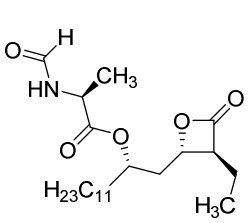
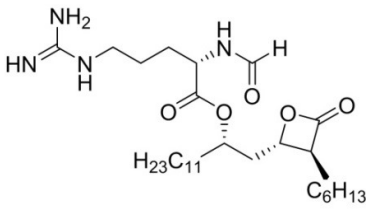
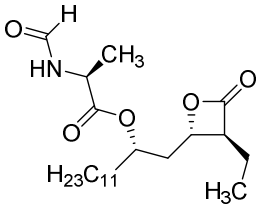
indices associated with these conditions. Accordingly, in some examples, provided herein are methods and compositions for limiting lipotoxicity and thereby reducing the likelihood of poor outcomes associated with acute pancreatitis and other severe systemic conditions.

In one aspect, the present disclosure refers to a compound selected from the group consisting of:

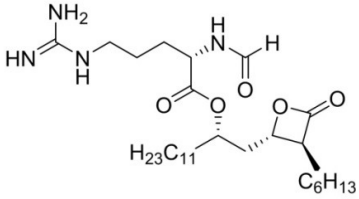



and

or a pharmaceutically acceptable salt thereof. In some examples, the compound is:



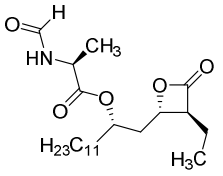
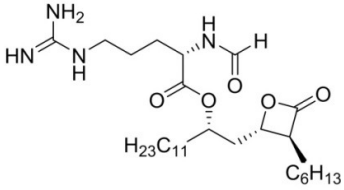
or a pharmaceutically acceptable salt thereof. In some examples, the compound is:



or a pharmaceutically acceptable salt thereof.

Further provided herein is a pharmaceutical composition comprising one or more of the compounds provided herein and a pharmaceutically acceptable excipient. In one aspect, the present disclosure refers to a pharmaceutical composition comprising any one of the compounds disclosed herein, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

In another aspect, the present disclosure refers to use of a compound selected from the group consisting of:

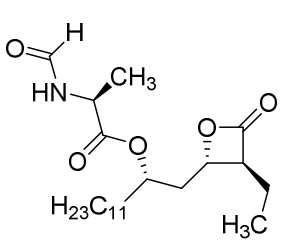
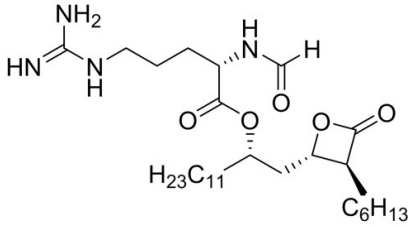



and

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating acute pancreatitis in a subject in need thereof. This disclosure also provides methods of treating acute pancreatitis in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound provided herein or a pharmaceutically acceptable salt thereof. In some examples, the acute pancreatitis is severe. In some examples, the acute pancreatitis is downgraded from severe to mild following administration. In some examples, the subject is obese. In some

examples, the risk of developing shock, renal failure, and/or pulmonary failure is reduced.

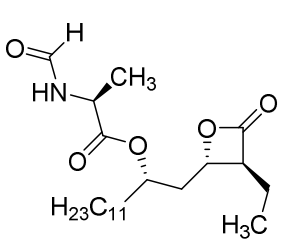
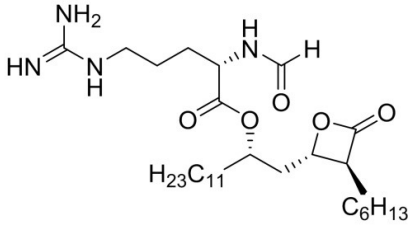
In yet another aspect, the present disclosure refers to use of a compound selected from the group consisting of:

and

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating acne in a subject in need thereof. Also provided herein is a method of treating acne in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound provided herein or a pharmaceutically acceptable salt thereof.

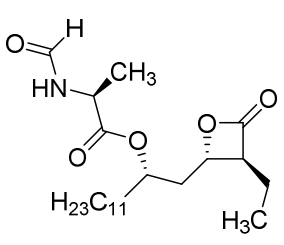
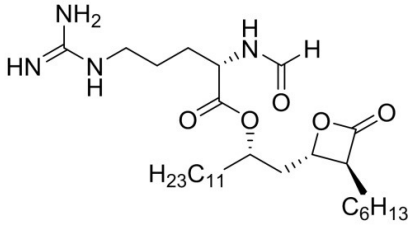
In yet a further aspect, the present disclosure refers to use of a compound selected from the group consisting of:

and

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating sepsis in a subject in need thereof. Further provided herein is a method of treating sepsis in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound provided herein or a pharmaceutically acceptable salt thereof. In some examples, the sepsis is culture negative sepsis.

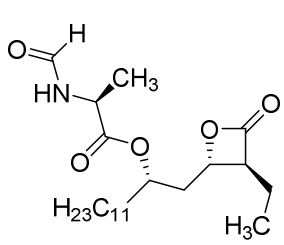
In another aspect, the present disclosure refers to use of a compound selected from the group consisting of:

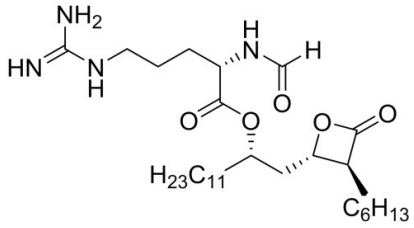
and

or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating burns in a subject in need thereof. This disclosure also provides methods of treating burns in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound provided herein or a pharmaceutically acceptable salt thereof.

In another aspect, the present disclosure refers to use of a compound selected from the group consisting of:

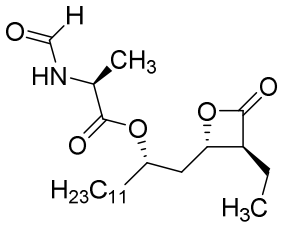


and

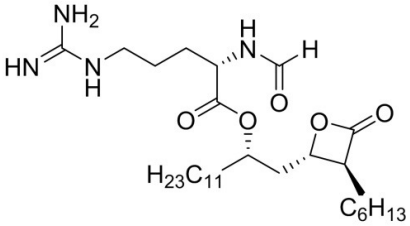


or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating infections in a subject in need thereof. Also provided herein is a method for treating infections in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound provided herein or a pharmaceutically acceptable salt thereof. In some examples, the infection is caused by one or more organisms selected from the group consisting of *P. auregenosa*, *S. aureus*, *B. subtilis*, and *B. cepecia*.

In some of the above examples, the compound is:



or a pharmaceutically acceptable salt thereof. In some examples, the compound is:



or a pharmaceutically acceptable salt thereof.

Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to

which this disclosure belongs. Methods and materials are described herein for use in the present disclosure; other, suitable methods and materials known in the art can also be used. The materials, methods, and examples are illustrative only and not intended to be limiting. All publications, patent applications, patents, sequences, database entries, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control.

Other features and advantages of the disclosure will be apparent from the following detailed description and figures, and from the claims.

DESCRIPTION OF DRAWINGS

FIG. 1 is a schematic of the structure of orlistat dividing the compound into three main regions.

FIG. 2 is a scheme detailing a synthetic route to prepare amino-ester modifications to the orlistat core.

FIG. 3 shows the structures of the various non-formylated amino ester modified analog compounds prepared.

FIG. 4 provides line graphs showing the results of a lipase inhibition assay testing the non-formylated amino ester modified analog compounds. **FIG. 4A** provides the results of freshly prepared solutions of the compounds while **FIG. 4B** provides the results of solutions stored overnight.

FIG. 5 is a scheme detailing a synthetic route to prepare formulated amino ester modified analogs.

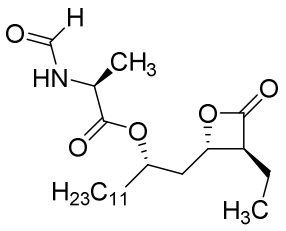
FIG. 6 shows the structures of the various formyl amino ester modified analog compounds prepared.

FIG. 7 provides line graphs showing the results of a lipase inhibition assay testing the formyl amino ester modified analog compounds. **FIG. 7A** provides the results of freshly prepared solutions of the compounds while **FIG. 7B** provides the results of solutions stored overnight.

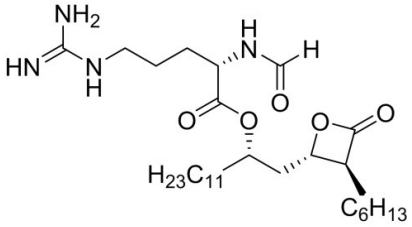
FIG. 8 provides bar graphs detailing the efficacy of selected analog compounds in reducing lipotoxic damage to acinar cells in acinar-adipocyce co-culture (**FIG. 8A**) while also assessing the toxicity of the compounds to these cells (**FIG. 8B**).

WHAT IS CLAIMED IS:

1. A compound selected from the group consisting of:

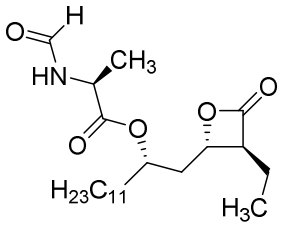


and



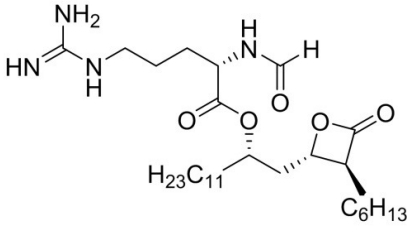
or a pharmaceutically acceptable salt thereof.

2. The compound of claim 1, wherein the compound is:



or a pharmaceutically acceptable salt thereof.

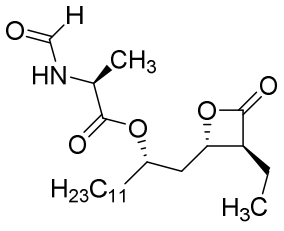
3. The compound of claim 1, wherein the compound is:

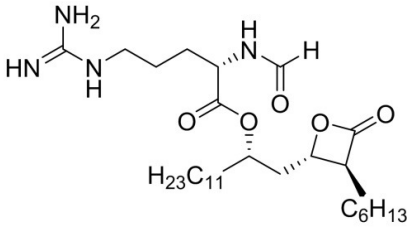


or a pharmaceutically acceptable salt thereof.

4. A pharmaceutical composition comprising a compound of any one of claims 1-3, or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable excipient.

5. Use of a compound selected from the group consisting of:



and


or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating acute pancreatitis in a subject in need thereof.

6. The use of claim 4, wherein the acute pancreatitis is severe.

7. The use of claim 4, wherein the acute pancreatitis is downgraded from severe to mild following administration.

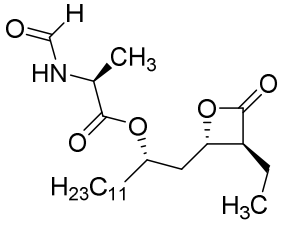
8. The use of claim 4, wherein the subject is obese.

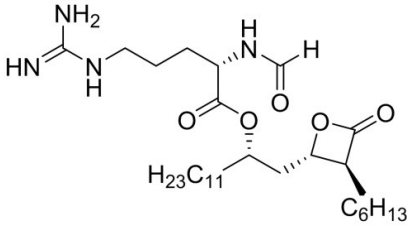
9. The use of claim 4, wherein the risk of developing shock is reduced.

10. The use of claim 4, wherein the risk of developing renal failure is reduced.

11. The use of claim 4, wherein the risk of developing pulmonary failure is reduced.

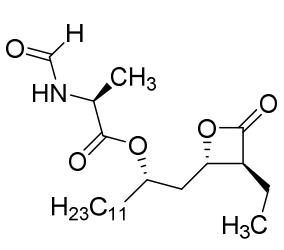
12. Use of a compound selected from the group consisting of:



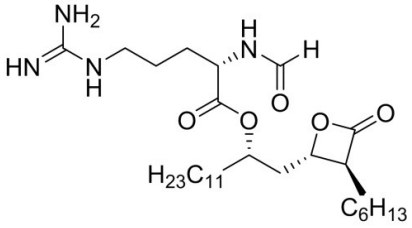
and


or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating acne in a subject in need thereof.

13. Use of a compound selected from the group consisting of:



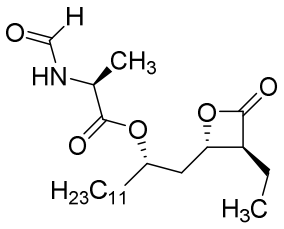
and



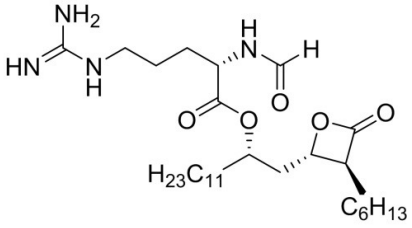
or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating sepsis in a subject in need thereof.

14. The use of claim 12, wherein the sepsis is culture negative sepsis.

15. Use of a compound selected from the group consisting of:

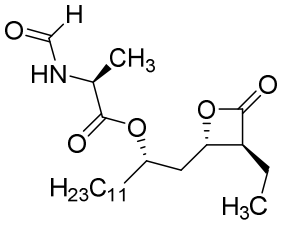


and

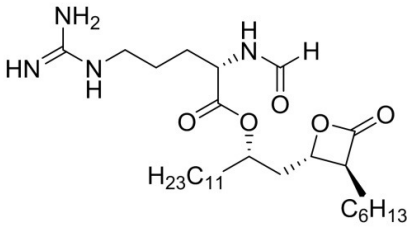


or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating burns in a subject in need thereof.

16. Use of a compound selected from the group consisting of:



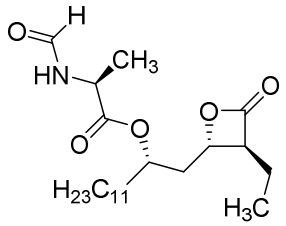
and



or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for treating infections in a subject in need thereof.

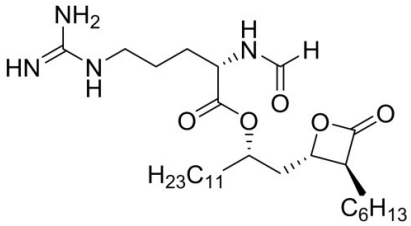
17. The use of claim 15, wherein the infection is caused by one or more organisms selected from the group consisting of *P. auregenosa*, *S. aureus*, *B. subtilis*, and *B. cepecia*.

18. The use of any one of claims 4-10, wherein the compound is:



or a pharmaceutically acceptable salt thereof.

19. The use of any one of claims 4-10, wherein the compound is:



or a pharmaceutically acceptable salt thereof.