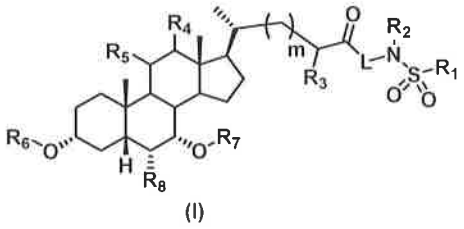
Claims

1. A compound represented by Formula I or a pharmaceutically acceptable salt, ester, stereoisomer, tautomer, solvate, or combination thereof:



(I)

wherein:

R_1 is selected from the group consisting of:

1) Halogen;
2) Substituted or unsubstituted $-C_1$-C_8 alkyl;
3) Substituted or unsubstituted $-C_2$-C_8 alkenyl;
4) Substituted or unsubstituted $-C_2$-C_8 alkynyl;
5) Substituted or unsubstituted $-C_3$-C_8 cycloalkyl;
6) Substituted or unsubstituted aryl;
7) Substituted or unsubstituted alkylaryl;
8) Substituted or unsubstituted heterocycloalkyl;
9) Substituted or unsubstituted heteroaryl;
10) Substituted or unsubstituted alkylheteroaryl; and
11) $-NR_9R_{10}$; wherein, R_9 and R_{10} are independently selected from hydrogen, substituted or unsubstituted $-C_1$-C_8 alkyl, substituted or unsubstituted $-C_2$-C_8 alkenyl, substituted or unsubstituted $-C_2$-C_8 alkynyl, substituted or unsubstituted $-C_3$-C_8 cycloalkyl, or R_9 and R_{10} are taken together with the nitrogen they attached to form a hetercyclic ring;

R_2 is hydrogen or Substituted or unsubstituted $-C_1$-C_8 alkyl;

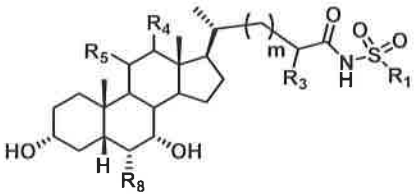
R_3 is independently selected from the group consisting of:

1) Hydrogen;
2) Substituted or unsubstituted $-C_1$-C_8 alkyl;
3) Substituted or unsubstituted $-C_2$-C_8 alkenyl;
4) Substituted or unsubstituted $-C_2$-C_8 alkynyl;
5) Substituted or unsubstituted alkylaryl; and
6) Substituted or unsubstituted aryl;

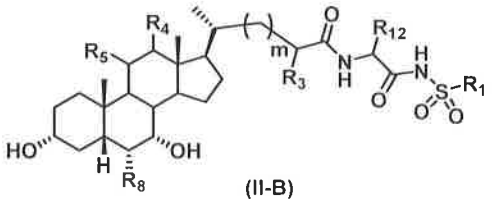
L is absent or $-NR_{11}CHR_{12}C(O)-$, wherein R_{11} and R_{12} are independently selected from R_3;
m is selected from 0, 1, 2 or 3;
R_4 is hydrogen, hydroxyl, $-OSO_3H$, $-OSO_3^-$, -OAc, $-OPO_3H_2$ or $-OPO_3^{2-}$;
R_5 is hydrogen, halogen, CN, N_3, hydroxyl, $-OSO_3H$, $-OSO_3^-$, -OAc, $-OPO_3H_2$, $-OPO_3^{2-}$, $-SR_2$ or $-NHR_2$, wherein, R_2 is as defined previously;
or R_4 and R_5 are taken together with the carbons they attached to form –CH=CH- or cycloalkyl ring or heterocycloalkyl ring such as, but not limited to cyclopropyl, or expoxide;
R_6 and R_7 are independently selected from hydrogen or hydroxyl protecting group such as, but not limited to acetyl, trimethyl silyl, or benzyl;
R_8 is selected from the group consisting of:

1) Hydrogen;
2) Halogen;
3) Substituted or unsubstituted $-C_1$-C_8 alkyl;
4) Substituted or unsubstituted $-C_2$-C_8 alkenyl;
5) Substituted or unsubstituted $-C_2$-C_8 alkynyl; and
6) Substituted or unsubstituted $-C_3$-C_8 cycloalkyl.

2. A compound of claim 1, represented by Formula II-A or Formula II-B or a pharmaceutically acceptable salt, ester, stereoisomer, tautomer, solvate, or combination thereof:



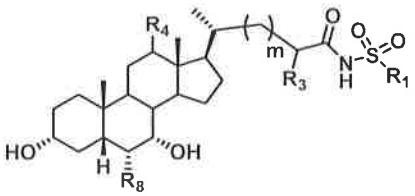
(II-A)



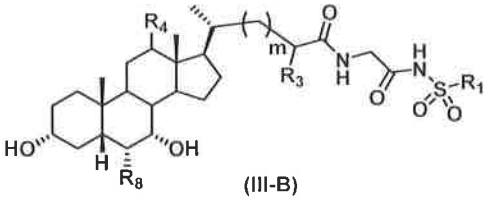
(II-B)

wherein, R_1, R_3, R_4, R_5, R_8, R_{12} and m are as defined in claim 1.

3. A compound of claim 1, represented by Formula III-A or Formula III-B or a pharmaceutically acceptable salt, ester, stereoisomer, tautomer, solvate, or combination thereof:



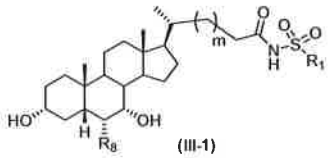
(III-A)



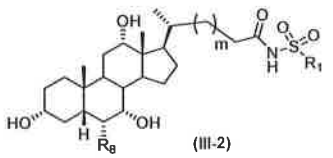
(III-B)

wherein, R_1, R_3, R_4, R_8 and m are as defined in claim 1.

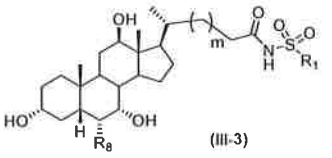
4. The compound of claim 1, represented by one of formulas (III-1) to (III-18), wherein R_1, R_8 and m are as defined in claim 1:



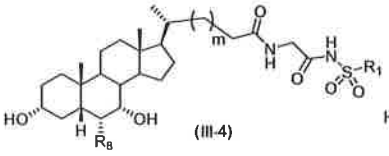
(III-1)



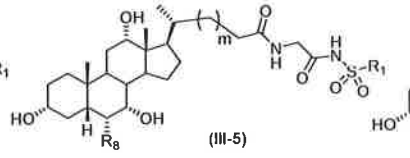
(III-2)



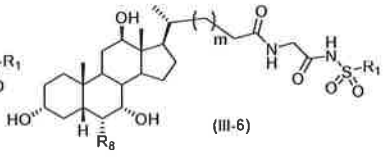
(III-3)



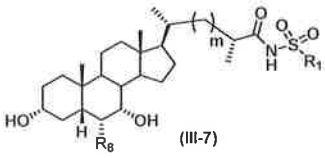
(III-4)



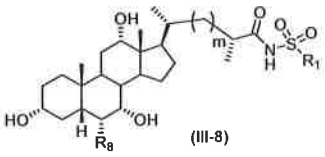
(III-5)



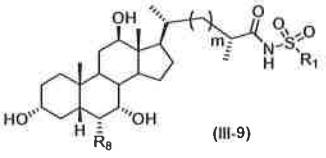
(III-6)



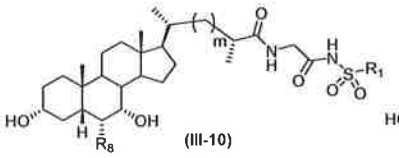
(III-7)



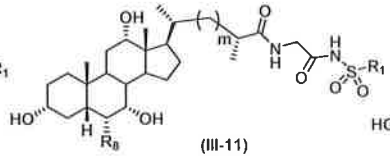
(III-8)



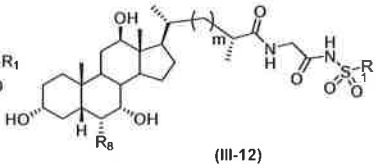
(III-9)



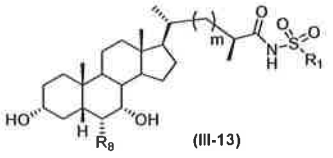
(III-10)



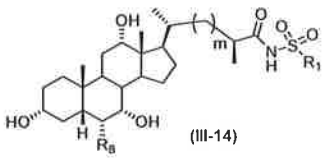
(III-11)



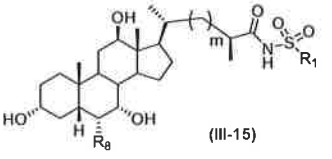
(III-12)



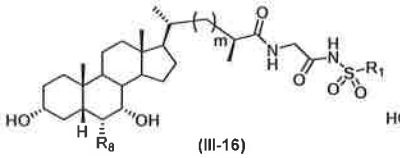
(III-13)



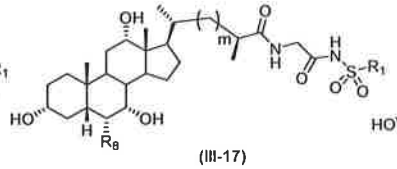
(III-14)



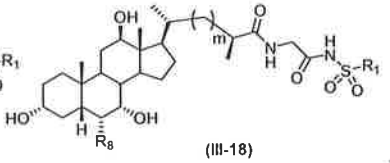
(III-15)



(III-16)

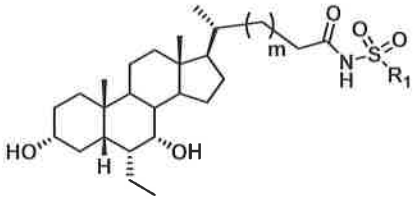


(III-17)

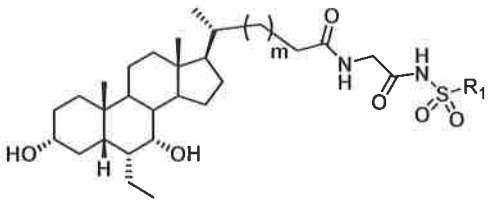


(III-18)

5. A compound of claim 1, represented by Formula IV-A or Formula IV-B or a pharmaceutically acceptable salt, ester, stereoisomer, tautomer, solvate, or combination thereof:



(IV-A)

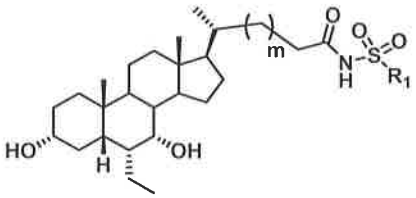


(IV-B)

wherein, R_1 and m are as defined in claim 1.

6. A compound according to claim 1, which is selected from:

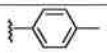
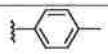
(a) Compounds according to Formula IV-A wherein, R_1 and m are delineated for each example in Table 1:



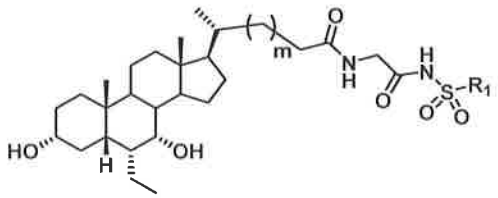
(IV-A)

Table 1

Compound	m	R_1	Compound	m	R_1	Compound	m	R_1
1	0	Methyl	26	1	Methyl	51	2	Methyl
2	0	Ethyl	27	1	Ethyl	52	2	Ethyl
3	0	Isopropyl	28	1	Isopropyl	53	2	Isopropyl
4	0	Butyl	29	1	Butyl	54	2	Butyl
5	0	t-Butyl	30	1	t-Butyl	55	2	t-Butyl
6	0	Propyl	31	1	Propyl	56	2	Propyl
7	0	Benzyl	32	1	Benzyl	57	2	Benzyl
8	0	Vinyl	33	1	Vinyl	58	2	Vinyl
9	0	Allyl	34	1	Allyl	59	2	Allyl
10	0	CF_3	35	1	CF_3	60	2	CF_3
11	0		36	1		61	2	
12	0		37	1		62	2	

13	0		38	1		63	2	
14	0		39	1		64	2	
15	0		40	1		65	2	
16	0		41	1		66	2	
17	0	NH_2	42	1	NH_2	67	2	NH_2
18	0		43	1		68	2	
19	0		44	1		69	2	
20	0		45	1		70	2	
21	0		46	1		71	2	
22	0		47	1		72	2	
23	0		48	1		73	2	
24	0		49	1		74	2	
25	0	F	50	1	F	75	2	F

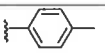
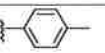
(b) Compounds according to Formula IV-B wherein, R_1 and m are delineated for each example in Table 2:



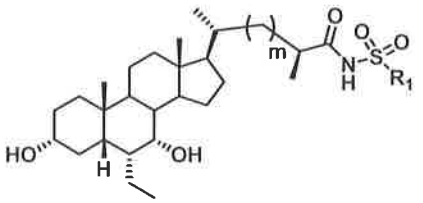
(IV-B)

Table 2

Compound	m	R_1	Compound	m	R_1	Compound	m	R_1
76	0	Methyl	101	1	Methyl	126	2	Methyl
77	0	Ethyl	102	1	Ethyl	127	2	Ethyl
78	0	Isopropyl	103	1	Isopropyl	128	2	Isopropyl
79	0	Butyl	104	1	Butyl	129	2	Butyl
80	0	t-Butyl	105	1	t-Butyl	130	2	t-Butyl
81	0	Propyl	106	1	Propyl	131	2	Propyl

82	0	Benzyl	107	1	Benzyl	132	2	Benzyl
83	0	Vinyl	108	1	Vinyl	133	2	Vinyl
84	0	Allyl	109	1	Allyl	134	2	Allyl
85	0	CF_3	110	1	CF_3	135	2	CF_3
86	0		111	1		136	2	
87	0		112	1		137	2	
88	0		113	1		138	2	
89	0		114	1		139	2	
90	0		115	1		140	2	
91	0		116	1		141	2	
92	0	NH_2	117	1	NH_2	142	2	NH_2
93	0		118	1		143	2	
94	0		119	1		144	2	
95	0		120	1		145	2	
96	0		121	1		146	2	
97	0		122	1		147	2	
98	0		123	1		148	2	
99	0		124	1		149	2	
100	0	F	125	1	F	150	2	F

7. The compound of claim 1, represented by Formula V-A or Formula V-B:

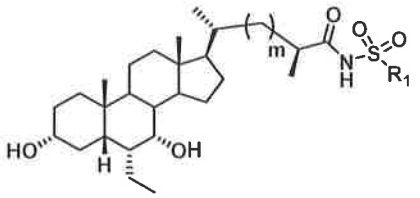


(V-A)

(V-B)

8. A compound according to claim 1, which is selected from:

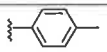
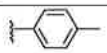
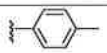
(a) compounds according to Formula V-A wherein, R_1 and m are delineated for each example in Table 3:



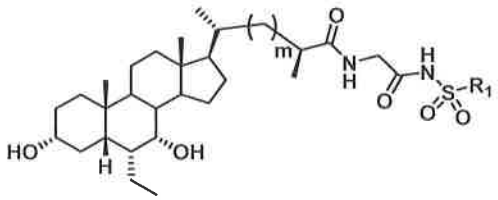
(V-A)

Table 3

Compound	m	R_1	Compound	m	R_1	Compound	m	R_1
151	0	Methyl	176	1	Methyl	201	2	Methyl
152	0	Ethyl	177	1	Ethyl	202	2	Ethyl
153	0	Isopropyl	178	1	Isopropyl	203	2	Isopropyl
154	0	Butyl	179	1	Butyl	204	2	Butyl
155	0	t-Butyl	180	1	t-Butyl	205	2	t-Butyl
156	0	Propyl	181	1	Propyl	206	2	Propyl
157	0	Benzyl	182	1	Benzyl	207	2	Benzyl
158	0	Vinyl	183	1	Vinyl	208	2	Vinyl
159	0	Allyl	184	1	Allyl	209	2	Allyl
160	0	CF_3	185	1	CF_3	210	2	CF_3
161	0		186	1		211	2	
162	0		187	1		212	2	
163	0		188	1		213	2	
164	0		189	1		214	2	
165	0		190	1		215	2	
166	0		191	1		216	2	
167	0	NH_2	192	1	NH_2	217	2	NH_2
168	0		193	1		218	2	
169	0		194	1		219	2	
170	0		195	1		220	2	

171	0		196	1		221	2	
172	0		197	1		222	2	
173	0		198	1		223	2	
174	0		199	1		224	2	
175	0	F	200	1	F	225	2	F

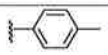
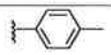
(b) Compounds according to Formula V-B wherein, R_1 and m are delineated for each example in Table 4:



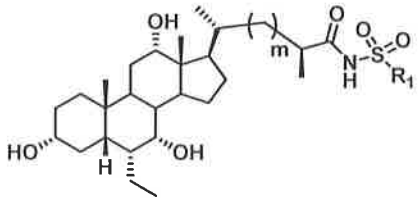
(V-B)

Table 4

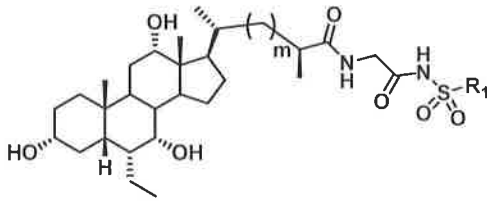
Compound	m	R_1	Compound	m	R_1	Compound	m	R_1
226	0	Methyl	251	1	Methyl	276	2	Methyl
227	0	Ethyl	252	1	Ethyl	277	2	Ethyl
228	0	Isopropyl	253	1	Isopropyl	278	2	Isopropyl
229	0	Butyl	254	1	Butyl	279	2	Butyl
230	0	t-Butyl	255	1	t-Butyl	280	2	t-Butyl
231	0	Propyl	256	1	Propyl	281	2	Propyl
232	0	Benzyl	257	1	Benzyl	282	2	Benzyl
233	0	Vinyl	258	1	Vinyl	283	2	Vinyl
234	0	Allyl	259	1	Allyl	284	2	Allyl
235	0	CF_3	260	1	CF_3	285	2	CF_3
236	0		261	1		286	2	
237	0		262	1		287	2	
238	0		263	1		288	2	
239	0		264	1		289	2	
240	0		265	1		290	2	

241	0		266	1		291	2	
242	0	NH_2	267	1	NH_2	292	2	NH_2
243	0		268	1		293	2	
244	0		269	1		294	2	
245	0		270	1		295	2	
246	0		271	1		296	2	
247	0		272	1		297	2	
248	0		273	1		298	2	
249	0		274	1		299	2	
250	0	F	275	1	F	300	2	F

9. A compound according to claim 1, represented by Formula VI-A or Formula VI-B:



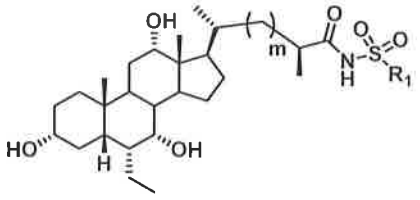
(VI-A)



(VI-B)

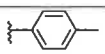
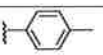
10. A compound according to claim 1, which is selected from:

(a) Compounds according to Formula VI-A wherein, R_1 and m are delineated for each example in Table 5,

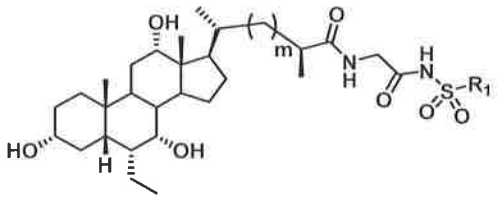


(VI-A)

Table 5

Compound	m	R_1	Compound	m	R_1	Compound	m	R_1
301	0	Methyl	326	1	Methyl	351	2	Methyl
302	0	Ethyl	327	1	Ethyl	352	2	Ethyl
303	0	Isopropyl	328	1	Isopropyl	353	2	Isopropyl
304	0	Butyl	329	1	Butyl	354	2	Butyl
305	0	t-Butyl	330	1	t-Butyl	355	2	t-Butyl
306	0	Propyl	331	1	Propyl	356	2	Propyl
307	0	Benzyl	332	1	Benzyl	357	2	Benzyl
308	0	Vinyl	333	1	Vinyl	358	2	Vinyl
309	0	Allyl	334	1	Allyl	359	2	Allyl
310	0	CF_3	335	1	CF_3	360	2	CF_3
311	0		336	1		361	2	
312	0		337	1		362	2	
313	0		338	1		363	2	
314	0		339	1		364	2	
315	0		340	1		365	2	
316	0		341	1		366	2	
317	0	NH_2	342	1	NH_2	367	2	NH_2
318	0		343	1		368	2	
319	0		344	1		369	2	
320	0		345	1		370	2	
321	0		346	1		371	2	
322	0		347	1		372	2	
323	0		348	1		373	2	
324	0		349	1		374	2	
325	0	F	350	1	F	375	2	F

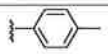
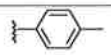
(b) Compounds according to Formula VI-B wherein, R_1 and m are delineated for each example in Table 6,



(VI-B)

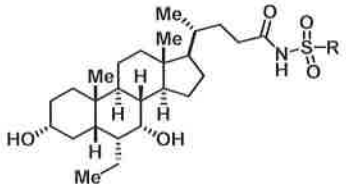
Table 6

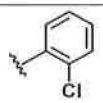
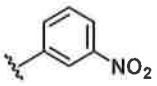
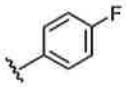
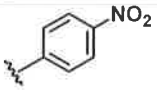
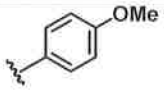
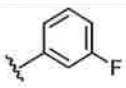
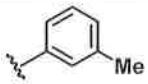
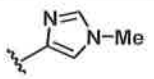
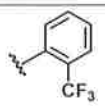
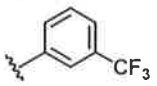
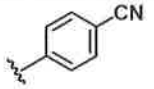
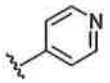
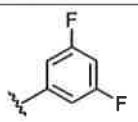
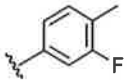
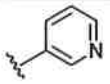
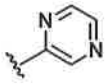
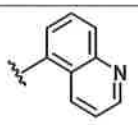
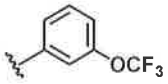
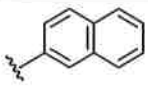
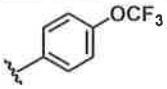
Compound	m	R_1	Compound	m	R_1	Compound	m	R_1
376	0	Methyl	401	1	Methyl	426	2	Methyl
377	0	Ethyl	402	1	Ethyl	427	2	Ethyl
378	0	Isopropyl	403	1	Isopropyl	428	2	Isopropyl
379	0	Butyl	404	1	Butyl	429	2	Butyl
380	0	t-Butyl	405	1	t-Butyl	430	2	t-Butyl
381	0	Propyl	406	1	Propyl	431	2	Propyl
382	0	Benzyl	407	1	Benzyl	432	2	Benzyl
383	0	Vinyl	408	1	Vinyl	433	2	Vinyl
384	0	Allyl	409	1	Allyl	434	2	Allyl
385	0	CF_3	410	1	CF_3	435	2	CF_3
386	0		411	1		436	2	
387	0		412	1		437	2	
388	0		413	1		438	2	
389	0		414	1		439	2	
390	0		415	1		440	2	
391	0		416	1		441	2	
392	0	NH_2	417	1	NH_2	442	2	NH_2
393	0		418	1		443	2	
394	0		419	1		444	2	
395	0		420	1		445	2	
396	0		421	1		446	2	

397	0		422	1		447	2	
398	0		423	1		448	2	
399	0		424	1		449	2	
400	0	F	425	1	F	450	2	F

11. A compound according to claim 1 selected from the group of compounds 451-492 shown below in table 7 and table 8, or a pharmaceutically acceptable salt thereof:

Table 7 Compounds 451-484



Compound	R	Compound	R	Compound	R
451		452		453	
454		455		456	
457		458		459	
460		461		462	
463		464		465	
466		467		468	
469		470		471	
472		473		474	

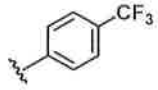
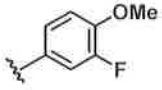
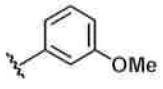
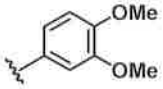
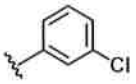
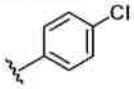
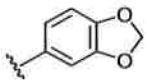
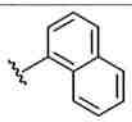
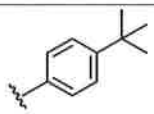
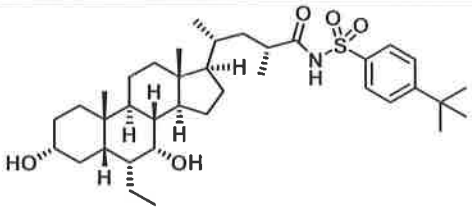
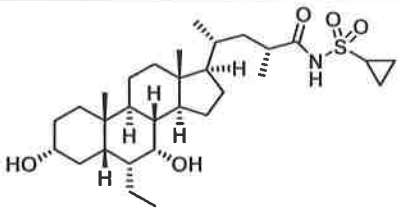
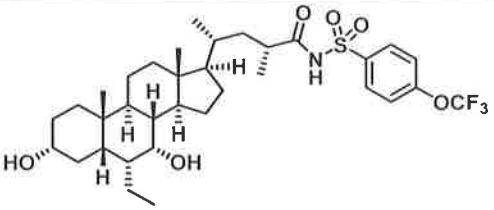
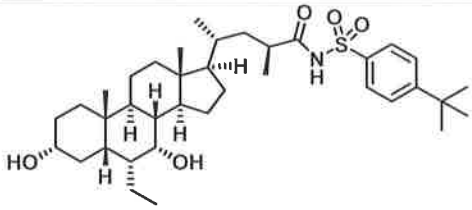
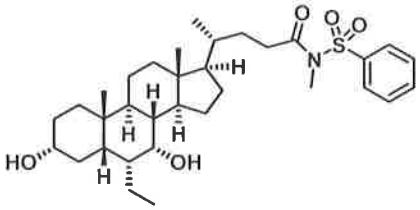
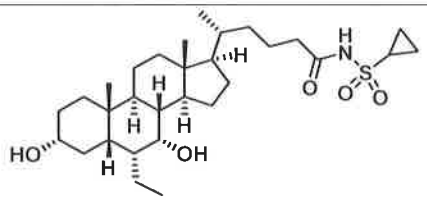
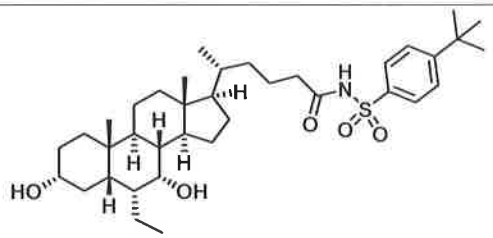
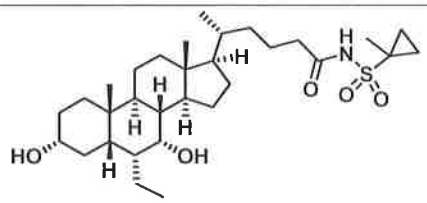
475		476		477	
478		479		480	
481		482		483	
484					

Table 8 Compounds 485-492

Compound	**Structure**
485	
486	
487	
488	
489	

490	
491	
492	

12. Use of a therapeutically effective amount of a compound according to any one of claims 1-11 in the manufacture of a medicament for the prevention or treatment of a disease or condition selected from the group consisting of primary biliary cirrhosis, cerebrotendinous xanthomatosis, primary sclerosing cholangitis, alcoholic liver disease, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, atherosclerosis, hypercholesterolemia, hypertriglyceridemia, Type II diabetes, and hepatocellular carcinoma in a mammal, wherein the medicament is to be administered to the mammal suffering from the disease or condition.

13. The use according to claim 12, wherein the disease or condition is primary biliary cirrhosis.

14. The use according to claim 12, wherein the disease or condition is nonalcoholic fatty liver disease.

15. The use according to claim 12, wherein the disease or condition is nonalcoholic steatohepatitis.

16. The use according to claim 12, wherein the disease or condition is Type II diabetes.

17. A pharmaceutical composition comprising a compound according to any one of claims 1-11 and a pharmaceutically acceptable carrier.

18. A compound according to any one of claims 1-11 or a pharmaceutical composition according to claim 17 for use as a medicament.

19. A compound according to any one of claims 1-11 or a pharmaceutical composition according to claim 17 for use as a medicament for the prevention or treatment of an FXR-mediated disease or condition.

20. A compound according to any one of claims 1-11 or a pharmaceutical composition according to claim 17 for use in the treatment of a disease or condition selected from the group consisting of primary biliary cirrhosis, cerebrotendinous xanthomatosis, primary sclerosing cholangitis, alcoholic liver disease, nonalcoholic fatty liver disease, nonalcoholic steatohepatitis, atherosclerosis, hypercholesterolemia, hypertriglyceridemia, Type II diabetes, and hepatocellular carcinoma.