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Supporting information for article:

Organism-specific differences in the binding of ketoprofen to serum albumin

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Human SA	1	DAHKSEVAHREFKDLGEENFKALVLIAFAQYLQCPFEDHVKLVNEVTEFAKTCVADESAA	60
Bovine SA	1	DTHKSEIAHREFKDLGEEHFKGLVLIAFSQYLOQCPFDEHVKLVNEVTEFAKTCVADESAA	60
Equine SA	1	DTHKSEIAHREFNDLGEKHFKGLVLVAFSQYLOQCPFEDHVKLVNEVTEFAKKGAAADESAE	60
Leporine SA	1	EAHKSEIAHRENNDVGEHEHFIGLVLTIFQSQYLKCPYEERAKLVKEVTDLAKAGVADESAA	60
		:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****	
61	NCDKSLHTLFGDKLCTVATLFETYGEMADCCAQKEPERNECFIQHKDDNPNLPLRVPEEV	120	
61	GEEKSLSHTLFGDKLCTVATLFETYGEMADCCAQKEPERNECFISHKDDSPDPLKL-KEDP	119	
61	NCDKSLHTLFGDKLCTVATLFATYGELADCEKEPERNECFIHKDDHPNLPLKL-KEEP	119	
61	NCDKSLHDIFGDKICALPSLRDTYGDVADCCKEPERNECFILHHKDLDKPDLEPPARFEA	120	
	:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****		
121	DVMCTAEHDEETFLKKYLYIEIARRHPYFYAPELLFFPKRYKAFTTECCQAADKAACILP	180	
120	NTLQDEEKAKDEEFLGKLYIEIARRHPYFYAPELLYYANKYNGVFQECQQAEDKGACLLP	179	
120	DAQCAAFQEDDPKFLGKLYIEVARRHPYFYPELLFHASEYKADFTTECCPADDKLACLLP	179	
121	DVLCKAEEHDEKAFFGHYLYIEVARRHPYFYAPELLYYAQKYKAILTECCEAADKGACILP	180	
	:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****		
181	KLDELRLDEGKASSAKORLKCGASLOKFGERAFKAWAVARLSQRFPKAEFAEVSKLVTDLTK	240	
180	KIETMREKVLIASSARQLRCAIQLKGERALKAWSVARLSQKFKAEFVEVTKLVTDLTK	239	
180	KLDALKERILLSSAKERILLCGCSFQNFGERAKVAVARLSQKFKADAEVSKIVTDLTK	239	
181	KLDALKERILLSSAKERILLCGCSFQNFGERAKVAVARLSQKFKADAEVSKIVTDLTK	240	
	:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****		
241	VHTECCHGDLLECADDRADLAKYICENQDSISSKLKECCEKPLLEKSHCIAEVENDMPA	300	
240	VHKECCCHGDLLECADDRADLAKYICDNQDTISSKLKECCEKPLLEKSHCIAEVENDMPA	299	
240	VHKECCCHGDLLECADDRADLAKYICHEQDSISGKLKACCDKPLLQKSHCIAEVENDMPA	299	
241	VHKECCCHGDLLECADDRADLAKYICHEQDTISSHLKECCEKPLLEKSHCIAEVENDMPA	300	
	:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****		
301	DLPLSLAADFVESKDVCKNVAEAKDVFLGMFLYEVARRHPDYSVVLLRLAKTYETTLEKC	360	
300	NLPLPLADFAEDKDVKCKNVAEAKDAFLGSFLYEVSSRRHPDYSVVLLRLAKTYETTLEEC	359	
300	DLPALAADFADKEICKHYKAOKDVELGFLYEVSSRRHPDYSVVLLRLAKTYETTLEKC	359	
301	GLPAVAREEFVEDKDVKCKNVAEAKDVLGKFLYEVSSRRHPDYSVVLLRLAKTYETTLEKC	360	
	:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****		
361	CAAADPHECYAKVDFEFKPPLVEEPQNLKIKONCELFEQLGEYKFQNALLVRYTAKVVPQVST	420	
360	CAKDDPHACYSTVFDKLKHILVDEPQNLKIKONCDQFEKLGEYGFQNALLVRYTAKVVPQVST	419	
360	CAEADPACYRTVFDQFTPPLVVEEPKSLVKKNCDLFEEVGEYDFQNALLVRYTAKVVPQVST	419	
361	CATDDPHACYAKVLDQFQPLVDEPQNLKIKONCELYEQLGDYNFQNALLVRYTAKVVPQVST	420	
	:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****		
421	PTLVEVSRLNLGVGSKCKKHPEAKRMPCAEDYLSVVLNQLCLVHLHEKTPVSDRVTKCCTES	480	
420	PTLVEVSRLNLGVGTRCCCKPESESRMPCTEDYLSLNLNPLCLVHLHEKTPVSEKVTKCCTES	479	
420	PTLVEISRTLGVGSRCCCKPESESRLPCSENHLALALNRLCLVHLHEKTPVSEKVTKCCTES	479	
421	PTLVEISRSLGKVGSKCKKHPEAERLPCVEDYLSVVLNRLCLVHLHEKTPVSEKVTKCCTES	480	
	:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****		
481	IVNRRPCFSALEVDETYVPKEFNAETFTFHADICTLSEKERQIKKQTALEVVKHKPKAT	540	
480	IVNRRPCFSALTPDETYVPKADEKLFTHADICTLPTEKEQIKKQTALEVLLKHKPKAT	539	
480	LAERRPCFSALELDEGYVPKEFNAETFTFHADICTLPEDEQIKKQSALELVVKHKPKAT	539	
481	IVDRRPCFSALGPDETYVPKEFNAETFTFHADICTLPETERKIKKQTALEVVKHKPKAT	540	
	:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****		
541	KEQLKAVMDPAAFVEKCCKADDKETCFREGKGLVVAASQAAALGL	585	
540	EEQLKTVMENFVAFVFDKCCAADDEKEACFAVEGPKLVNSTQTLALA-	583	
540	KEQLKTVLGNESAFVAKCCGREDEKEACFAEEGPKLVASSQALALA-	583	
541	NDQLKTIVGEGTALLDKCCSAEDKEACFAVEGPKLVESSKATLG-	584	
	:*****:*****:*****:*****:*****:*****:*****:*****:*****:*****		

Figure S1 Amino acid sequence alignment of human, bovine, equine, and leporine serum albumin.

Identical amino acids are labeled in dark gray and with an asterisk. Similar amino acids are labeled with light gray and dots.

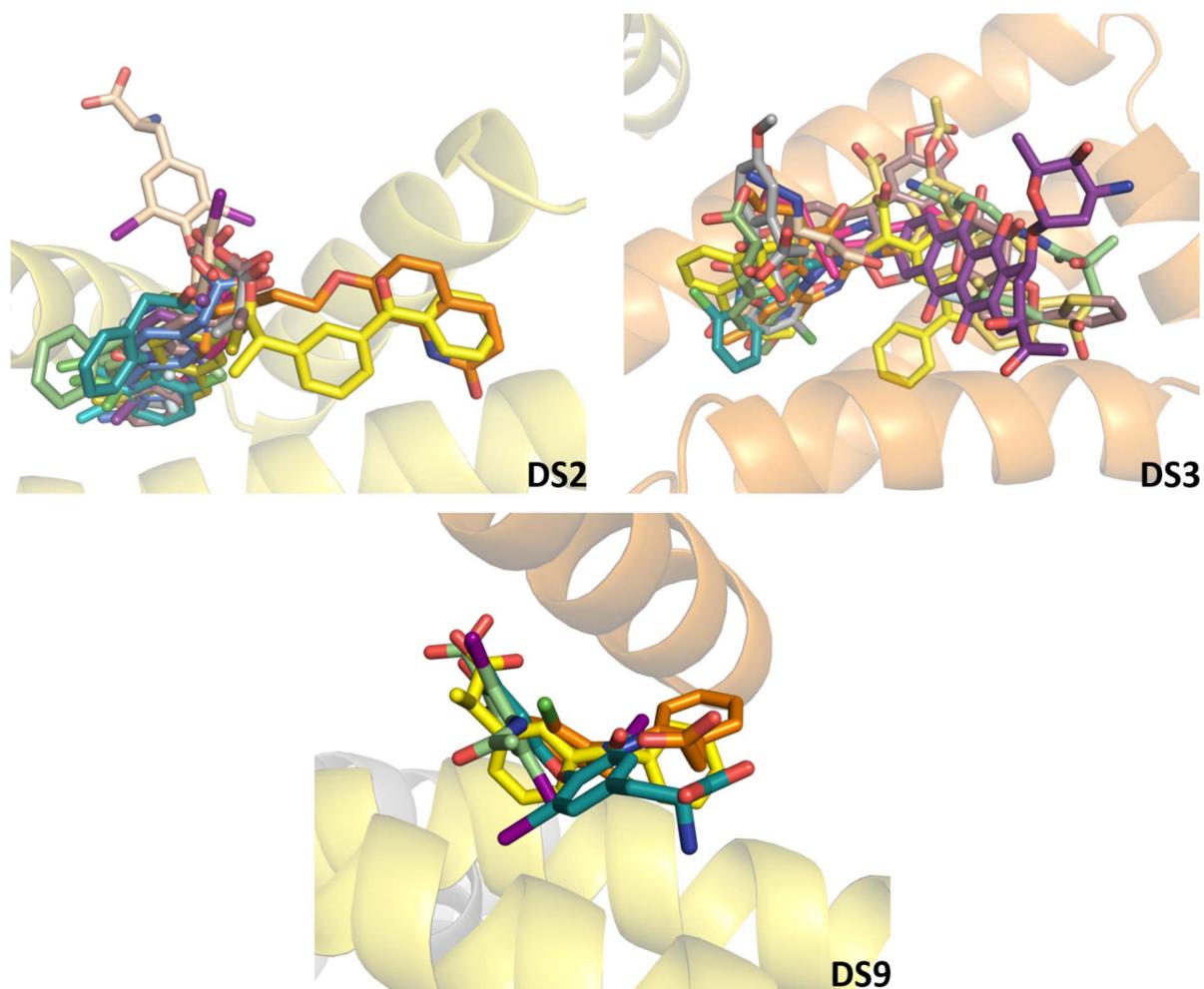


Figure S2 Superposition of the HSA-ketoprofen structure (PDB ID: 7JWN) and SA complexes with FDA-approved drugs known to bind to drug sites 2, 3 and 9. Ketoprofen molecules are shown with carbom atoms in yellow on all panels. DS2: aripiprazole (PDB ID: 6A7P), diazepam (PDB ID: 2BXF), diclofenac (PDB ID: 4ZBQ), diflunisal (PDB ID: 2BXE), halothane (PDB ID: 1E7B), ibuprofen (PDB ID: 2BXG), ketoprofen (PDB ID: 6OCK), nabumetone (PDB ID: 6U5A), naproxen (PDB ID: 4ZBR), phenylbutyric acid (PDB ID: 5YOQ), propofol (PDB ID: 1E7A), suprofen (PDB ID: 6OCJ), thyroxine (PDB ID: 1HK1). DS3: azapropazone (PDB ID: 2BXI), bicalutamide (PDB ID: 4LA0), diclofenac (PDB ID: 4Z69), etodolac (PDB ID: 5V0V), fusidic acid (PDB ID: 2VUF), idarubicin (PDB ID: 4LB2), indomethacin (PDB ID: 2BXM), naproxen (PDB ID: 2VDB), salicylic acid (PDB ID: 3B9M), teniposide (PDB ID: 4L9Q), zidovudine (PDB ID: 3B9L). DS9: diclofenac (PDB ID: 6HN0), iodipamine (PDB ID: 2BXN), thyroxine (PDB ID: 1HK4).

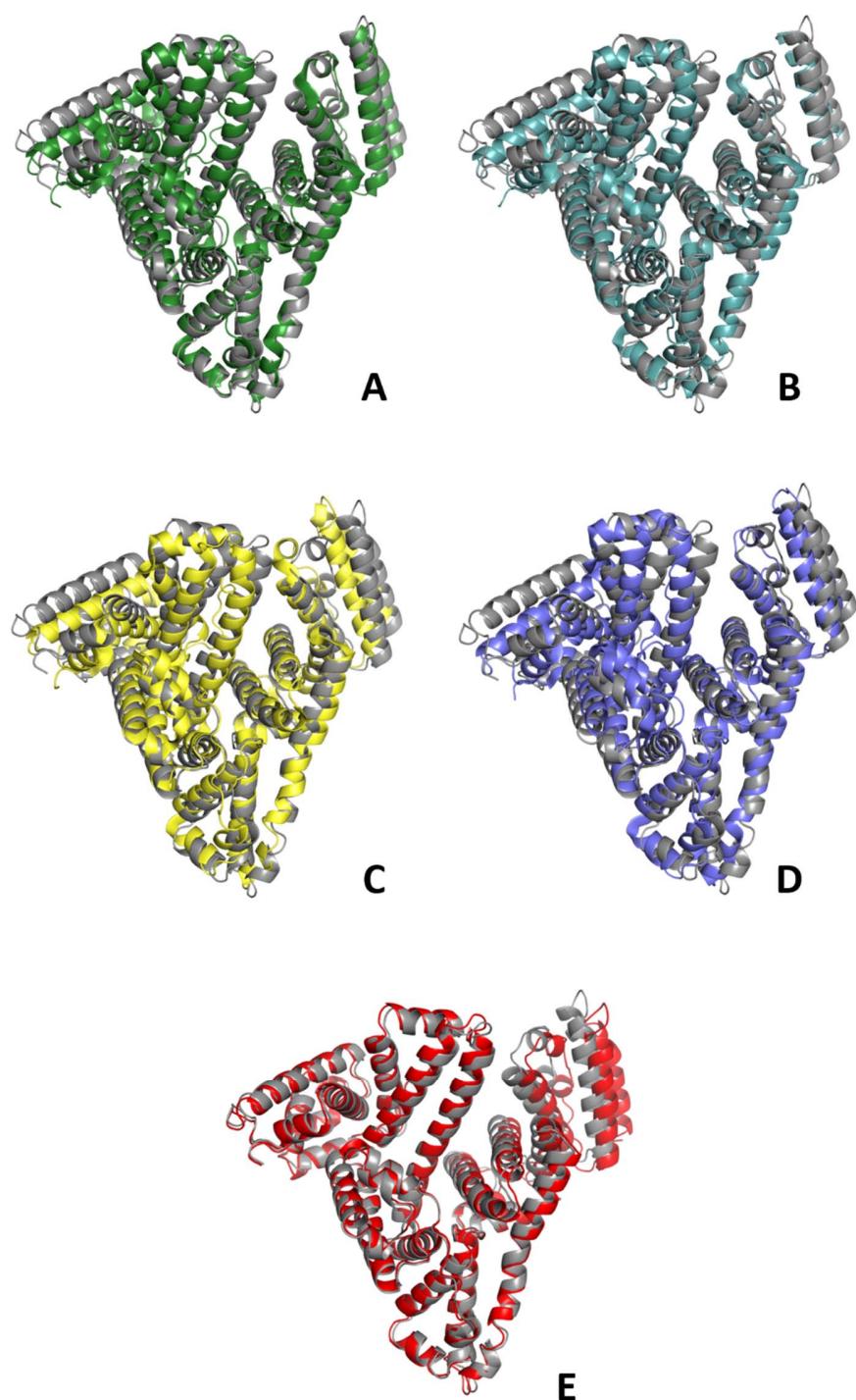


Figure S3 Superposition of structure of the HSA-ketoprofen complex (cartoon shown in gray) with the following complexes: A) ESA-ketoprofen (PDB ID: 6U4R); B) BSA-ketoprofen (PDB ID: 6QS9); C) LSA-ketoprofen (PDB ID: 6OCK); D) HSA-ligand free (PDB ID: 4K2C); E) HSA-myristic acid (PDB ID: 1BJ5).

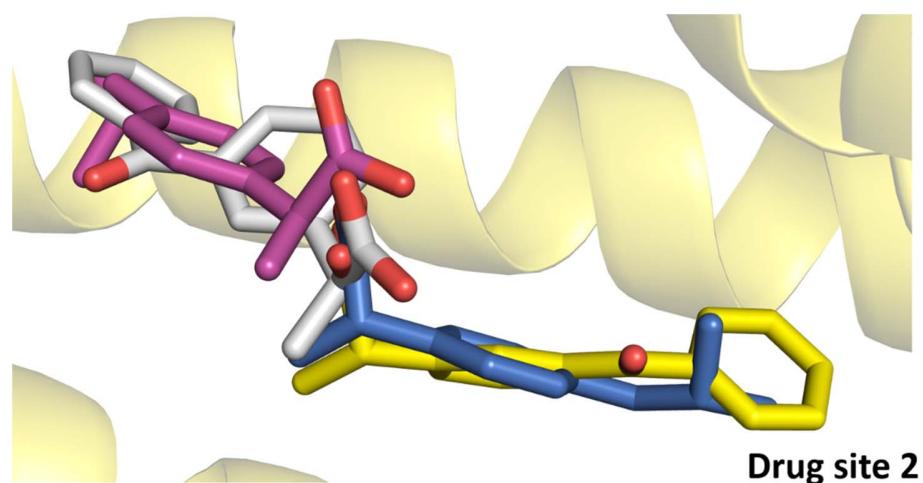


Figure S4 Superposition of the crystal structures of ketoprofen complexes with HSA (PDB ID: 7JWN), carbon atoms of the ligand are shown in yellow) and LSA (PDB ID: 6OCK, a ligand in gray) and ibuprofen complexes with HSA (PDB ID: 2BXG, a ligand in pink) and ESA (PDB ID: 6U4X, a ligand in blue).

Table S1 RMSD values [Å] between the aligned C α atoms of SA-ketoprofen complexes, ligand-free SAs, and HSA complex with myristic acid.

-	HSA-ket (7JWN)	LSA-ket (6OCK)	BSA-ket (6QS9)	ESA-ket (6U4R)	BSA (3V03)	ESA (4F5T)	HSA (4K2C)	LSA (4F5V)	HSA-myrs (1BJ5)
HSA-ket (7JWN)	-	4.5	4.0	3.7	4.5	3.6	3.9	4.6	1.5
LSA-ket (6OCK)	4.5	-	1.5	2.4	1.5	2.3	1.8	0.7	5.2
BSA-ket (6QS9)	4.0	1.5	-	1.7	0.5	1.7	1.6	1.7	4.8
ESA-ket (6U4R)	3.7	2.4	1.7	-	1.6	0.8	1.9	2.6	3.9
BSA (3V03)	4.5	1.5	0.5	1.6	-	1.7	1.6	1.7	4.9
ESA (4F5T)	3.6	2.3	1.7	0.8	1.7	-	1.8	2.5	3.9
HSA (4K2C)	3.9	1.8	1.6	1.9	1.6	1.8	-	1.9	4.2
LSA (4F5V)	4.6	0.7	1.7	2.6	1.7	2.5	1.9	-	5.2
HSA-myrs (1BJ5)	1.5	5.2	4.8	3.9	4.9	3.9	4.2	5.2	-