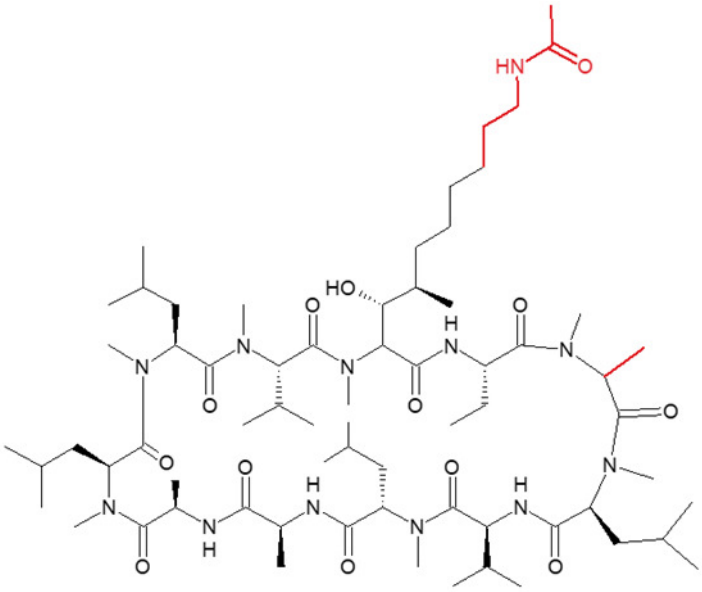


(CRV431);

(b) Vitamin E;

(c) ~~Maisine® CC~~ glyceryl monolinoleate;

(d) propylene glycol;

(e) ~~Transcutol®~~ diethylene glycol monoethyl ether;

(f) ethanol; and

(g) ~~Cremophor® RH40~~ polyoxyl castor oil, wherein Vitamin E, ~~Maisine® CC~~ glyceryl monolinoleate, propylene glycol, ~~Transcutol®~~ diethylene glycol monoethyl ether, ethanol, and ~~Cremophor® RH40~~ polyoxyl castor oil are at a weight ratio, respectively, of about 1/(1-2)/(2-5)/(2-5)/(2-2.4)/(4-6) and wherein polyoxyl castor oil and glyceryl monolinoleate are at a weight ratio equal to or greater than 3 ~~(0.75-1.5)/(0.5-2)/(2-5)/(2-5)/(2-2.4)/(4-8)~~.

[0004b] In another aspect, the present disclosure refers to the pharmaceutical composition as described herein for use as a medicament.

[0004c] In another aspect, the present disclosure refers to a use of a pharmaceutical composition as described herein in the manufacture of a medicament.

[0004d] In yet another aspect, the present disclosure refers to the pharmaceutical composition as described herein for use in the treatment or prevention of a disease in a subject, wherein the disease is liver disease.

[0004e] In yet another aspect, the present disclosure refers to a use of a pharmaceutical composition as described herein in the manufacture of a medicament for the treatment or prevention of a disease in a subject, wherein the disease is liver disease.

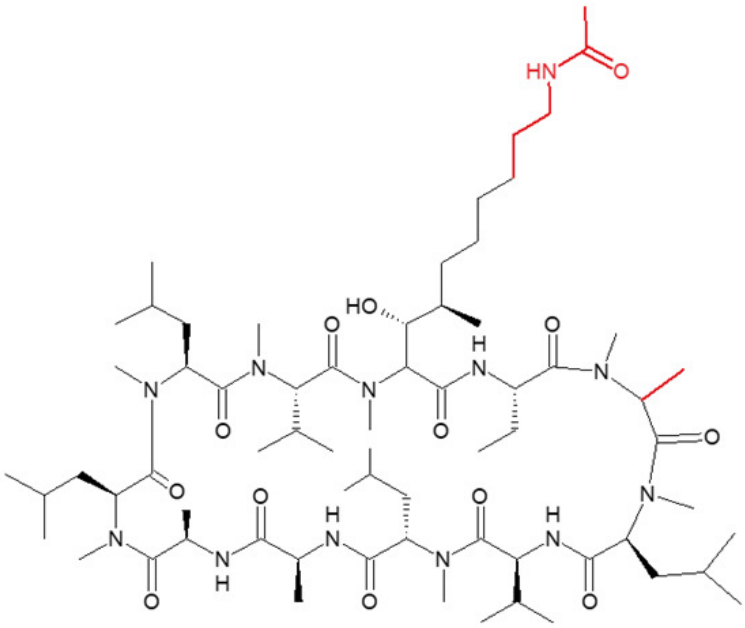
[0005] In one example, the present disclosure provides a self-microemulsifying drug delivery system (SMEDDS) comprising a derivative or an analog, of cyclosporine A, such as CRV431:

CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising:

(a) CRV431 at a concentration of from about 10 mg/mL to about 90 mg/mL:



(CRV431);

(b) Vitamin E;

(c) ~~Maisine® CC~~ glyceryl monolinoleate;

(d) propylene glycol;

(e) ~~Transcutol®~~ diethylene glycol monoethyl ether;

(f) ethanol; and

(g) ~~Cremophor® RH40~~ polyoxyl castor oil, wherein Vitamin E, ~~Maisine® CC~~ glyceryl monolinoleate, propylene glycol, ~~Transcutol®~~ diethylene glycol monoethyl ether, ethanol, and ~~Cremophor® RH40~~ polyoxyl castor oil are at a weight ratio, respectively, of about 1/(1-2)/(2-5)/(2-5)/(2-2.4)/(4-6) and wherein polyoxyl castor oil and glyceryl monolinoleate are at a weight ratio equal to or greater than 3~~(0.75-1.5)/(0.5-2)/(2-5)/(2-5)/(2-2.4)/(4-8)~~.

2. The pharmaceutical composition of claim 1 for use as a medicament.

3. Use of a pharmaceutical composition of claim 1 in the manufacture of a medicament.

4. The pharmaceutical composition of claim 1 for use in the treatment or prevention of a disease in a subject, wherein the disease is liver disease.

5. Use of a pharmaceutical composition of claim 1 in the manufacture of a medicament for

the treatment or prevention of a disease in a subject, wherein the disease is liver disease.

6. The ~~pharmaceutical composition of claim 4 or the~~ use of claim 4 or 5, wherein the disease is a severe liver disease.

7. The ~~pharmaceutical composition of claim 4 or the~~ use of claim 4 or 5, wherein the disease is hepatitis B (HBV).

8. The ~~pharmaceutical composition of claim 4 or the~~ use of claim 4 or 5, wherein the disease is liver fibrosis.

9. The ~~pharmaceutical composition of claim 4 or the~~ use of claim 4 or 5, wherein the disease is hepatocellular carcinoma.

10. The ~~pharmaceutical composition or the~~ use of any one of claims 4-9, wherein an area under curve (AUC) of a plot of a concentration of CRV431 in a blood of the subject over time is from about 5000 ng.hr/ml to about 150000 ng.hr/ml.

11. The ~~pharmaceutical composition or the~~ use of any one of claims 4-10, wherein a maximum concentration (C_{max}) of CRV431 in a blood of the subject is from about 1500 ng/ml to about 2500 ng/ml.

12. The ~~pharmaceutical composition or the~~ use of any one of claims 4-11, wherein a time (T_{max}) to reach a maximum concentration of CRV431 in a blood of the subject is from about 0.5 hour to about 8 hours.

13. The ~~pharmaceutical composition or the~~ use of any one of claims 4-12, wherein an elimination half-life ($T_{1/2}$) of CRV431 in a blood of the subject is from about 10 hours to about 200 hours.

14. The ~~pharmaceutical composition or the~~ use of any one of claims 4-13, wherein a concentration of CRV431 in a liver of the subject relative to a concentration of CRV431 in a blood of the subject is from about 1 to about 20.

15. The ~~pharmaceutical composition or the~~ use of any one of claims 4-14, wherein a therapeutically effective amount of the pharmaceutical composition ~~or CRV431~~ is from about 0.5 mg/kg to about 5 mg/kg.

16. The ~~pharmaceutical composition or the~~ use of any one of claims 4-15, thereby a symptom of the disease in the subject is alleviated and/or a severity of the disease in the subject decreases.

17. The ~~pharmaceutical composition or the~~ use of any one of claims 4-16, thereby a function

of a liver of the subject is improved.

18. The ~~pharmaceutical composition or the~~ use of any one of claims 4-17, thereby a load of a virus causing the disease decreases.

19. The pharmaceutical composition or the use of any of the preceding claims, wherein the pharmaceutical composition is stable at room temperature.

20. The pharmaceutical composition or the use of any of the preceding claims, wherein the pharmaceutical composition is stable for from at least about 25 days to at least about 200 days.

21. The pharmaceutical composition or the use of any of the preceding claims, wherein the diameter of particles formed by the pharmaceutical composition dispersed in an aqueous solution is from about 15 nm to about 40 nm.

22. The pharmaceutical composition or the use of any of the preceding claims, wherein the concentration of CRV431 is from about 50 mg/mL to about 90 mg/mL, optionally wherein the concentration of CRV431 is about 70 mg/mL.

23. The pharmaceutical composition or the use of any of the preceding claims, wherein Vitamin E, ~~Maisine® CC~~ glyceryl monolinoleate, propylene glycol, ~~Transcutol®~~ diethylene glycol monoethyl ether, ethanol, and ~~Cremophor® RH40~~ polyoxyl castor oil are at a weight ratio, respectively, of about 1/1/5/5/2.4/4 to about 1/1.5/2.5/5/2.4/5.