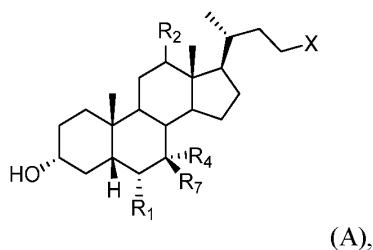


CLAIMS

1. A pharmaceutical composition comprising an FXR agonist, at least one PPAR-alpha agonist, PPAR-delta agonist, and/or PPAR-alpha and delta dual agonist, and optionally one or more pharmaceutically acceptable carriers.
2. The pharmaceutical composition of claim 1, wherein the at least one PPAR-alpha agonist is a fibrate.
3. The pharmaceutical composition of claim 2, wherein the fibrate is selected from bezafibrate, ciprofibrate, clofibrate, fenofibrate, gemfibrozil, binifibrate, clinofibrate, clofibric acid, nicofibrate, pirifibrate, plafibrade, ronifibrate, theofibrate, and tocofibrate, or a pharmaceutically acceptable salt or ester thereof, and a derivative of 2-phenoxy-2-methylpropanoic acid in which the phenoxy moiety is substituted with an optionally substituted piperidine, 4-hydroxypiperidine, piperid-3-ene or piperazine.
4. The pharmaceutical composition of claim 3, wherein the fibrate is selected from bezafibrate, fenofibrate, and clofibrate, or a pharmaceutically acceptable salt or ester thereof.
5. The pharmaceutical composition of claim 4, wherein the fibrate is fenofibrate.
6. The pharmaceutical composition of claim 3, wherein the fibrate is 2-[3-[1-(4-fluorobenzoyl)-piperidin-4-yl]phenoxy]-2-methylpropanoic acid.
7. The pharmaceutical composition of claim 1, wherein the at least one PPAR-delta agonist is {4-[(4-methyl-2-[4-(trifluoromethyl)phenyl]-1,3-thiazol-5-yl)methyl]sulfanyl}-2-methylphenoxy}acetic acid, {2-methyl-4-[5-methyl-2-(4-trifluoromethyl-phenyl)-2H-[1,2,3]triazol-4-ylmethylsulfanyl]-phenoxy}-acetic acid, or [4-[[[2-[3-fluoro-4-(trifluoromethyl)phenyl]-4-methyl-5-thiazolyl]methyl]thio]-2-methyl phenoxy]-acetic acid, or a pharmaceutically acceptable salt thereof.
8. The pharmaceutical composition of claim 1, wherein the at least one PPAR-alpha and delta dual agonist is 2-[2,6 dimethyl-4-[3-[4-(methylthio)phenyl]-3-oxo-1(E)-propenyl]phenoxy]-2-methylpropanoic acid, (2S)-2-methoxy-3-[4-[2-(5-methyl-2-phenyl-4-

oxazolyl)ethoxy]-7-benzothiophenyl]propanoic acid, N-[(4-methoxyphenoxy)carbonyl]-N-{4-[2-(5-methyl-2-phenyl-1,3-oxazol-4-yl)ethoxy]benzyl}glycine, (2S)-2-ethoxy-3-[4-[2-(4-methylsulfonyloxyphenyl)ethoxy]phenyl]propanoic acid, or (2S)-2-ethoxy-3-[4-(2-{2-methyl-5-[4-(methylsulfanyl)phenyl]-1H-pyrrol-1-yl}ethoxy)phenyl]propanoic acid, or a pharmaceutically acceptable salt thereof.

9. The pharmaceutical composition of claim 1, further comprising a statin.
10. The pharmaceutical composition of claim 9, wherein the statin is selected from simvastatin, fluvastatin, pravastatin, rivastatin, mevastatin, atorvastatin, cerivastatin, lovastatin, pitavastatin, fluindostatin, velostatin, dalvastatin, rosuvastatin, dihydrocompactin, and compactin.
11. A pharmaceutical composition comprising an FXR agonist, at least one statin, and optionally one or more pharmaceutically acceptable carriers.
12. The pharmaceutical composition of claim 1, 9, or 11, wherein the FXR agonist is a compound of formula A:

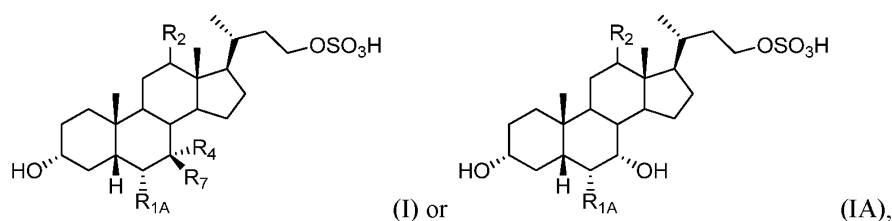


or a pharmaceutically acceptable salt, or amino acid conjugate thereof, wherein:

- R₁ is hydrogen or unsubstituted C₁-C₆ alkyl;
- R₂ is hydrogen or α -hydroxyl;
- X is C(O)OH, C(O)NH(CH₂)_mSO₃H, C(O)NH(CH₂)_nCO₂H or OSO₃H;
- R₄ is hydroxyl or hydrogen;
- R₇ is hydroxyl or hydrogen;
- m is 1, 2, or 3; and
- n is 1, 2, or 3.

13. The pharmaceutical composition of claim 12, wherein R₁ is unsubstituted C₁-C₆ alkyl.

14. The pharmaceutical composition of claim 13, wherein R_1 is methyl, ethyl, or propyl.
15. The pharmaceutical composition of claim 14, wherein R_1 is ethyl.
16. The pharmaceutical composition of claim 12, wherein X is selected from $C(O)OH$, $C(O)NH(CH_2)SO_3H$, $C(O)NH(CH_2)CO_2H$, $C(O)NH(CH_2)_2SO_3H$, and $C(O)NH(CH_2)_2CO_2H$.
17. The pharmaceutical composition of claim 16, wherein X is $C(O)OH$.
18. The pharmaceutical composition of claim 12, wherein X is OSO_3H .
19. The pharmaceutical composition of claim 12, wherein R_4 is hydroxyl and R_7 is hydrogen.
20. The pharmaceutical composition of claim 12, wherein the FXR agonist is a compound of formula I or IA:



or a pharmaceutically acceptable salt or amino acid conjugate thereof, wherein

R_{1A} is hydrogen or unsubstituted C_1 - C_6 alkyl;

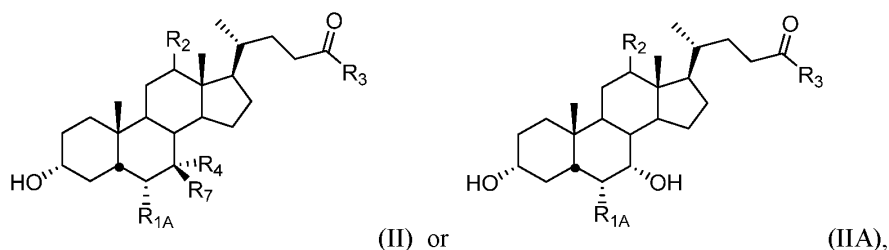
R_2 is hydrogen or α -hydroxyl;

R_4 is hydroxyl or hydrogen; and

R_7 is hydroxyl or hydrogen.

21. The pharmaceutical composition of claim 20, wherein R_{1A} is unsubstituted C_1 - C_6 alkyl.
22. The pharmaceutical composition of claim 21, wherein R_{1A} is methyl, ethyl, or propyl.
23. The pharmaceutical composition of claim 22, wherein R_{1A} is ethyl.

24. The pharmaceutical composition of claim 12, wherein the FXR agonist is a compound of formula II or IIA:



or a pharmaceutically acceptable salt or amino acid conjugate thereof, wherein:

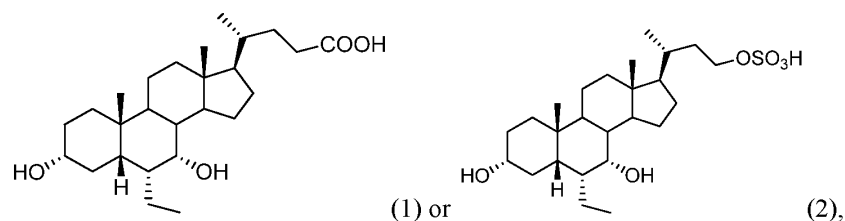
- R_{1A} is hydrogen or unsubstituted C₁-C₆ alkyl;
- R_2 is hydrogen or α -hydroxyl;
- R_3 is hydroxyl, $\text{NH}(\text{CH}_2)_m\text{SO}_3\text{H}$, or $\text{NH}(\text{CH}_2)_n\text{CO}_2\text{H}$;
- R_4 is hydroxyl or hydrogen;
- R_7 is hydroxyl or hydrogen;
- m is 1, 2, or 3; and
- n is 1, 2, or 3.

25. The pharmaceutical composition of claim 24, wherein R_{1A} is unsubstituted C₁-C₆ alkyl.

26. The pharmaceutical composition of claim 25, wherein R_{1A} is methyl, ethyl, or propyl.

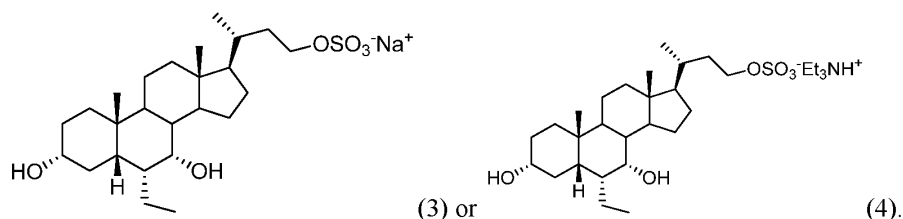
27. The pharmaceutical composition of claim 26, wherein R_{1A} is ethyl.

28. The pharmaceutical composition of claim 12, wherein the FXR agonist is:



or a pharmaceutically acceptable salt or amino acid conjugate thereof.

29. The pharmaceutical composition of claim 12, wherein the FXR agonist is:



30. A method of treating or preventing an FXR mediated disease or condition or a condition related to elevated lipid levels, comprising administering the pharmaceutical composition of claim 1, 9, or 11 to a subject in need thereof.

31. The method of claim 30, wherein the disease or condition is selected from primary biliary cirrhosis (PBC), primary sclerosing cholangitis (PSC), portal hypertension, bile acid diarrhea, a chronic liver disease, nonalcoholic fatty liver disease (NAFLD), nonalcoholic steatohepatitis (NASH), hepatitis C infection, an alcoholic liver disease, liver damage due to progressive fibrosis, liver fibrosis, a cardiovascular disease, and hyperlipidemia.

32. The method of claim 30, wherein the condition is selected from resistant primary biliary cirrhosis; primary biliary cirrhosis where there is associated liver function test elevation and hyperlipidemia; primary sclerosing cholangitis; non-alcohol-induced steatohepatitis; chronic liver disease associated with hepatitis B, C or alcohol; hyperlipidemia where the hyperlipidemia is primary hyperlipidemia with or without a genetic component; and hyperlipidemia associated with coronary artery disease, cerebrovascular arterial disease, peripheral vascular disease, aortic aneurisms, or carotid atherosclerosis.

33. A method of inhibiting or reversing fibrosis, comprising administering the pharmaceutical composition of claim 1, 9, or 11 to a subject in need thereof.

34. The method of claim 33, wherein the fibrosis is selected from liver fibrosis, kidney fibrosis, and intestinal fibrosis.