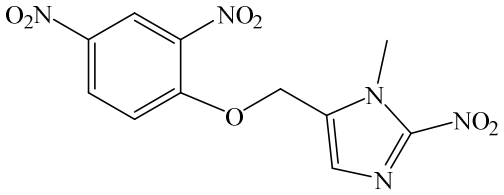
mitochondrial proton leak, an ongoing process in the body that dissipates energy, and accounts for 20% - 40% of daily calories. 5-[(2,4-Dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole leverages a mitochondrial uncoupling mechanism to increase substrate utilization.

[0006] A primary concern for the manufacture of pharmaceutical compounds is the stability of an active substance. An active substance having a stable crystalline morphology may provide consistent processing parameters and pharmaceutical quality. Unstable active substances may affect the reproducibility of the manufacturing process and thus lead to final formulations that do not meet the high quality and other stringent requirements imposed on formulations of pharmaceutical compositions.

[0007] There is thus a continuing need for polymorphic forms of 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole and manufacturing processes for preparing thereof.

SUMMARY

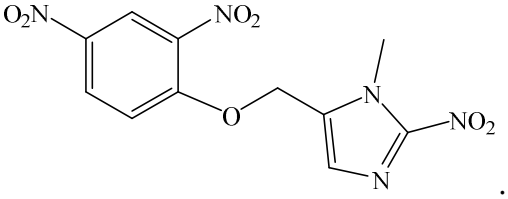
[0008] In one example, the present disclosure provides a compound of 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole having the structure:



Compound **(I)**

wherein the compound **(I)** is in a substantially crystalline form.

[0008a] In one aspect, the present disclosure refers to a crystalline form of 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole having the structure:



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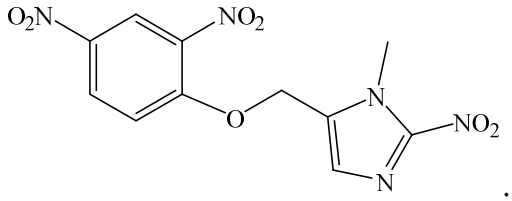
[0008b] In one aspect, the present disclosure refers to a micronized crystalline form of 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole having the structure:



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[0009] In another example, the present disclosure provides polymorphic Form **A** of freebase Compound **(I)** having an X-ray powder diffraction pattern with characteristic peaks expressed in degrees two-theta at approximately 17.6 ± 0.2, 24.9 ± 0.2, 26.1 ± 0.2, and 30.0 ± 0.2.

[0010] In another example, the present disclosure provides polymorphic Form **A** of freebase Compound **(I)** having an X-ray powder diffraction pattern with characteristic peaks expressed in degrees two-theta at approximately 16.1 ± 0.2, 16.4 ± 0.2, 17.6 ± 0.2, 17.9 ± 0.2, 24.9 ± 0.2, 26.1 ± 0.2, and 30.0 ± 0.2.

[0011] In another example, the present disclosure provides polymorphic Form **A** of freebase Compound **(I)** having an X-ray powder diffraction pattern with characteristic peaks

expressed in degrees two-theta at approximately 13± 0.2, 16.1 ± 0.2, 16.4 ± 0.2, 17.6 ± 0.2, 17.9 ± 0.2, 20.4 ± 0.2, 20.7 ± 0.2, 24.9 ± 0.2, 26.1 ± 0.2, and 30.0 ± 0.2.

[0012] In another example, the present disclosure provides polymorphic Form **A** of freebase Compound **(I)** having XRPD pattern as shown in Figure 1.

[0013] In another example, the present disclosure provides polymorphic Form **B** of freebase Compound **(I)** having an X-ray powder diffraction pattern with characteristic peaks expressed, in degree two-theta, at approximately 8.9 ± 0.2, 13.30 ± 0.2, and 26.2 ± 0.2.

[0014] In another example, the present disclosure provides polymorphic Form **B** of freebase Compound **(I)** having an X-ray powder diffraction pattern with characteristic peaks expressed, in degree two-theta, at approximately 8.9 ± 0.2, 9.8 ± 0.2, 13.3 ± 0.2, 21.6 ± 0.2, 23.8 ± 0.2, and 26.2 ± 0.2.

[0015] In another example, the present disclosure provides polymorphic Form **B** of freebase Compound **(I)** having an X-ray powder diffraction pattern with characteristic peaks expressed, in degree two-theta, at approximately 8.9 ± 0.2, 9.8 ± 0.2, 13.3 ± 0.2, 14.0 ± 0.2, 15.7 ± 0.2, 21.6 ± 0.2, 23.8 ± 0.2, 26.2 ± 0.2, 27.3 ± 0.2, and 31.1 ± 0.2.

[0016] In certain examples, the present disclosure provides polymorphic Form **B** of freebase Compound **(I)** having XRPD pattern as shown in Figure 2.

[0016a] In one aspect, the present disclosure refers to a pharmaceutical composition comprising (i) the crystalline form disclosed herein or the micronized crystalline form disclosed herein; and (2) a pharmaceutically acceptable carrier.

[0017] In some examples, the crystalline forms of 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole are useful for regulating mitochondria activities, reducing adiposity, treating diseases including metabolic disorders, diabetes or diabetes-associated complications such as heart disease and renal failure, and moderating or controlling of weight gain in a subject. In one aspect, the present disclosure refers to use of a crystalline form disclosed herein or the micronized crystalline form disclosed herein, in the manufacture of a medicament:

(A) to treat a mitochondria-related disorder or condition in a subject in need thereof;

optionally wherein the disorder or condition is metabolic disorders, diabetes, type 2 diabetes (T2DM), diabetes-associated complications, obesity, excess body fat, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), hepatic steatosis, insulin resistance or intolerance, dyslipidemia, cardiovascular disease, or artherosclerosis;

(B) for reducing adiposity, controlling or preventing of weight gain in a subject in need thereof; or

(C) for stimulating oxygen consumption rate (OCR) in a subject.

[0018] In some examples, the disorder is metabolic disorders, diabetes, or diabetes-associated complications, such as heart disease and renal failure, and moderating or controlling of weight gain in a subject.

[0019] In some examples, the disorder is obesity or excess body fat, diabetes, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), hepatic steatosis, insulin resistance or intolerance, dyslipidemia, cardiovascular disease, atherosclerosis.

[0020] In some examples, the crystalline forms of 5-[(2,4-dinitrophenoxy)methyl]-1-methyl-2-nitro-1H-imidazole are used to reduce adiposity, controlling or preventing of weight gain in a subject, and/or to stimulate oxygen consumption rate (OCR) in a subject, and/or to treat inflammation and fibrosis resulting in NASH in a subject.