The present disclosure also relates to a pharmaceutical composition comprising a compound of the application or a pharmaceutically acceptable salt, solvate, ester, tautomer, amino acid conjugate, or metabolite thereof, and at least one pharmaceutically acceptable excipient.

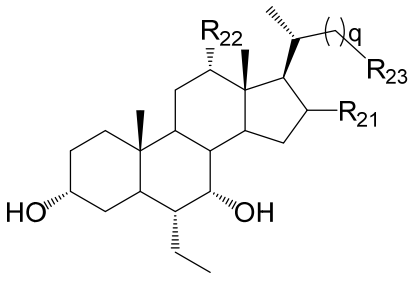
The present disclosure also relates to a method of treating or preventing a disease or disorder in a subject, comprising administering to the subject an effective amount of a compound of the application, or a pharmaceutically acceptable salt, solvate, ester, tautomer, amino acid conjugate, or metabolite thereof.

The present disclosure also relates to a compound of the application, or a pharmaceutically acceptable salt, solvate, ester, tautomer, amino acid conjugate, or metabolite thereof, for use in a method of treating or preventing a disease or disorder in a subject.

The present disclosure also relates to use of a compound of the application, or a pharmaceutically acceptable salt, solvate, ester, tautomer, amino acid conjugate, or metabolite thereof, in the manufacture of a medicament for treating or preventing a disease or disorder in a subject.

The present disclosure also relates to TGR5 is involved in the disease or disorder. The present disclosure also relates to TGR5 plays a role in the activation/upregulation of the cellular pathway which results in the disease or disorder. The present disclosure also relates to TGR5 plays a role in the de-activation/downregulation of the cellular pathway which results in the disease or disorder. In a further embodiment, the disease or disorder is selected from a metabolic disease, an inflammatory disease, an autoimmune disease, a cardiac disease, a kidney disease, a gastrointestinal disease, a pulmonary disease, and a cancer.

In one aspect of the present disclosure, there is provided a compound of formula II:



(II),

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

q is 0, 1, or 2;

R_{21} and R_{22} are each independently H or OH; and

R_{23} is tetrazolyl, oxadiazolyl, oxadiazolonyl, or thiazolidine-dionyl optionally substituted with $NHS(O)_2$-(C_1-C_3) alkyl.

In another aspect of the present disclosure, there is provided a pharmaceutical composition comprising the compound as described herein, and at least one pharmaceutically acceptable excipient.

In yet another aspect of the present disclosure, there is provided a compound as described herein for use in treating or preventing a TGR5-mediated disease.

In a further aspect of the present disclosure, there is provided a compound as described herein for use in treating or preventing a metabolic disease.

In another aspect of the present disclosure, there is provided a compound as described herein for use in treating or preventing type II diabetes.

In yet another aspect of the present disclosure, there is provided a use of a compound as described herein in the manufacture of a medicament for the treatment or prevention of a TGR5-mediated disease.

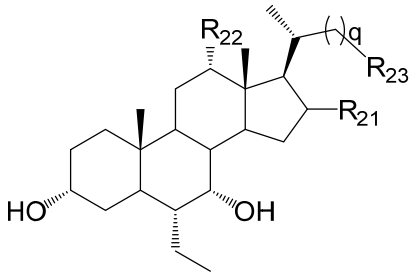
In a further aspect of the present disclosure, there is provided a use of a compound as described herein in the manufacture of a medicament for the treatment or prevention of a metabolic disease.

In another aspect of the present disclosure, there is provided a use of a compound as described herein in the manufacture of a medicament for the treatment of type II diabetes.

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 application belongs. In the specification, the singular forms also include the plural unless the context clearly dictates otherwise. Although methods and materials similar or equivalent to those described herein can be used in the practice or testing of the present application, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference. The references cited herein are not admitted to be prior art to the present application. In the case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and are not intended to be limiting.

CLAIMS

1. A compound of formula II:



(II),

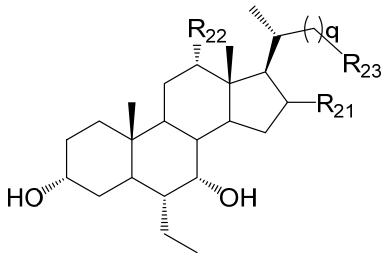
or a pharmaceutically acceptable salt, solvate, ester, tautomer, or amino acid conjugate thereof, wherein:

q is 0, 1, or 2;

R_{21} and R_{22} are each independently H or OH; and

R_{23} is tetrazolyl, oxadiazolyl, oxadiazolonyl, or thiazolidine-dionyl optionally substituted with $NHS(O)_2$-(C_1-C_3) alkyl.

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



(II).

3. The compound of claim 1, wherein q is 1.

4. The compound of claim 1, wherein q is 2.

5. The compound of claim 1, wherein R_{21} is H.

6. The compound of any one of claims 1-4, wherein R_{21} is OH.

7. The compound of any one of claim 1-5, wherein R_{22} is H.

8. The compound of any one of claim 1-5, wherein R_{22} is OH.

9. The compound of any one of claim 1-8, wherein R_{23} is tetrazolyl, oxadiazolyl, oxadiazolonyl, or thiazolidine-dionyl.

10. A pharmaceutical composition comprising the compound of any one of claims 1-9, and at least one pharmaceutically acceptable excipient.

11. A compound of any one of claims 1-9 for use in treating or preventing a TGR5-mediated disease.

12. A compound of any one of claims 1-9 for use in treating or preventing a metabolic disease.

13. A compound of any one of claims 1-9 for use in treating or preventing type II diabetes.

14. Use of a compound of any one of claims 1-9 in the manufacture of a medicament for the treatment or prevention of a TGR5-mediated disease.

15. Use of a compound of any one of claims 1-9 in the manufacture of a medicament for the treatment or prevention of a metabolic disease.

16. Use of a compound of any one of claims 1-9 in the manufacture of a medicament for the treatment of type II diabetes.