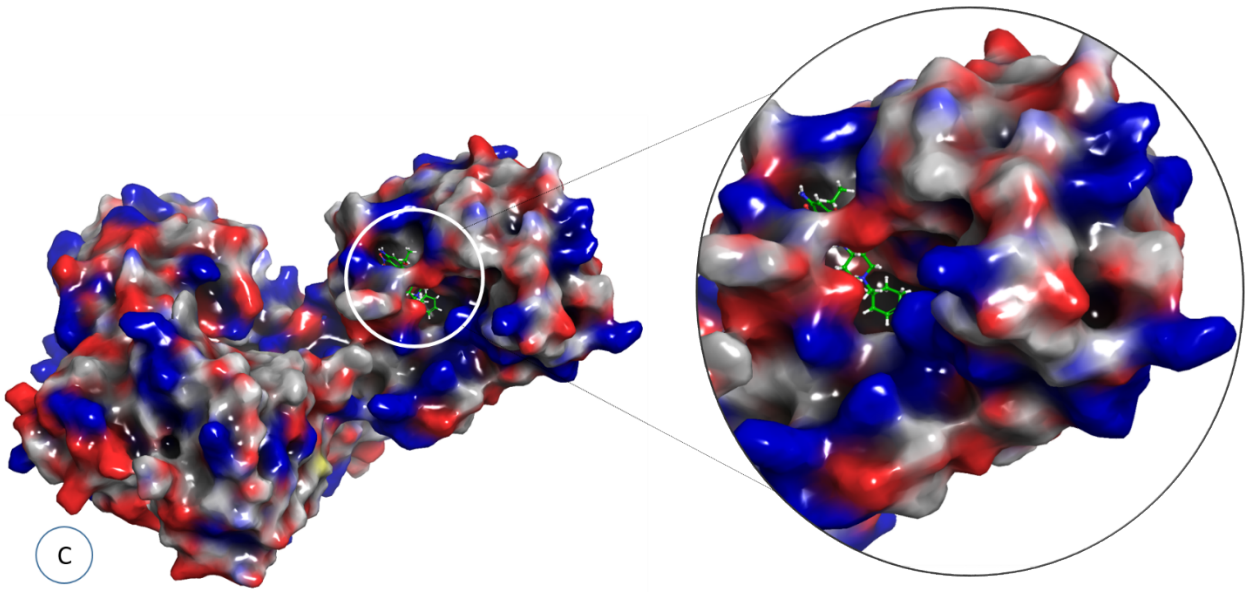
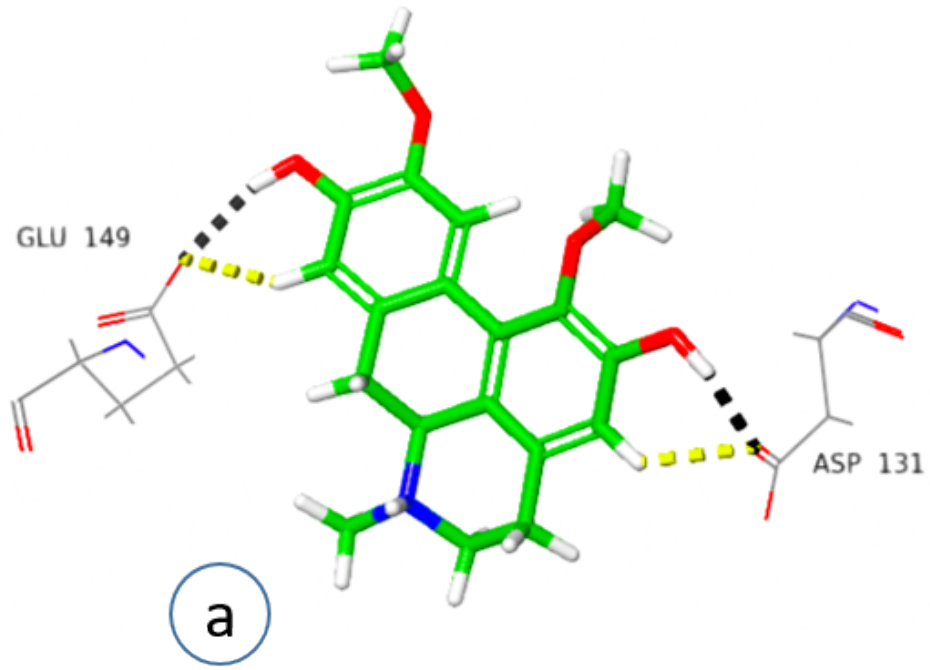


Fig. S19. Docked pose of compound **10** (cinitapride): a) 3D representation of ligand-protein interaction in dotted lines indicating aromatic interaction (yellow) and pi pi stacking (magenta).b) 2D representation of ligand-protein profile. c) Solid surface representation of ligand protein profile, depicting the electrostatic potential distribution over the surface (red, negative regions; blue, positive regions



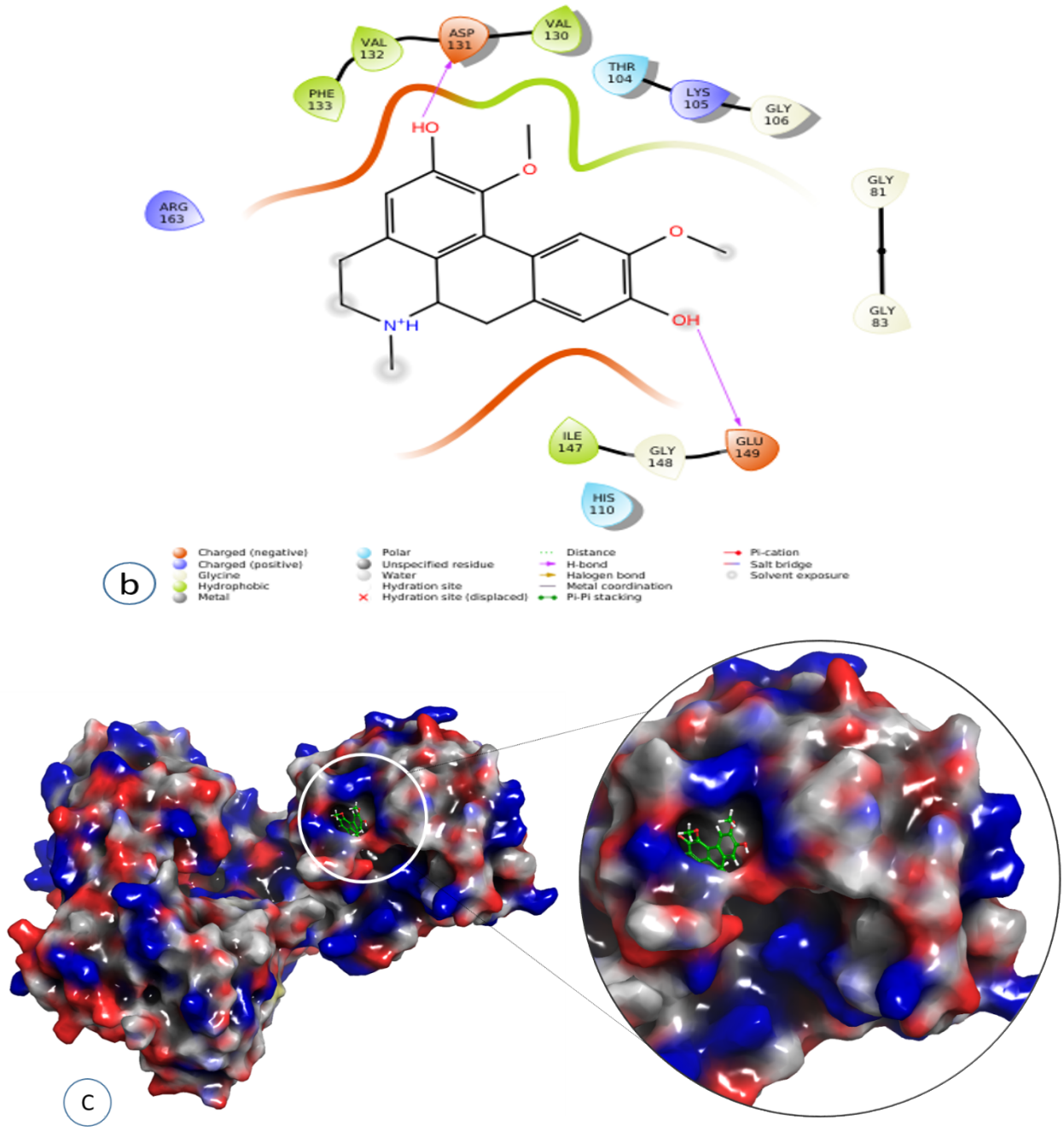


Fig. S20. Docked pose of compound **11** (Boldin): a) 3D representation of ligand-protein interaction in dotted lines indicating hydrogen bond (black) and aromatic hydrogen bond (yellow). b) 2D representation of ligand-protein profile.c) Solid surface representation of ligand-protein profile, depicting the electrostatic potential distribution over the surface (red, negative regions; blue, positive regions

Details of Mixtures made for STD-NMR Studies

Mixture (Codes of Molecular Bank PCMD)	**Drug / Molecule Name**
Mix 1	
SS024	L-Hyoscyamine
SS087	Nordihydroguaiaretic acid
3RTN024	Isopulegol
AAB535	
3RTN006	Chelidonic acid
Mix 2	
SS022	Lapachol
SS016	Silymarin
DB089	Ceftriaxone Sodium. 3.5 H_2O
DB022	Lisinopril Dihydrate
3RTN012	Phloridzin
Mix 3	
DB087	Cefixime Trihydrate
DB018	Leflunomide
DB033	Ropinirole HCl
DB008	Captopril
DB017	Itopride Hydrochloridescopl
Mix 4	
DB040	Gamma-Aminobutyric Acid
DB029	Paracetamol (Acetaminophen
DB086	Cefadroxil monohydrate
DB014	Enalaprilat Dihydrate
3RTN022	Baicalein
Mix 5	
DB050	Clopidogrel bisulfate
DB073	Nabumetone
DB003	Ampicillin Trihydrate

3RTN019	Menthofuran
3RTN011	Carvacrol
Mix 6	
DB043	Bromazepam
DB047	Chlorthalidone
DB095	Labetalol Hydrochloride
DB021	Linezolid
DB083	Valsartan
Mix 7	
AAB471	
DB094	Hydrocortisone Sodium Succinate
SS008	Strychnine Free base
DB093	Gliclazide
DB041	Aripiprazole
Mix 8	
SS023	Rotenone
DB035	Sodium valproate
SS030	Noscapine
AAB435	
DB026	Nimesulide
Mix 9	
DB092	Famotidine
DB039	Acetylsalicylic Acid (Aspirin)
DB030	Piroxicam
DB042	Atenolol
DB045	Celecoxib
Mix 10	
DB053	Diphenhydramine Hydrochloride
DB056	Enalapril Maleate

SS079	Quinidine
3RTN016	Carveol
DB063	Levocetirizine Dihydrochloride
Mix 11	
DB060	Gemfibrozil
DB019	Levosulpiride
SS033	Scopolamine cloxa hydrobromide trihydrate
3RTN023	Hesperidin
SS086	Digitoxin
Mix 12	
DB049	Cinnarizine
DB061	Hydrochlorothiazide
DB065	Loratadine
DB064	Levofloxacin Hemihydrate
DB062	Ibuprofen
Mix 13	
DB048	Cilostazol
SS069	Caffeine
DB020	Lidocaine Hydrochloride monohydrate
DB002	Amoxicillin trihydrate
DB070	Mesterolone
Mix 14	
SS013	Camptothecin
3RTN015	Neohesperidin dihydrochalcone
DB052	Diclofenac Sodium
DB068	Lumefantrine
3RTN005	Boldine
Mix 15	

DB110	Bupropion Hydrochloride
DB084	Epinephrine Bitartrate/Adrenaline Bitartrate
DB032	Probucol
DB111	Cinitapride
DB101	Cloxacillin Sodium Hydrate