absorbed in the stomach. The high concentration rapidly distributes and uncouples immediately, producing high levels of heat in a short period of time. Thus, DNP has a small therapeutic index and is extremely dangerous in overdose. DNP was labelled as “extremely dangerous and not fit for human consumption” by the Federal Food, Drug and Cosmetic Act of 1938. Accordingly, there is a need for uncouplers that can safely treat mitochondria-related disorders or conditions.

[0005] 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole is a novel small molecule uncoupler (Compound 1). It works as a controlled metabolic accelerator (CMA). It is designed to effectively address the root cause of metabolic diseases, the accumulation of fat and sugars in the body. CMAs work to improve cellular metabolism and increase energy expenditure and calorie consumption, reducing the accumulation of fat. Using a new controlled and targeted approach, Compound 1 can increase mitochondrial proton leak, an ongoing process in the body that dissipates energy, and accounts for 20% - 40% of daily calories. Compound 1 leverages a mitochondrial uncoupling mechanism to increase substrate utilization.

[0006] In recent years, the increase of incidence and prevalence of muscle wasting in the obese population has been observed. In patients with obese sarcopenia, the retention of muscle mass is critical, and the loss of muscle mass is not only counterproductive for these patients to regain metabolic health but can be a direct cause for subsequent morbidities and loss of quality of life due to falls and increase dependence on daily care. There is, henceforth, a dire need for pharmaceutical interventions that can address excess adiposity without detrimental effects on muscle mass.

SUMMARY

[0006a] In a first aspect of the present disclosure, there is provided a use of 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for preserving skeletal muscle mass during bodyweight reduction in a subject in need thereof.

[0007] In one example, the present disclosure provides a method of preserving skeletal muscle mass during bodyweight reduction in a subject in need thereof, wherein the method comprises administering to the subject a therapeutically effective amount of 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole, or a pharmaceutically acceptable salt thereof.

[0008] In another example, the bodyweight reduction is attributed to fat reduction.

[0009] In another example, the subject suffers from obesity, excess body fat, diabetes, high blood pressure (hypertension), dyslipidemia, hypertriglyceridemia, acquired lipodystrophy, inherited lipodystrophy, partial lipodystrophy, or metabolic syndrome.

[0010] In another example, the subject suffers from disorders selected from non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH).

[0011] In another example, the subject suffers from decreased muscle mass or obese sarcopenia.

[0012] In another example, the subject has a body mass index greater than 28 kg/m2.

[0013] In another example, the therapeutically effective amount of Compound 1 is from about 30mg to about 1400mg per day, from about 50mg to about 100mg per day, from about 150mg to about 600mg per day, or from 200mg to 550mg orally once daily.

[0014] In another example, the subject experiences fat reduction greater than 5%, 10%, 20%, 30%, or 40%.

[0015] In one example, the method slows the progression of obesity, hypertension, or diabetes.

BRIEF DESCRIPTION OF THE DRAWINGS

[0016] FIG. 1 shows the Phase 2 study design flowchart.

[0017] FIG. 2 shows body fat mass changes in FAS population.

[0018] FIG. 3 shows body fat changes in the elevated HbA1c population.

[0019] FIG. 4 shows reduction of glycated albumin (percent %) in overall (FAS) population.

[0020] FIG. 5 shows the skeletal muscle mass and fat mass change in FAS population.

[0021] FIG. 6 shows the skeletal muscle mass and fat mass change in HbA1c population.

DETAILED DESCRIPTION

Definitions

[0022] While various embodiments and aspects of the present invention are shown and described herein, it will be obvious to those skilled in the art that such embodiments and aspects are provided by way of example only. Numerous variations, changes, and substitutions will now occur to those skilled in the art without departing from the invention. It should be understood that various alternatives to the embodiments of the invention described herein may be employed in practicing the invention.

[0023] The section headings used herein are for organizational purposes only and are not to be construed as limiting the subject matter described. All documents, or portions of documents, cited in the application including, without limitation, patents, patent applications, articles, books,

CLAIMS

We claim:

1. Use of 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole, or a pharmaceutically acceptable salt thereof, in the manufacture of a medicament for preserving skeletal muscle mass during bodyweight reduction in a subject in need thereof.

2. The use of claim 1, wherein the bodyweight reduction is attributed to fat reduction.

3. The use of claim 1 or 2, wherein the subject suffers from obesity, excess body fat, diabetes, high blood pressure (hypertension), dyslipidemia, hypertriglyceridemia, acquired lipodystrophy, inherited lipodystrophy, partial lipodystrophy, or metabolic syndrome.

4. The use of claim 1 or 2, wherein the subject suffers from obesity or excess body fat.

5. The use of claim 1 or 2, wherein the subject suffers from diabetes.

6. The use of claim 5, wherein the diabetes is type 2 diabetes (T2DM).

7. The use of claim 1 or 2, wherein the subject suffers from disorders selected from non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH).

8. The use of claim 1 or 2, wherein, the subject suffers from sarcopenia.

9. The use of claim 1 or 2, wherein the subject suffers from sarcopenic obesity.

10. The use of claim 1 or 2, wherein the subject suffers from decreased muscle mass, loss of muscle mass, muscle weakness, decline in muscle strength, slow walking speed, or difficulty performing normal daily activities.

11. The use of claim 1 or 2, wherein the use slows the progression of obesity, hypertension, or diabetes.

12. The use of any one of claims 1-11, wherein the subject has an abnormal HbA1c level.

13. The use of claim 12, wherein the abnormal HbA1c level is an elevated HbA1c.

14. The use of any one of claims 1-13, wherein the subject has a body mass index greater than 28 kg/m2.

15. The use of any one of claims 1-14, wherein 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole is to be administered at from about 30mg to about 1400mg per day, from about 100mg to about 1000mg per day, from about 150mg to about 600mg per day, from 200mg to 550mg per day, or from about 50mg to about 100mg per day.

16. The use of any one of claims 1-15, wherein 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole is to be administered at about 100mg, 150mg, 200mg, 250mg, 300mg, 350mg, 400mg, 450mg, 500mg, or 600mg per day.

17. The use of any one of claims 1-16, wherein 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole is to be administered at about 150mg, 300mg, or 450mg per day.

18. The use of any one of claims 1-15, wherein 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole is to be administered at about 30mg, 35mg, 40mg, 45mg, 50mg, 55mg, 60mg, 65mg, 70mg, 75mg, 80 mg, 85mg, 90mg, or 95mg, per day.

19. The use of any one of claims 1-18, wherein 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole is to be administered orally once daily.

20. The use of any one of claims 1-19, wherein the subject experiences fat reduction greater than 5%, 10%, 20%, 30%, or 40%.

21. The use of claim 20, wherein the subject has an elevated HbA1c level and experiences fat reduction of approximately 40%.

22. The use of any one of claims 1-21, wherein the subject experiences at least one of:
i) a reduction of lipids by at least 10% or at least 30%;
ii) a reduction of blood pressure of at least 5 mmHg; and/or
iii) a reduction of liver fat by at least 50%.

23. The use of any one of claims 1-21, wherein the subject experiences at least one of:

i) a reduction of lipids by at least 10% or at least 30%;

ii) a reduction of blood pressure of at least 5 mmHg; and/or

iii) a reduction of liver fat by at least 30%.