Future potentials of bile acids and their oxo derivatives in nano chemistry.

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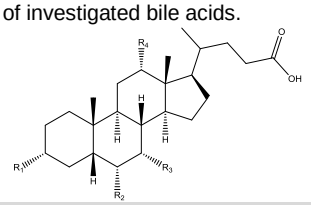
Abstract

Bile acids and their oxo derivatives have pharmacological characteristic to act as drug carriers, absorption enhancers and as cholesterol lowering agents. Bile acids have also potential to regulate hepatic lipid, glucose, and energy homeostasis and maintain metabolic process. Acting as signaling molecules these compounds have ability to interact with several receptors such as: farensoid X receptor (FXR) and G protein coupled receptor (GPCR). In our study 13 different bile acids and their derivatives (Figure 1.) were examined. Using their lipophilicity the parameters of bioactivity were investigated and validated. Multiple linear regression was performed considering lipophilicity of molecules with addition of two molecular descriptors: polar surface area (TPSA) and molecular weight (Mw).

Parameters of bioactivity are an essential part of modern QSAR studies because binding with different classes of proteins in human body is responsible for a specific desired or undesired effect. Bioactivity scores were calculated using Molinspiration software. These parameters are G Protein-coupled receptors ligand (GPCR), ion channel modulation (ICM), nuclear receptor ligand (NCR) and protease inhibition (PI) and they are shown in Table 1. Calculated values can indicate binding affinity of investigated bile acids to the mentioned receptors and enzymes. Negative values represent low affinity, while positive values indicate greater affinity. The compounds investigated were expected to bind for GPCR, ion channels and nuclear receptors, and they should not inhibit kinase.

Figure 1. Structure of investigated bile acids.



Name of bile acid	Groups
Deoxycholic acid (1)	R_1=OH, R_2=H, R_3=H, R_4=OH
Chenodeoxycholic acid (2)	R_1=OH, R_2=H, R_3=OH, R_4=H
3α-hydroxy-12-oxo-5ß-cholanoic acid(3)	R_1=OH, R_2=H, R_3=H, R_4=O
3α-hydroxy-7-oxo-5ß-cholanoic acid(4)	R_1=OH, R_2=H, R_3=O, R_4=H
3α-hydroxy-7,12-dioxo-5ß-cholanoic(5)	R_1=OH, R_2=H, R_3=O, R_4=O
12α-hydroxy-3,7-dioxo-5ß-cholanoic acid(6)	R_1=O, R_2=H, R_3=O,R_4=OH
3,7,12- Trioxo-5ß-cholanoic acid(7)	R_1=O, R_2=H, R_3=O, R_4=O
Hyodeoxycholic acid(8)	R_1=OH, R_2=OH, R_3=H, R_4=H
Ursodeoxycholic acid(9)	R_1=OH ,R_2=H, R_3=OH(β), R_4=H
3,12-dioxo-5ß-cholanoic acid(10)	R_1=0, R_2=H, R_3=H, R_4=O
3,7-dioxo-5ß-cholanoic acid (11)	R_1=0, R_2=H, R_3=0, R_4=H
3α , 7α-dihdroxy-12-oxo- 5ß-cholanoic acid(12)	R_1=0H, R_2=H, R_3=OH, R_4=O
3α , 12α-dihdroxy-7-oxo- 5ß-cholanoic acid (13)	R_1=0H, R_2=H, R_3=O, R_4=OH

Table 1. Calculated bioactivity scores of examined bile acids.

Compound	GPCR	ICM	NRL	PI
1	0,28	0,31	0,74	0,25
2	0,33	0,33	0,86	0,29
3	0,20	0,23	0,74	0,22
4	0,25	0,27	0,74	0,27
5	0,22	0,19	0,67	0,19
6	0,22	0,18	0,69	0,22
7	0,15	0,10	0,61	0,05
8	0,33	0,34	0,89	0,29
9	0,33	0,33	0,86	0,29
10	0,13	0,14	0,68	0,08
11	0,18	0,18	0,68	0,13
12	0,24	0,21	0,82	0,25
13	0,25	0,22	0,70	0,26

Recent Publications

1.Anjul K, Rajesh KC, Pramod SP., 2010. Synthesis of click bile acid polymers and their application in stabilization of silver nanoparticles showing Iodide Sensing Property. Org. Lett. 12(1), 24–27

2. Armstrong JM, Carey CM., 1982. The hydrophobic-hydrophilic balance of bile salts. Inverse correlation between reverse-phase high performance liquid chromatographic mobilities and micellar cholesterol-solubilizing capacities. J. Lipid. Res. 23, 6362-6370.

3. Calabresi M, Andreozzi P, La Mesa C., 2012. Supra-molecular association and polymorphic behavior in systems containing bile acid salts, Molecules. 12, 1731-1754.

4. Ceryak S, Bouscarel B, Fromm H., 1993. Comparative binding of bile acids to serum lipoproteins and albumin. J. Lipid. Res. 34, 661-1674Chiang JY., 2009. Bile acids: regulation of synthesis, J Lipid Res. 50(10), 1955–1966.

5. Chong HS, Hyun AS, Xiang M, Sooyoun L, Xiang S, Mhaske Santosh B., 2009. Bile acid-based polyaminocarboxylate conjugates as targeted antitumor agents. J. Chem. Commun. 21, 3011-3013.

Biography

Jovana Trifunović has completed her Ph.D. in Pharmacy from University of Novi Sad and currently, she is Post-doctoral student at University of Vienna. She was visiting student at Department of Chemistry, University of Graz and at Department of Organic Chemistry at Graz University of Technology, Austria during 2012/2013 and 2014.