THERAPEUTIC COMPOUNDS, FORMULATIONS, AND USE THEREOF

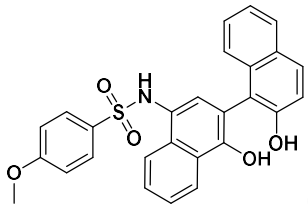
CROSS REFERENCE

[0001] This application claims the benefit of and priority to U.S. Provisional Patent Application No. 63/369,055, filed July 21, 2022, which is incorporated by reference in its entirety herein.

SUMMARY

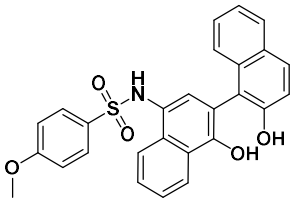
[0002] Disclosed herein, in certain examples, are compositions comprising a compound of formula (I), wherein the compositions are substantially free of an impurity, processes of producing said compositions, and uses thereof such as in treating, preventing, or reducing the risk or severity of certain diseases or disorders (e.g., cancer, fibrosis, and inflammatory diseases or disorders).

[0003] In certain examples, disclosed herein is a composition, comprising a compound of formula (I):

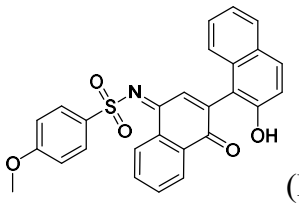


(I),

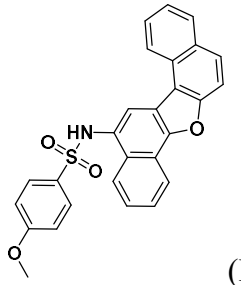
wherein the composition is substantially free of an impurity.**[0003a]** In one aspect, the present disclosure refers to a composition, comprising a compound of formula (I):



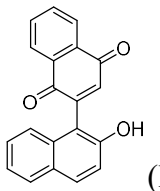
(I), wherein the composition is substantially free of an impurity selected from the group consisting of a compound of formula (II), a compound of formula (III), and a compound of formula (IV), or a combination thereof:



(II),

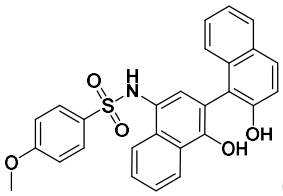
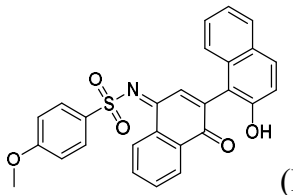
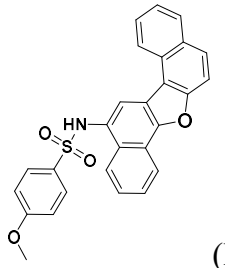
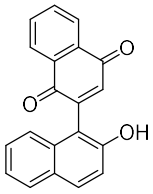


(III),



(IV).

[0004] In certain examples, disclosed herein is a composition, comprising a compound of formula (I), and a pharmaceutically acceptable carrier, wherein the composition is substantially free of an impurity.

[0004a] In one aspect, the present disclosure refers to a composition, comprising: (a) a compound of formula (I):  (I); and (b) a pharmaceutically acceptable carrier, wherein the composition is substantially free of an impurity selected from the group consisting of a compound of formula (II), a compound of formula (III), and a compound of formula (IV), or a combination thereof:  (II),  (III),  (IV).

[0005] In certain examples, disclosed herein is a composition, comprising a compound of formula (I), wherein the composition comprises no more than about 2% of a compound of formula (II).

[0006] In certain examples, disclosed herein is a composition, comprising a compound of formula (I), and a pharmaceutically acceptable carrier, wherein the composition comprises no more than about 2% of a compound of formula (II).

[0007] In certain examples, disclosed herein is a composition, comprising a compound of formula (I), wherein the composition comprises no more than about 0.05% of a compound of formula (III).

[0008] In certain examples, disclosed herein is a composition, comprising a compound of formula (I), and a pharmaceutically acceptable carrier, wherein the composition comprises no more than about 0.05% of a compound of formula (III).

[0008a] In one aspect, the present disclosure refers to a composition disclosed herein for use in therapy.

[0009] In certain examples, provided herein is a method of treating a cancer in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of the composition disclosed herein.

[0009a] In one aspect, the present disclosure refers to use of a composition disclosed herein in the manufacture of a medicament for treating cancer in an individual in need thereof.

[00010] In certain examples, provided herein is a method of treating fibrosis in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of the composition disclosed herein.

[00010a] In one aspect, the present disclosure refers to use of a composition disclosed herein in the manufacture of a medicament for treating fibrosis in an individual in need thereof.

[00011] In certain examples, provided herein is a method of treating an inflammatory disease or disorder in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of the composition disclosed herein.

[00011a] In one aspect, the present disclosure refers to use of a composition disclosed herein in the manufacture of a medicament for treating an inflammatory disease or disorder, chemotherapy-induced peripheral neuropathy, diabetic neuropathy, familial amyloid polyneuropathy, cachexia, anaphylaxis, non-alcoholic fatty liver disease, or steatohepatitis in an individual in need thereof.

[00012] In certain examples, provided herein is a method of treating chemotherapy-induced peripheral neuropathy in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of the composition disclosed herein.

[00013] In certain examples, provided herein is a method of treating diabetic neuropathy in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of the composition disclosed herein.

[00014] In certain examples, provided herein is a method of treating familial amyloid polyneuropathy in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of the composition disclosed herein.

[00015] In certain examples, provided herein is a method of treating cachexia in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of the composition disclosed herein.

[00016] In certain examples, provided herein is a method of treating anaphylaxis in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of the composition disclosed herein.

[00017] In certain examples, provided herein is a method of treating non-alcoholic fatty liver disease or steatohepatitis in an individual in need thereof, the method comprising administering to the individual a therapeutically effective amount of the composition disclosed herein.

[00018] In certain examples, provided herein is a use of a composition disclosed herein for treating cancer in an individual in need thereof.

[00019] In certain examples, provided herein is a use of a composition disclosed herein for treating fibrosis in an individual in need thereof.

[00020] In certain examples, provided herein is a use of a composition disclosed herein for treating an inflammatory disease or disorder in an individual in need thereof.

[00021] In certain examples, provided herein is a use of a composition disclosed herein for treating chemotherapy-induced peripheral neuropathy in an individual in need thereof.

[00022] In certain examples, provided herein is a use of a composition disclosed herein for treating diabetic neuropathy in an individual in need thereof.

[00023] In certain examples, provided herein is a use of a composition disclosed herein for treating familial amyloid polyneuropathy in an individual in need thereof.

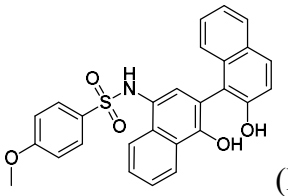
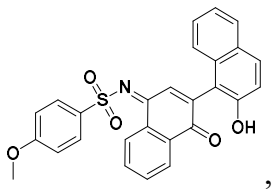
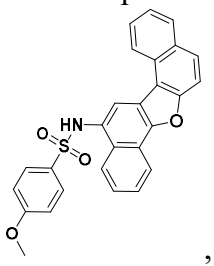
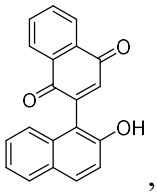
[00024] In certain examples, provided herein is a use of a composition disclosed herein for treating cachexia in an individual in need thereof.

[00025] In certain examples, provided herein is a use of a composition disclosed herein for treating anaphylaxis in an individual in need thereof.

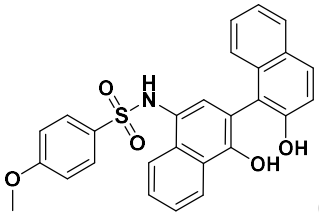
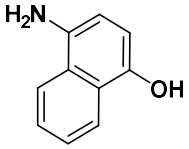
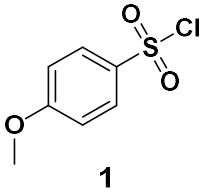
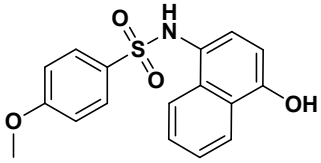
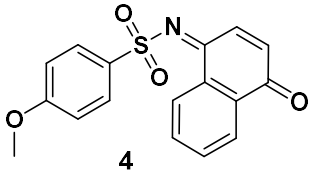
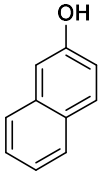
[00026] In certain examples, provided herein is a use of a composition disclosed herein for treating anaphylaxis in an individual in need thereof.

[00027] In certain examples, provided herein is a use of a composition disclosed herein for treating non-alcoholic fatty liver disease or steatohepatitis in an individual in need thereof.

[00028] In certain examples, disclosed herein is a method of evaluating the purity of a composition comprising a compound of formula (I), comprising assaying the composition for the presence of a compound selected from the group consisting of a compound of formula (II), a compound of formula (III), and a compound of formula (IV).

[00028a] In one aspect, the present disclosure refers to a method of evaluating the purity of a composition comprising a compound of formula (I):  (I), the method comprising assaying the composition for the presence of a compound selected from the group consisting of: , , and , optionally wherein the assaying comprises analysis using HPLC.

[00029] In certain examples, disclosed herein is a process for preparing a compound of formula (I), substantially free of an impurity.

[00029a] In one aspect, the present disclosure refers to a process for preparing a compound of formula (I):  (I) substantially free of an impurity, the process comprising: (a) contacting Compound 2:  2 , with Compound 1:  1 , to produce Compound 3:  3 , (b) contacting Compound 3 with an oxidizing agent to produce Compound 4:  4 , (c) contacting Compound 4 with Compound 5:  5 , in the presence of a coupling agent to produce the crude compound of formula (I); (d) contacting the compound of formula (I) of step (c) with an alcohol, water, or a combination thereof, to form a mixture; and (e) filtering the mixture of step (d) to isolate a precipitate, wherein the precipitate is the compound of formula (I) substantially free of an impurity.

[00029b] In one aspect, the present disclosure refers to a composition, comprising a compound of Formula (I) prepared according to the processes disclosed herein.

[00030] Other objects and advantages will become apparent to those skilled in the art from a consideration of the ensuing **Detailed Description**, **Examples**, and **Claims**.

BRIEF DESCRIPTION OF THE DRAWINGS

[00031] FIG. 1 shows an exemplary ^{1}H-NMR spectrum of Compound 7 in DMSO-d6.

[00032] FIG. 2 shows an exemplary ^{13}C-NMR spectrum of Compound 7 in DMSO-d6.