Supporting Information.

Conformational Properties of Cholic Acid, a Lead Compound at the Crossroads of Bile Acid Inspired Drug Discovery.

Authors: Antimo Gioiello, Francesco Venturoni, Sara Tamimi, Chiara Custodi, Roberto Pellicciari, Antonio Macchiarulo.

Table of Contents:

Table S1. Distance matrix of RMSD values (Å) between minima conformations of CA.

	Conf.1	Conf.4	Conf.11	Conf.12	Conf.13	Conf.14	Conf.15	Conf.29	Conf.32	Conf.33	Conf.35	Conf.36	Conf.37	Conf.38	Conf.39	Conf.54	Conf.56	Conf.61	Conf.63
Conf.1	0.000	0.455	1.064	0.975	1.334	1.339	1.174	1.279	0.932	0.916	0.964	1.380	0.628	1.332	1.264	0.751	1.343	1.385	0.846
Conf.4	0.485	0.000	1.249	0.949	1.137	1.131	1.043	1.072	0.841	0.764	1.103	1.291	0.949	1.404	1.421	0.594	1.118	1.243	0.644
Conf.11	1.064	1.249	0.000	0.591	1.351	1.136	1.566	1.510	0.737	1.403	0.363	1.039	0.732	0.549	0.373	1.347	1.731	1.012	1.470
Conf.12	0.975	0.949	0.591	0.000	1.107	0.766	1.351	1.271	0.216	1.125	0.371	0.889	0.982	0.720	0.718	1.046	1.436	0.747	1.262
Conf.13	1.334	1.137	1.351	1.107	0.000	0.769	0.725	0.352	1.072	0.833	1.272	0.535	1.439	1.181	1.303	0.829	0.692	0.797	0.951
Conf.14	1.339	1.131	1.136	0.766	0.769	0.000	0.990	0.921	0.671	1.025	0.966	0.876	1.451	1.032	1.118	1.046	0.959	0.392	1.081
Conf.15	1.174	1.043	1.566	1.351	0.725	0.990	0.000	0.582	1.233	0.499	1.471	1.087	1.426	1.600	1.661	0.689	0.459	1.115	0.619
Conf.29	1.279	1.072	1.510	1.271	0.352	0.921	0.582	0.000	1.21	0.732	1.425	0.745	1.453	1.351	1.486	0.763	0.604	0.946	0.781
Conf.32	0.932	0.841	0.737	0.216	1.072	0.671	1.233	1.210	0.000	1.010	0.494	0.947	1.042	0.884	0.888	0.944	1.308	0.736	1.124
Conf.33	0.916	0.764	1.403	1.125	0.833	1.025	0.499	0.732	1.010	0.000	1.269	1.025	1.239	1.506	1.539	0.340	0.704	1.135	0.687
Conf.35	0.964	1.103	0.363	0.371	1.272	0.966	1.471	1.425	0.494	1.269	0.000	0.988	0.853	0.652	0.540	1.201	1.589	0.869	1.372
Conf.36	1.380	1.291	1.039	0.889	0.535	0.876	1.087	0.745	0.947	1.025	0.988	0.000	1.320	0.824	0.959	1.022	1.118	0.728	1.312
Conf.37	0.628	0.949	0.732	0.982	1.439	1.451	1.426	1.453	1.042	1.239	0.853	1.320	0.000	1.008	0.919	1.145	1.635	1.380	1.170
Conf.38	1.332	1.404	0.549	0.720	1.181	1.032	1.600	1.351	0.884	1.506	0.652	0.824	1.008	0.000	0.359	1.457	1.677	0.776	1.586
Conf.39	1.264	1.421	0.373	0.718	1.303	1.118	1.661	1.486	0.888	1.539	0.540	0.959	0.919	0.359	0.000	1.466	1.779	0.921	1.636
Conf.54	0.751	0.594	1.347	1.046	0.829	1.046	0.689	0.763	0.944	0.340	1.201	1.022	1.145	1.457	1.466	0.000	0.832	1.176	0.700
Conf.56	1.343	1.118	1.731	1.436	0.692	0.959	0.459	0.604	1.308	0.704	1.589	1.118	1.635	1.677	1.779	0.832	0.000	1.098	0.707
Conf.61	1.385	1.243	1.012	0.747	0.797	0.392	1.115	0.946	0.736	1.135	0.869	0.728	1.380	0.776	0.921	1.176	1.098	0.000	1.225
Conf.63	0.846	0.644	1.470	1.262	0.951	1.081	0.619	0.781	1.124	0.687	1.372	1.312	1.170	1.586	1.636	0.700	0.707	1.225	0.000

Table S2. ^{13}C and ^{1}H resonance assignments for CA and its sodium salt at 300 K.[30]

#	Type	Cholic Acid			Sodium Cholate		
		Carbon	Proton		Carbon	Proton	
			Ha	Hb		Ha	Hb
1	CH_2	36.5	1.81	0.99	36.6	1.75	0.90
2	CH_2	31.2	1.45	1.59	31.6	1.41	1.51
3	CH	72.9	-	3.37	71.8	-	3.24
4	CH_2	40.5	2.29	1.66	40.8	2.36	1.57
5	CH	43.2	-	1.38	43.1	-	1.30
6	CH_2	35.9	1.53	1.95	36.0	1.49	1.87
7	CH	69.1	-	3.80	67.7	-	3.71
8	CH	41.0	-	1.55	40.9	-	1.43
9	CH	27.9	2.25	-	27.3	2.33	-
10	C	35.9	-	-	35.5	-	-
11	CH_2	29.6	1.58	1.58	29.5	1.55	1.46
12	CH	74.0	-	3.97	72.6	-	3.89
13	C	47.6	-	-	46.9	-	-
14	CH	43.0	2.00	-	42.4	2.13	-
15	CH_2	24.2	1.12	1.76	24.0	1.02	1.77
16	CH_2	28.7	1.90	1.32	28.5	1.87	1.28
17	CH	48.1	1.86	-	47.5	1.94	-
18	CH_3	13.0	0.72		13.0	0.67	
19	CH_3	23.2	0.92		23.2	0.88	
20	CH	37.8	1.43		36.9	1.35	
21	CH_3	17.7	1.02		18.0	1.01	
22	CH_2	32.4	1.79[a]	1.35[a]	33.6	1.77[a]	1.31[a]
23	CH_2	32.0	2.37[a]	2.21[a]	35.8	2.11[a]	1.94[a]
24	C	178.3	-	-	180.1	-	-

[a] In the case of the H_{23} and H_{22} (*R* and *S*) protons, arbitrary assignments have been made.

Table S3. RMSD values (Å) of bioactive conformations of CA as superimposed on conf.4, conf.1 and conf.39 minima. In bold are highlighted the closest most populated minima points to the relative bioactive conformation.

Name	Resolution (Å)	Target Type	PDB code-#Bioactive Conf. Model	Conf.4	Conf.1	Conf.39
Alcohol dehydrogenase[40]	1.54	Enzyme	1EE2-1	**0.405**	0.630	1.339
			1EE2-2	**0.448**	0.644	1.322
Carboxyl esterase[41]	3.0	Enzyme	2DQY-1	**0.419**	0.510	1.337
			2DQY-2	**0.323**	0.580	1.408
Choloylglycine hydrolase	1.80	Enzyme	2RLC-1	0.922	**0.597**	1.036
Phospholipase A2[42]	1.90	Enzyme	2AZY-1	0.768	**0.427**	1.197
Ileal bile Acid Binding Protein (IBABP)[43]	2.20	Transporter	3ELZ-1	**0.483**	0.537	1.478
			3ELZ-2	**0.304**	0.452	1.347
			3ELZ-3	0.541	**0.471**	1.158
			3ELZ-4	**0.297**	0.508	1.382
			3ELZ-5	0.704	**0.534**	1.258
			3ELZ-6	**0.519**	0.631	1.330
			3ELZ-7	**0.425**	0.517	1.280
			3ELZ-8	0.802	**0.464**	1.062
			3ELZ-9	0.554	**0.506**	1.170
			3ELZ-10	0.823	**0.434**	1.174
			3ELZ-11	**0.502**	0.616	1.360
			3ELZ-12	**0.326**	0.559	1.398
			3ELZ-13	0.636	**0.354**	1.153
	2.20	Transporter	3EM0-1	**0.419**	0.621	1.356
			3EM0-2	**0.422**	0.709	1.380
			3EM0-3	**0.470**	0.744	1.499
			3EM0-4	**0.470**	0.553	1.432

			3EM0-5	0.861	**0.610**	1.032
			3EM0-6	**0.233**	0.515	1.407
			3EM0-7	**0.333**	0.653	1.468
			3EM0-8	0.641	**0.509**	1.352
			3EM0-9	**0.438**	0.676	1.454
Liver Bile Acid Binding Protein (LBABP)[44]	2.20	Transporter	2FT9-1	**0.386**	0.635	1.322
			2FT9-2	0.616	**0.323**	1.203
Liver Bile Acid Binding Protein (LBABP)[45]	1.50	Transporter	2QO4-1	0.772	**0.395**	1.136
			2QO5-2	**0.296**	0.477	1.358
			2QO5-3	**0.328**	0.597	1.498
			2QO6-4	0.765	**0.381**	1.147
Liver basic type Fatty Acid Binding Protein (Lb-FABP)[46]	2.00	Transporter	1TW4-1	**0.386**	0.569	1.270
			1TW4-2	**0.264**	0.560	1.489
			1TW4-3	**0.520**	0.605	1.178
			1TW4-4	**0.245**	0.591	1.521

Figure.S1 NOE effect between the methyl at C21 position and the protons located at C_{23}Ha and C_{23}Hb at 300 K.

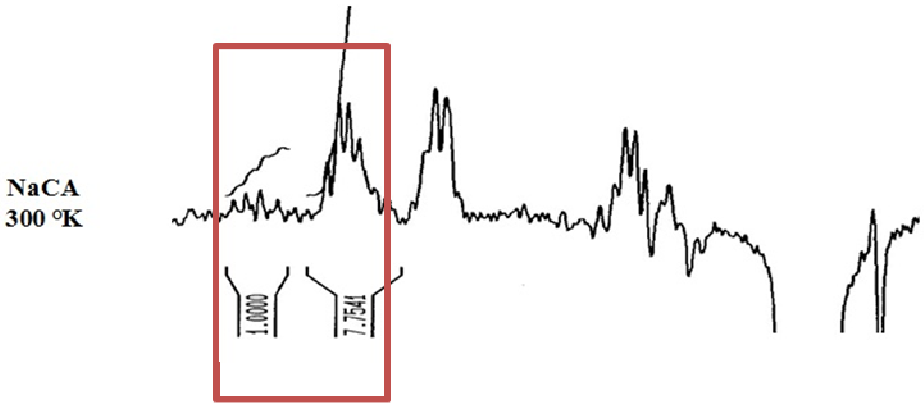

Figure.S2 Row associated with the selective irradiation of the proton at $C_{12}\alpha$ position.