Electronic Supplementary Information

Table S1 PDB codes and ligand/drug and myristic acids binding sites for selected HSA crystal structures.

PDB code	Ligand/drug name	Ligand/drug binding site[a]	Myristic acid binding site[a]
1HA2	S-Warfarin	IIA	FA1, FA2, FA3, FA4, FA5, FA6
1HK1	L-Thyroxine	IIA IIIA IIIB	-
1O9X	Hemin	IB	FA2, FA3, FA4, FA5, FA6, FA7
2BXB	Oxyphenbutazone	IIA	-
2BXD	R-Warfarin	IIA	-
2BXF	Diazepam	IIIA	-
2BXI	Azapropazone	IB IIA	FA2, FA3, FA4, FA5, FA6
2BXK	Indomethacin, Azapropazone	IIA	FA1, FA2, FA3, FA4, FA5, FA6
2VUE	4*Z*,15*E*-Bilirubin-IXalpha	IB	-
2VUF	Fusidic acid	IB IIIB	-
2XVU	Dansyl-L-Asparagine	IIA IIIA	-
3CX9	Lysophosphatidylethanolamine	IIA	FA2, FA3, FA4, FA5, FA6
4L9K	Camptothecin	IB	-
4L9Q	Tenoposide	IB	-
4LA0	R-Bicalutamide	IB	-
1E7G	-	-	FA1, FA2x2, FA3, FA4, FA5, FA6, FA7

[a] Binding sites notations are taken from Ref. 29 of the main text.

Table S2 Overlapping of proposed phycocyanobilin binding sites (IB and IIA) and binding sites for ligands/drugs on 14 HSA crystal structures found in the PDB.

PDB code	Ligand/drug name	Binding site IB on HSA	Binding site IIA on HSA
1HA2	S-Warfarin	-	R222, H242, R257
1HK1	L-Thyroxine	-	K195, K199, W214, R218, R222, H242, R257
1O9X	Hemin	R114, R117, Y138, Y161	-
2BXB	Oxyphenbutazone	-	K195, Q196, K199, W214, R218, R222, H242, R257
2BXD	R-Warfarin	-	K199, R222, H242, R257
2BXI	Azapropazone	R117, Y138, R186	K199, R218, R222, H242, R257
2BXK	Indomethacin	-	K199, W214, R218
	Azapropazone	-	K199, R218, R222, H242, R257
2VUE	4*Z*,15*E*-Bilirubin-IXalpha	R117, F134, Y138, R145, Y161, R186	-
2VUF	Fusidic acid	R117, F134, Y138, Y161, R186	-
2XVU	Dansyl-L-Asparagine	-	K199, W214, R222, H242, R257
3CX9	Lysophosphatidyl-ethanolamine	-	Q196, K199, W214, R222, H242, R257
4L9K	Camptothecin	R117, Y138, Y161, R186	-
4L9Q	Tenoposide	R117, F134, Y138, E141, Y161, D183, R186,	-
4LA0	R-Bicalutamide	R117, F134,Y138, E141	-

Table S3 Re-docking simulations RMSD values and phycocyanobilin binding energies for 16 HSA crystal structures extracted from PDB.

PDB code	Ligand/drug binding site	Re-dock RMSD value	PCB binding site	Binding energy (kcal/mol)
1HA2	IIA	0.2243	IIA	10.5
			IB	10.8
1HK1	IIA IIIB IIIA	0.6964 IIA 0.2995 IIIB 0.8722 IIIA	IIA	9.9
			IB	8.7
1O9X	IB	0.5652	IIA	9.7
			IB	10.5
2BXB	IIA	0.3047	IIA	8.5
			IB	8.8
2BXD	IIA	0.0000	IIA	8.7
			IB	9.7
2BXF	IIIA	0.2091	IIA	9.1
			IB	8.8
2BXI	IB IIA	0.5567 IB 0.8713 IIA	IIA	9.3
			IB	10.5
2BXK	IIA IMN[a] IIA AZQ[a]	0.1384 IMN[a] 0.9941 AZQ[a]	IIA	10.2
			IB	9.7
2VUE	IB	0.3310	IIA	8.6
			IB	8.4
2VUF	IB IIIB	0.3017 IB 2.2162 IIIB	IIA	8.5
			IB	9.1
2XVU	IIA IIIA	0.3467 IIA 0.3239IIIB	IIA	9.5
			IB	9.3
3CX9	IIA	0.5311	IIA	9.5
			IB	9.5
4L9K	IB	0.2581	IIA	8.9
			IB	10.2
4L9Q	IB	0.2293	IIA	9.6
			IB	10.3
4LA0	IB	3.8581	IIA	9.2
			IB	10.3
1E7G	-	-	IIA	9.3
			IB	10.7

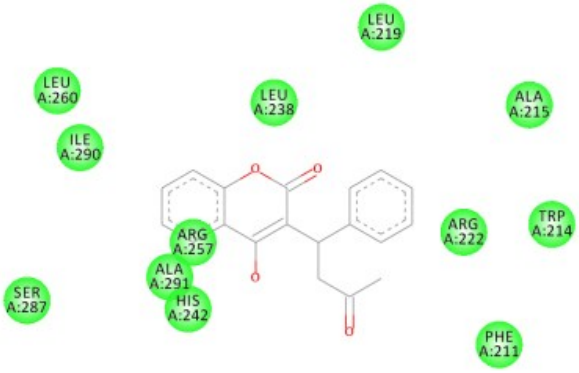
[a] IMN - Indomethacin; AZQ - Azapropazone

Table S4 Phycocyanobilin binding energies for 6 HSA crystal structures with myristic acids extracted from PDB.

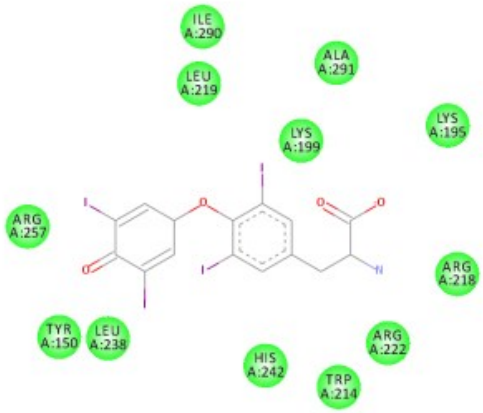
PDB code	Myristic acid binding site	PCB binding site	Binding energy (kcal/mol)
1HA2	FA1, FA2, FA3, FA4, FA5, FA6	IIA	10.5
		IB	-
1O9X	FA2, FA3, FA4, FA5, FA6, FA7	IIA	10.4
		IB	10.5
2BXI	FA2, FA3, FA4, FA5, FA6	IIA	9.3
		IB	10.6
2BXK	FA1, FA2, FA3, FA4, FA5, FA6	IIA	10.3
		IB	-
3CX9	FA2, FA3, FA4, FA5, FA6	IIA	9.5
		IB	9.5
1E7G	FA1, FA2x2, FA3, FA4, FA5, FA6, FA7	IIA	8.2
		IB	-

Table S5 Phycocyanobilin binding energies for 14 HSA crystal structures with ligand present at the same binding site on protein.

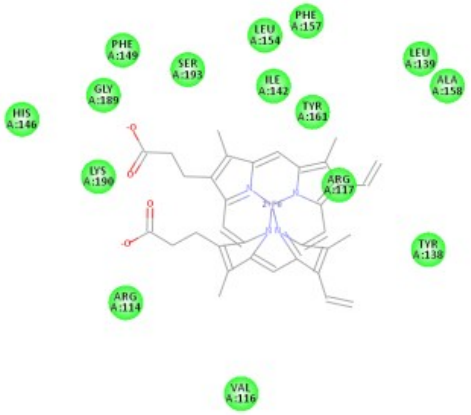
PDB code	Ligand/Myristic acid binding site	PCB binding site	Binding energy (kcal/mol)
1HA2	IIA, FA1, FA2, FA3, FA4, FA5, FA6	IIA	-
1HK1	IIA	IIA	-
1O9X	IB, FA2, FA3, FA4, FA5, FA6, FA7	IB	-
2BXB	IIA	IIA	-
2BXD	IIA	IIA	-
2BXI	IB, IIA, FA2, FA3, FA4, FA5, FA6	IIA IB	8.6 -
2BXK	IIA IMN, IIA AZQ	IIA	9.0
2VUE	IB	IB	-
2VUF	IB, IIIB	IB	-
2XVU	IIA, IIIA	IIA	-
3CX9	IIA, FA2, FA3, FA4, FA5, FA6	IIA	9.0
4L9K	IB	IB	-
4L9Q	IB	IB	-
4LA0	IB	IB	-



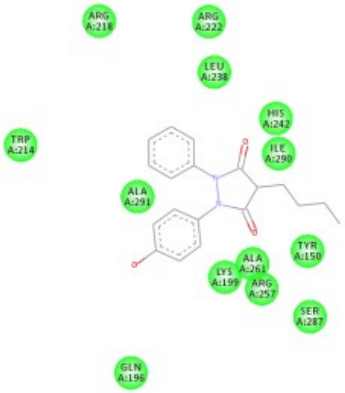
1HA2 IIA



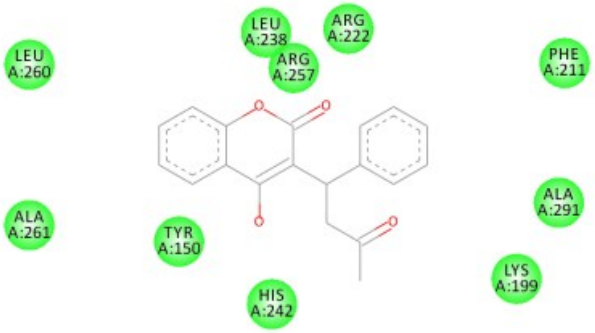
1HK1 IIA



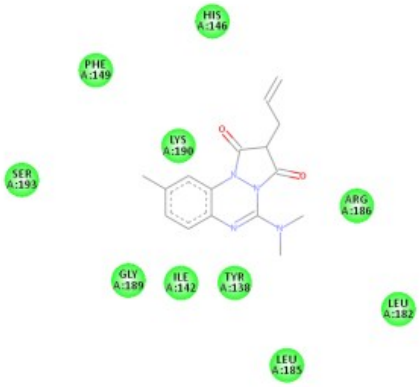
109X IB



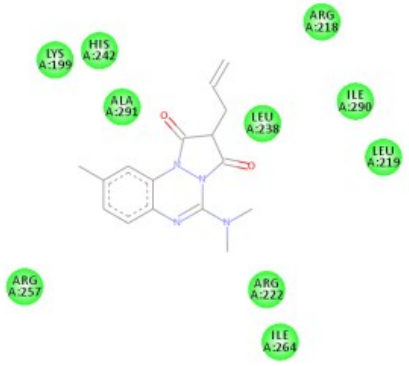
2BXB IIA



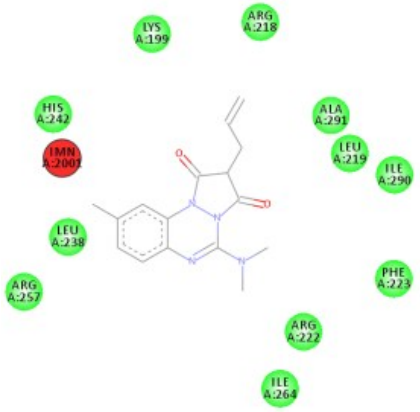
2BXD IIA



2BXI IB



2BXI IIA



2BXK AZQ IIA

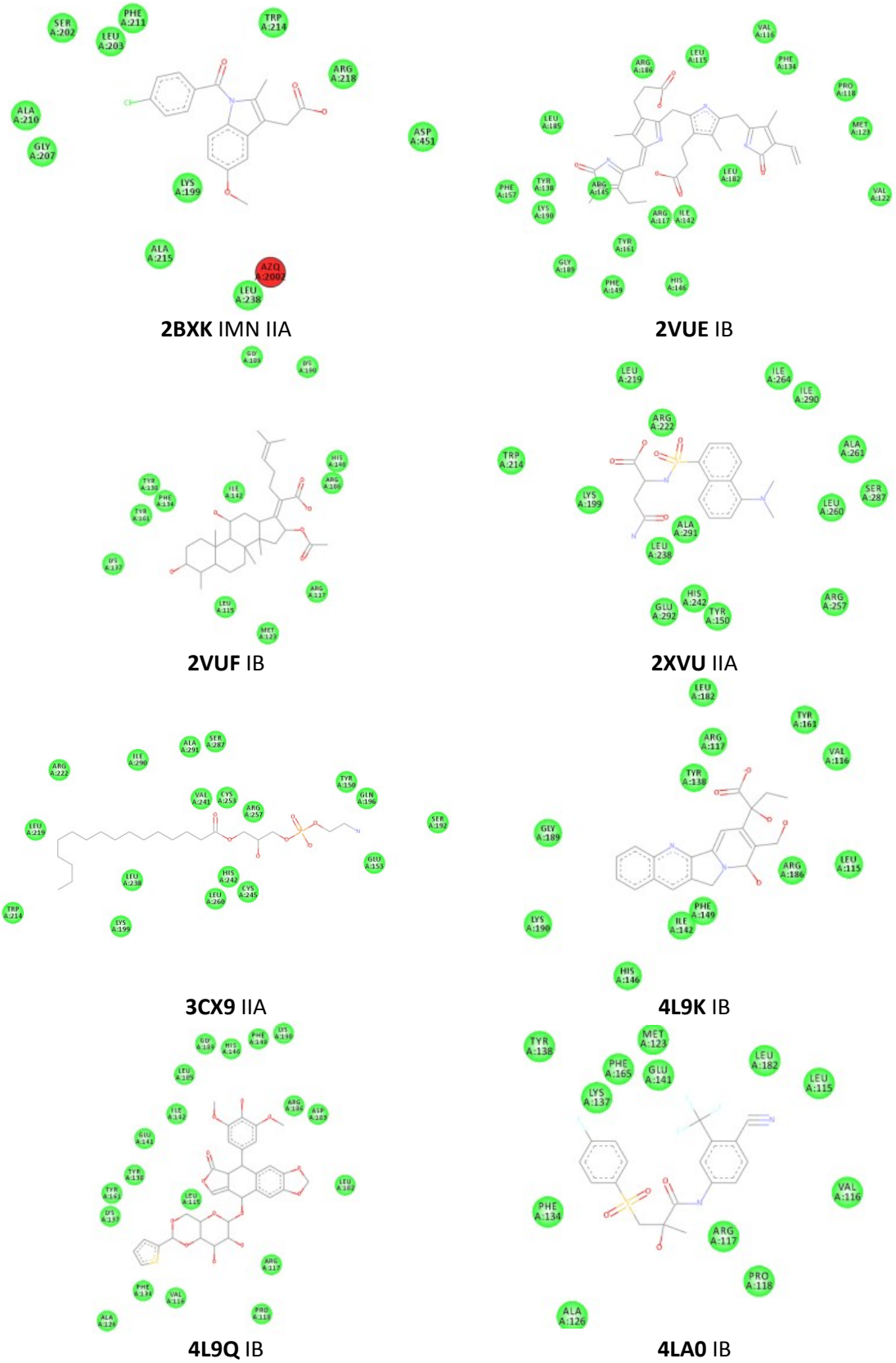


Figure S1 Amino acid residues within 3.5Å from the ligand/drug binding site (IIA or IB) for ligands/drugs from selected HSA crystal structures.

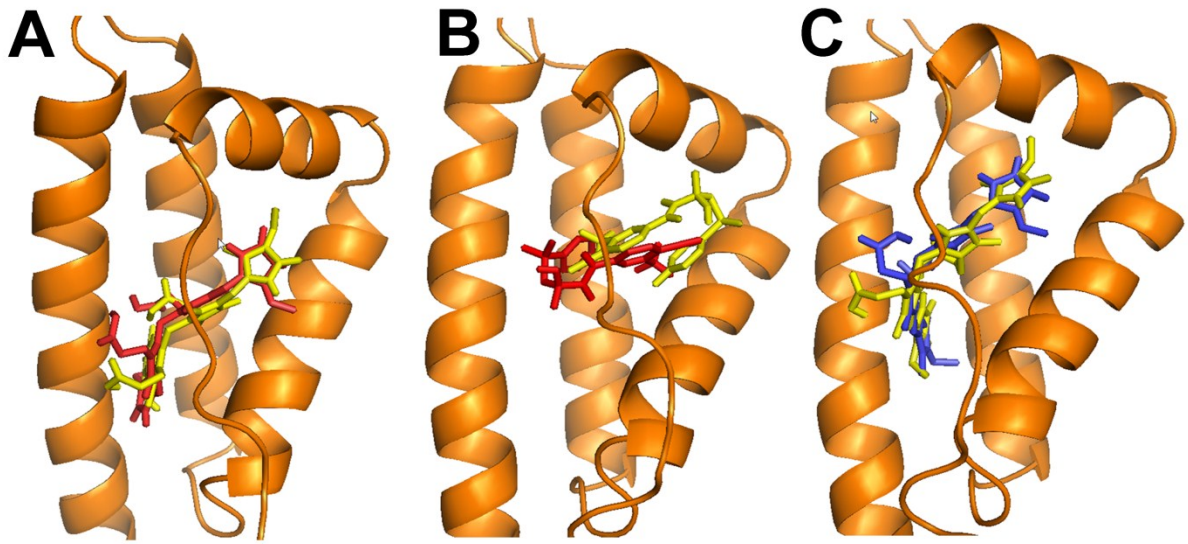


Figure S2 Re-docked (yellow) and crystallographic (red) positions for: **(A)** 2VUE (RMSD value 0.3310) structure and **(B)** 4LA0 (RMSD value 3.8581) structure; **(C)** Superimposition of docked phycocyanobilin (purple) and cristalographically found 4*Z*,15*E*-bilirubin-IXα (yellow) in PDB 2VUE structure.

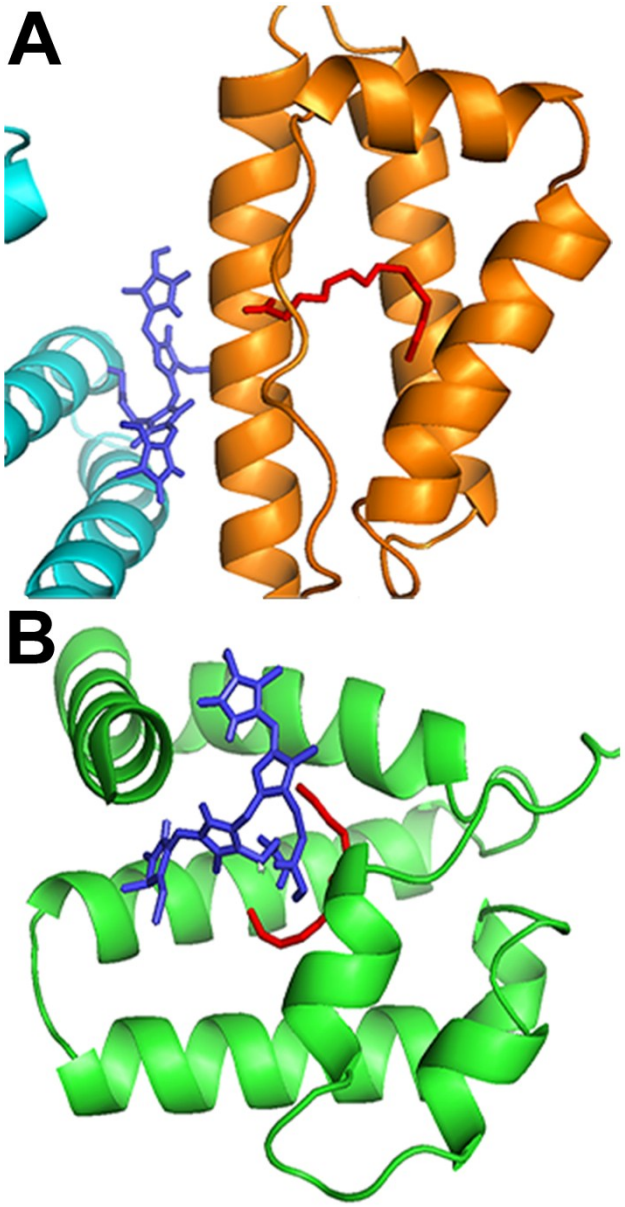


Figure S3 (A) Myristic acid (red) at the FA1 site and docked phycocyanobilin (purple) towards the cleft binding site; **(B)** Myristic acid (red) at the FA7 site and docked phycocyanobilin (purple) in the IIA binding site.

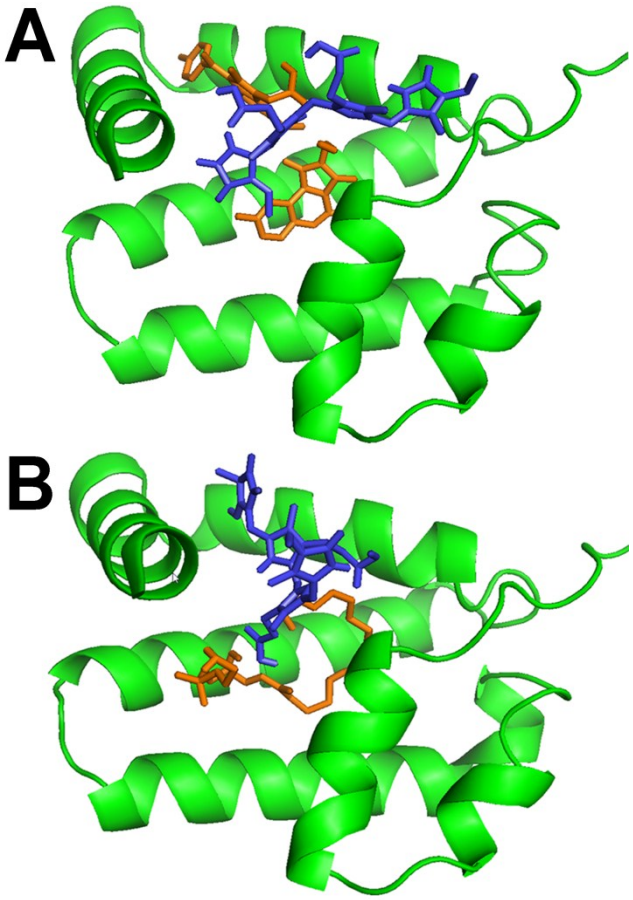


Figure S4 Ligand(s) (orange) and docked phycocyanobilin (purple) in the IIA binding site, PDB codes: 2BXK **(A)** and 3CX9 **(B)**.

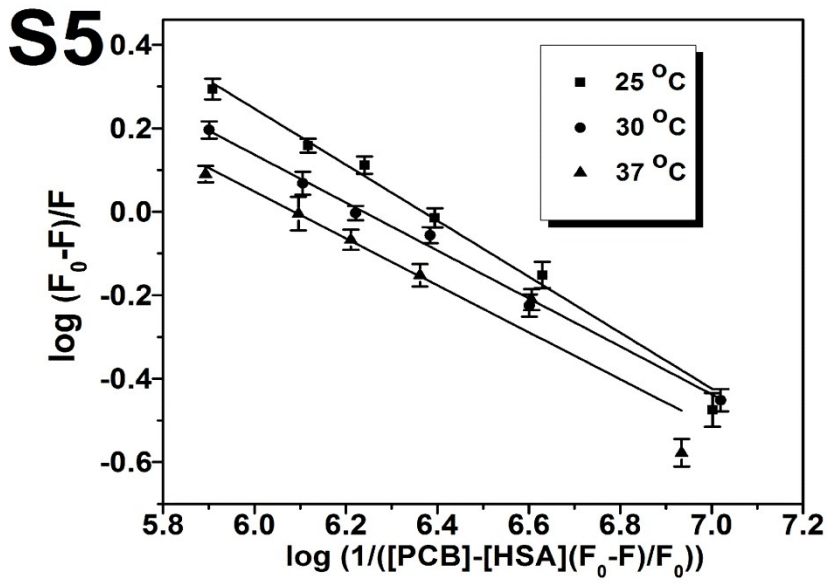


Figure S5 Fluorescence quenching based plots (from data for determination of binding constants and number of binding sites of HSA-phycocyanobilin complex at different temperatures). Error bars represent standard deviation.

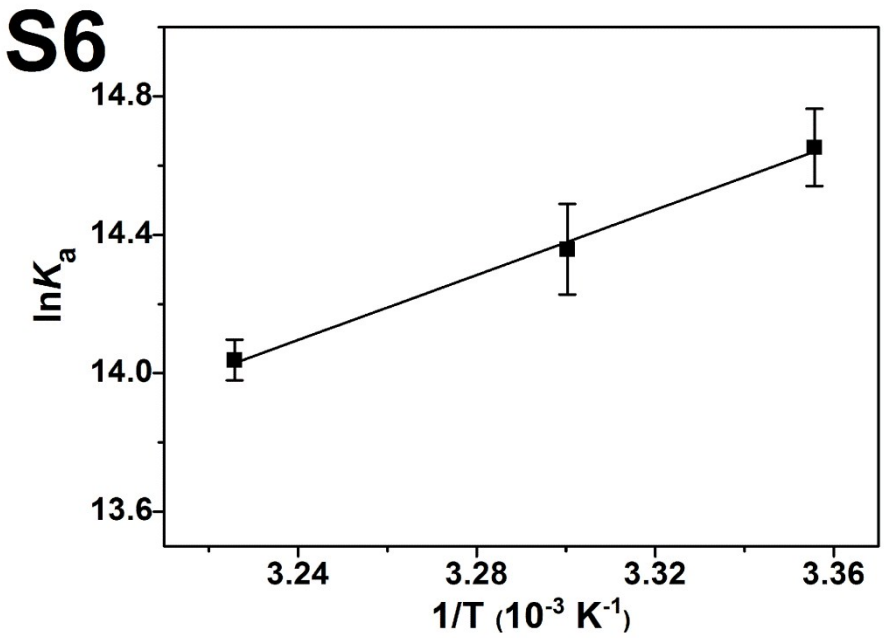


Figure S6 Plot based on Van't Hoff equation for determination of thermodynamic parameters of HSA-phycocyanobilin system. Error bars represent standard deviation.

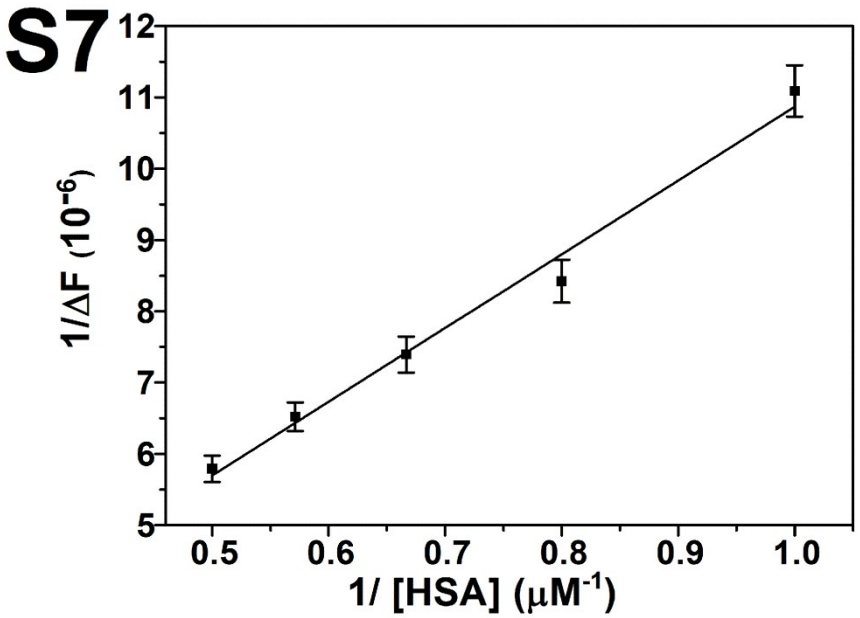


Figure S7 Fluorescence enhancement based plots for determination of binding constant of HSA-phycocyanobilin complex. Error bars represent standard deviation.

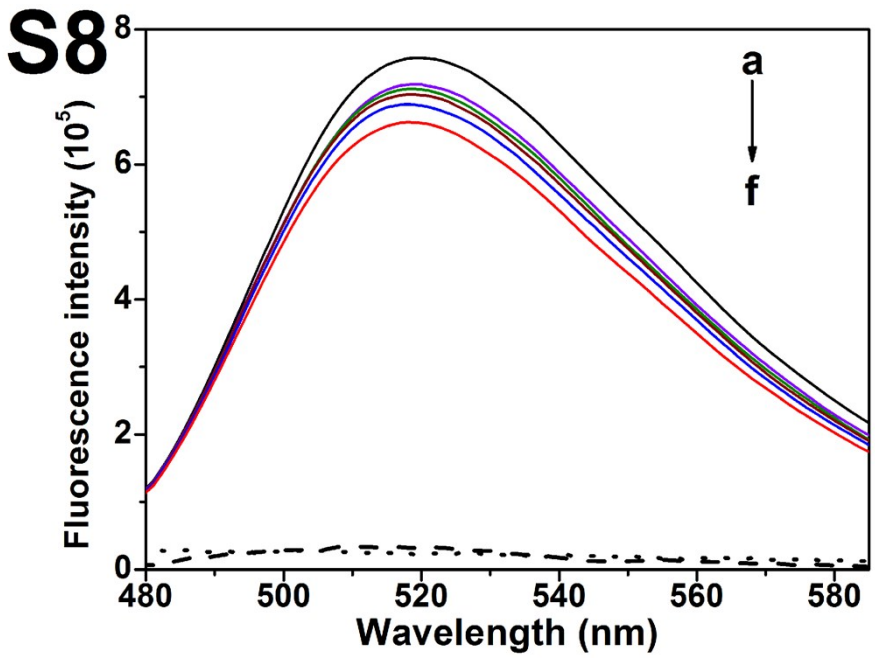


Figure S8 Quenching of HSA-bilirubin complex (2 μM both) by warfarin (0, 2, 4, 6, 8 and 20 μM, for curves a to f, respectively) (excitation wavelength 460 nm). Dot line curve: 2 μM bilirubin, dash line curve: 2 μM HSA in presence of 20 μM warfarin.

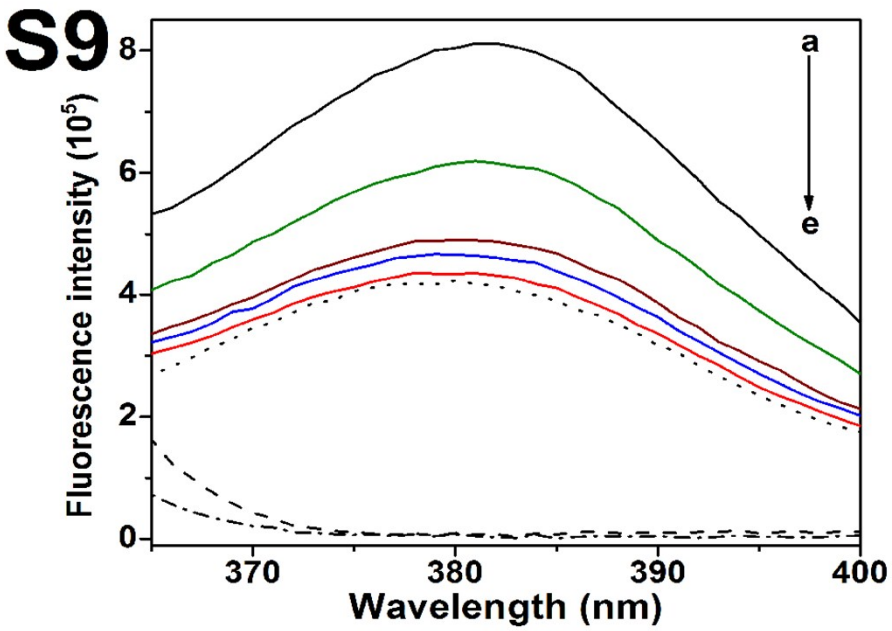


Figure S9 Quenching of HSA-warfarin complex (0.25 μM both) by bilirubin (0, 0.125, 0.25, 0.375, and 0.5, for curves a to e, respectively) using synchronous fluorescence spectroscopy, Δλ 64 nm. Dash line curve: 0.25 μM HSA. Dot line curve: 0.25 μM warfarin. Dash-dot line curve represents 0.25 μM HSA in presence of 0.5 μM bilirubin.

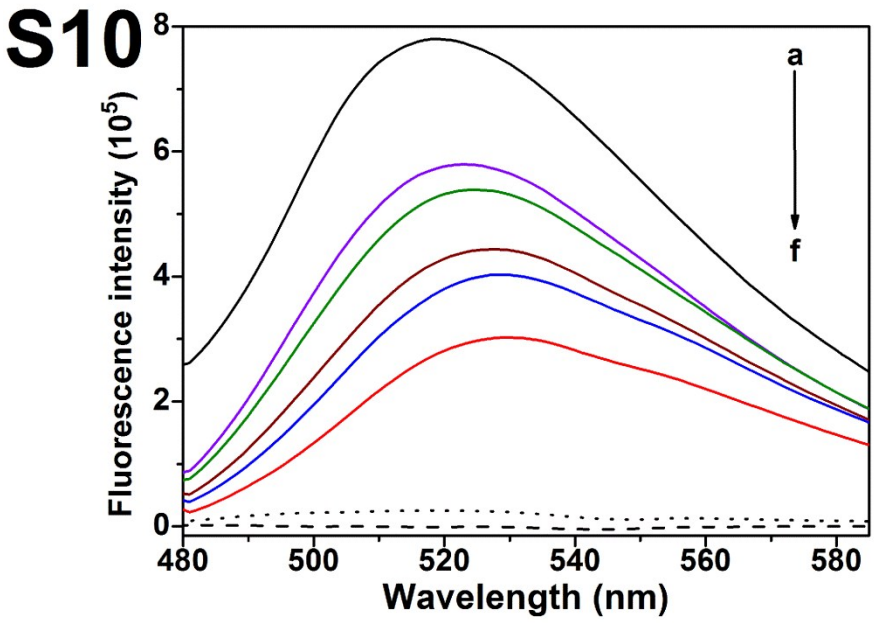


Figure S10 Quenching of HSA-bilirubin complex (2 μM both) by hemin (0, 1, 2, 3, 4, and 5 μM, for curves a to f, respectively) (excitation wavelength 460 nm). Dot line curve: 2 μM bilirubin, dash line curve: 2 μM HSA in presence of 5 μM hemin.