Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Morphological changes in human serum albumin in presence of cationic amphiphilic drugs

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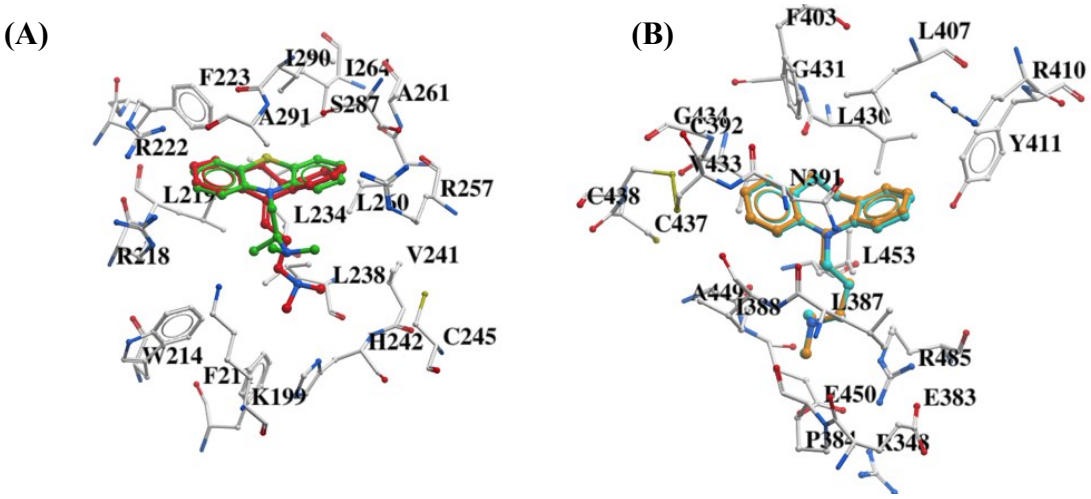
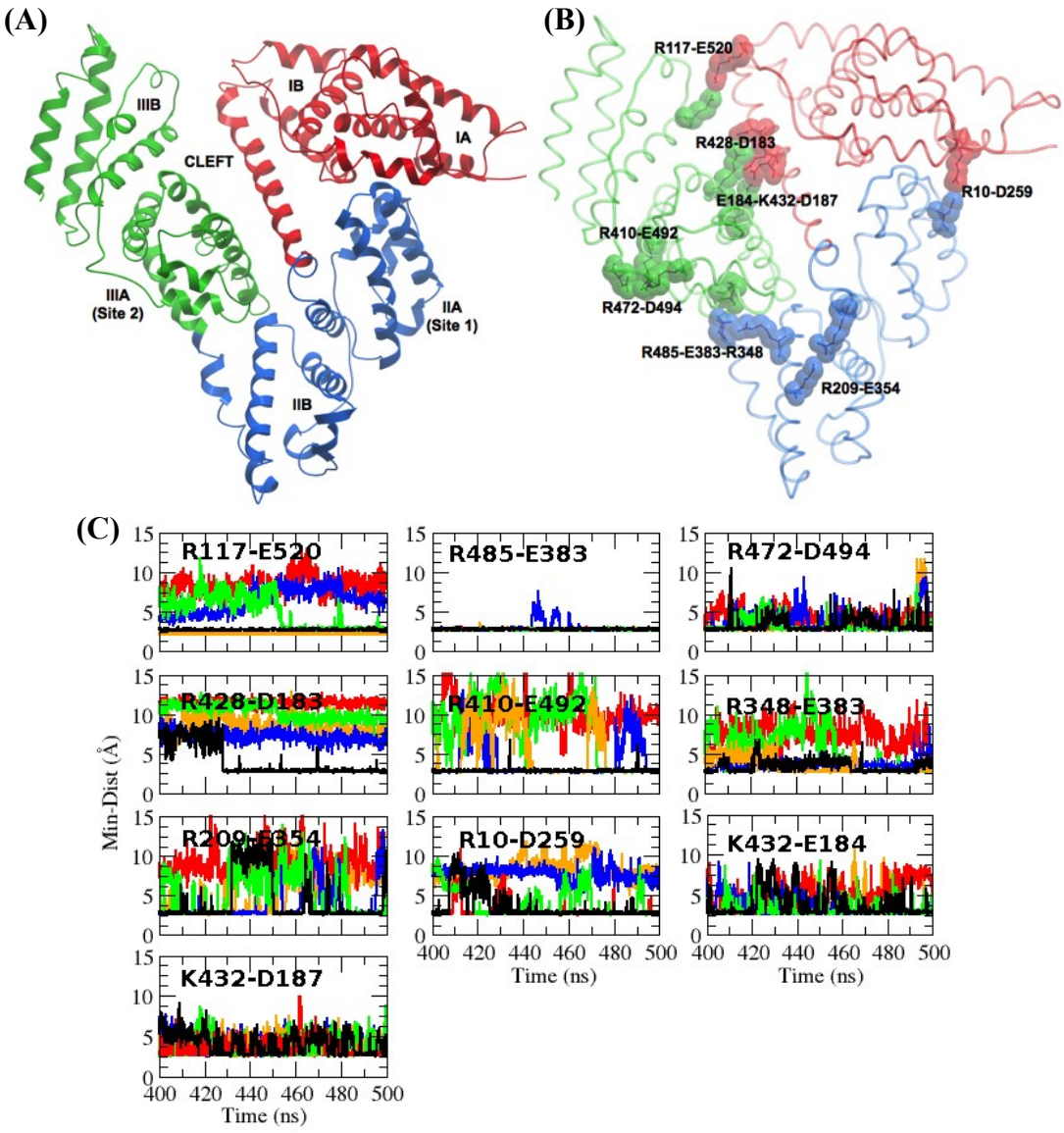
Supplementary Information

Supplementary Figure 1:



Supplementary Figure 1: A detailed view of (A) site 1 and (B) site 2. The binding sites display a predominantly hydrophobic character. AMT (red) and PMT (green) bind to site 1 in an orientation similar to that of Diclofenac as observed in PDB id 4Z69, where as AMT (orange) and IMP (cyan) dock to site 2 in a pose similar to that of Diazepam, as observed in PDB id 2BXF

Supplementary Figure 2:



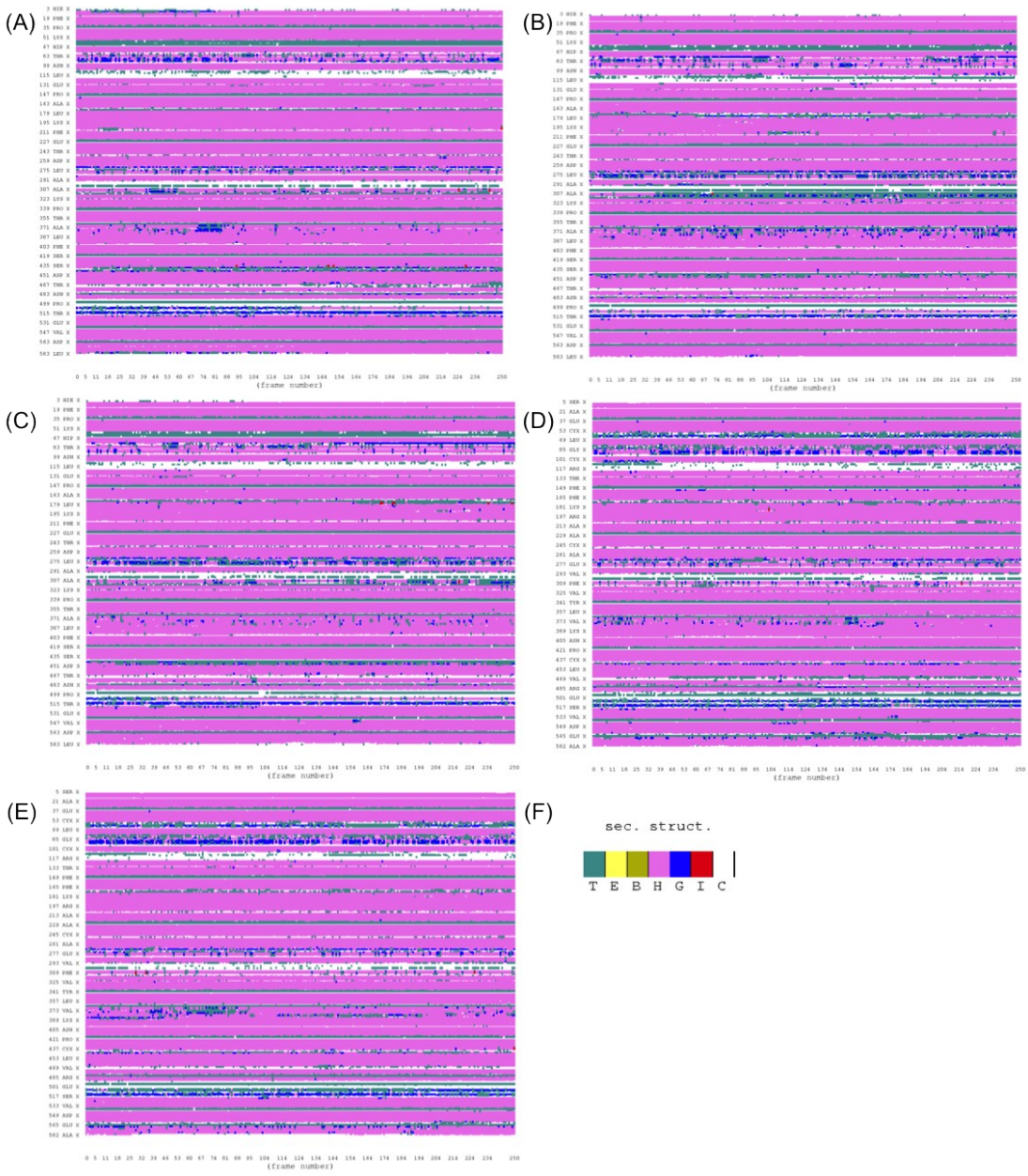
Supplementary Figure 2: (A) HSA consists of three domains, namely I (residues 1-195, red), II (residues (196-383, blue) and III (residues 384-585, green). Domains are further divided into two subdomains A and B. Binding site 1 is located in domain IIA, while site 2 is present in domain IIIA. (B) The spatial positions of ion-pair interactions used to monitor conformational drift during the simulations. (C) Ten ion-pair interactions are present at the interface between domains and were monitored to assess conformational perturbations.

Supplementary Table 1:

	RMSD (nm)				Rg (nm)				SASA (nm^2)			
	1	2	3	Av	1	2	3	Av	1	2	3	Av
HSA (apo)	0.54	**0.34**	0.31	0.39 (0.04)	2.68	2.69	2.71	2.69 (0.02)	328.6	323.8	324.2	325.5 (3.1)
HSA-AMT (site1)	0.52	0.37	**0.4**	0.43 (0.04)	2.69	2.74	2.71	2.75 (0.02)	331.4	335.1	329.6	332.1 (3.0)
HSA-PMT (site1)	0.36	**0.41**	0.43	0.40 (0.04)	2.69	2.74	2.71	2.72 (0.02)	329.9	329.8	330.9	330.2 (3.0)
HSA-AMT (site2)	0.29	0.25	**0.26**	0.27 (0.01)	2.69	2.64	2.64	2.66 (0.02)	332.5	330.1	329	330.5 (3.1)
HSA-IMP (site2)	0.26	**0.24**	0.31	0.25 (0.02)	2.69	2.64	2.65	2.65 (0.01)	329.9	324.5	325.8	326.7 (3.0)

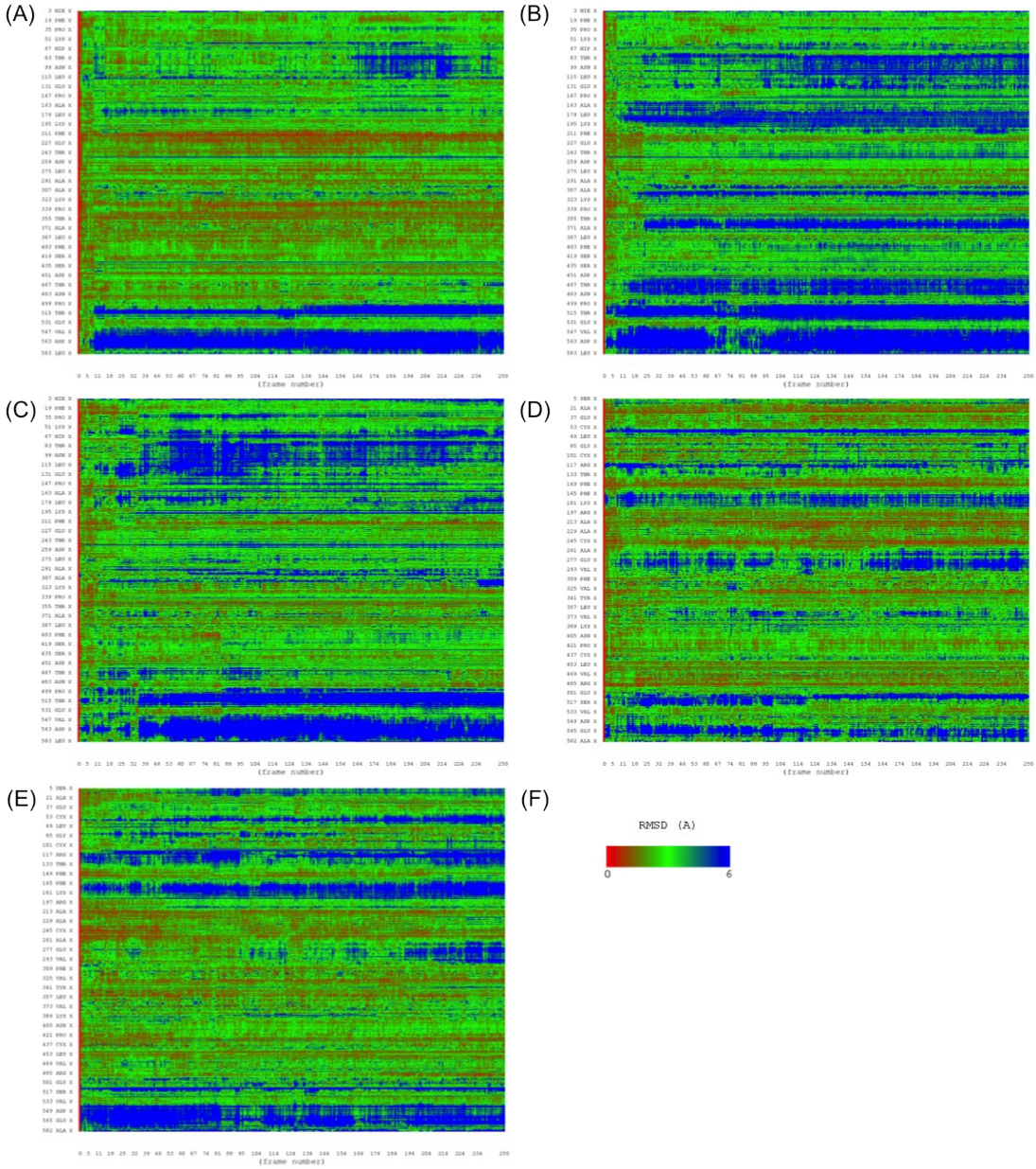
Supplementary Table 1: Root mean squared deviation (RMSD), Radius of gyration (Rg) and solvent accessible surface area (SASA) values calculated from the final 100ns (400-500ns) of the simulation run. The average values were calculated for each system and the simulation, which displayed the closest RMSD value to the average, was selected for further structural analysis (highlighted red). For example, simulation 2 of HSA(apo) was chosen for further structural analysis.

Supplementary Figure 3:



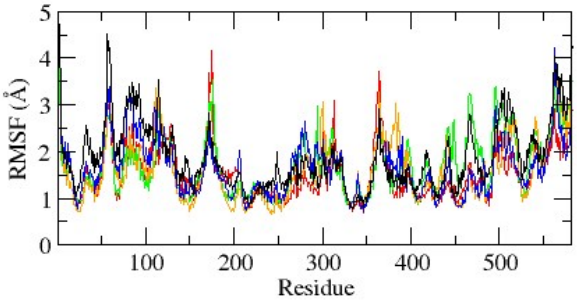
Supplementary figure 3: Secondary structure calculated at every 20th frame from (A) HSA(apo), simulation 2, (B) HSA-AMT (site 1), simulation 3, (C) HSA-PMT (site 1), simulation 2 (D) HSA-AMT (site 2), simulation 3 and (E) HSA-IMP (site 2), simulation 2. (F) The legend for secondary structure is illustrated and colour coded as: teal – turn; yellow – extended configuration; brown – isolated bridge; pink – alpha helix; blue – 3_{10} helix; red – Pi helix and white – coil (none of the above). The x-axis is the frame number and y-axis is the residue number.

Supplementary Figure 4:



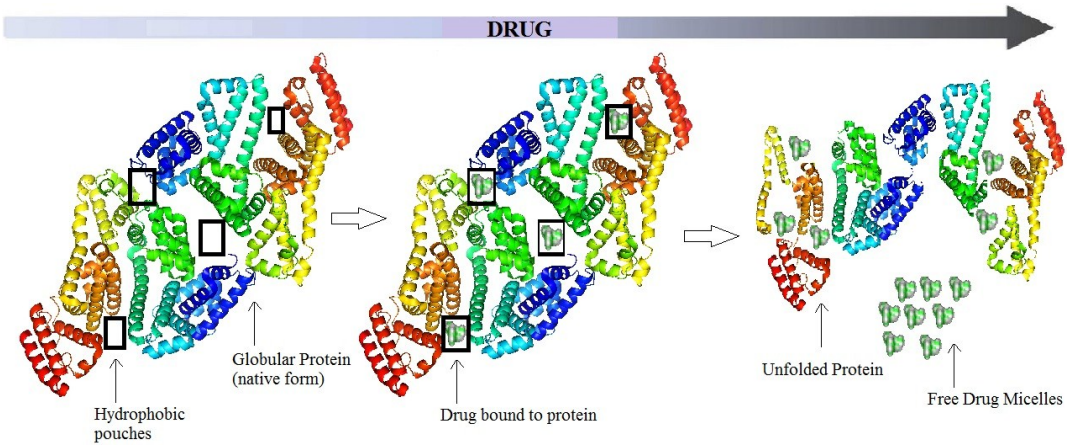
Supplementary figure 4: RMSD per residue, calculated at every 20th frame from (A) HSA(apo), simulation 2, (B) HSA-AMT (site 1), simulation 3, (C) HSA-PMT (site 1), simulation 2 (D) HSA-AMT (site 2), simulation 3 and (E) HSA-IMP (site 2), simulation 2. (F) The RMSD scale is illustrated over a range of 0-6Å. The x-axis is the frame number and y-axis is the residue number.

Supplementary Figure 5:



Supplementary figure 5: Root means squared fluctuation (RMSF), highlighting residual fluctuations. The analysis indicates that that the drugs, when bound in site 1 exhibited pronounced structural effects on the protein than when bound in site 2.

Supplementary Figure 6:



Supplementary figure 6: Predicted model of HSA(apo) and cationic amphiphilic drugs. Both SANS and DLS studies suggest that the protein gets unfolded in presence of the cationic amphiphillic drugs, and after saturation of protein, there is formation of free micelles of the drugs.