[0008] Previously pharmaceutical formulations of Compound I have been prepared as a solid blend formulation containing drug substance at strengths of 5.0 mg, 10.0 mg, 20.0 mg and 40.0 mg, with the drug substance blended with conventional excipients for such formulations. However, it has since been found that lower dosage strengths are required. In particular, per capsule dosages of 0.5 mg and 1.0 mg are now required. It is difficult to achieve the required homogeneity and content uniformity of capsules using conventional manufacturing approaches at lower dosage strengths in a solid blend formulation.

[0009] It is an aim of certain embodiments of this invention to provide a pharmaceutical formulation comprising Compound I in an effective dose. It is an aim of certain embodiments of this invention to provide a pharmaceutical formulation comprising Compound I in a low dose, e.g. a lower strength than is described in certain clinical studies.

[0010] It is an aim of certain embodiments of this invention to provide method of making a pharmaceutical formulation comprising Compound I.

[0011] It is an aim of certain embodiments of this invention to provide method of making a pharmaceutical formulation comprising Compound I which is homogeneous at low doses. It is an aim of certain embodiments of this invention to provide method of making a pharmaceutical formulation comprising Compound I which is homogeneous at low doses within a batch, e.g. which complies with requirements for uniformity of dosage units (content uniformity) described in relevant pharmacopoeia, an example being section 2.9.40 of the European Pharmacopoeia. It is an aim of certain embodiments of this invention to provide method of making a pharmaceutical formulation comprising Compound I which is of consistent strength in relation to Compound 1 at low doses between capsules with both the mean and individual dosage units demonstrating active agent content in the range 90-110% of the label claim as measured by HPLC analysis.

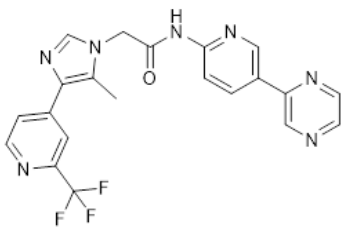
[0012] It is an aim of certain embodiments of this invention to provide a method of making a stable pharmaceutical formulation comprising Compound I which is homogeneous at low doses.

[0013] Certain embodiments of this invention satisfy some or all of the above aims.

SUMMARY

[0013a] In a first aspect of the present disclosure, there is provided a semi-solid pharmaceutical formulation comprising:

Compound I;



Compound I

distributed in a semi-solid diluent.

[0013b] In another aspect of the present disclosure, there is provided a method of making a semi-solid pharmaceutical formulation, the method comprising the steps of:

(i) melting a semi-solid diluent;

(ii) distributing Compound I in the molten semi-solid diluent to form a molten blend;

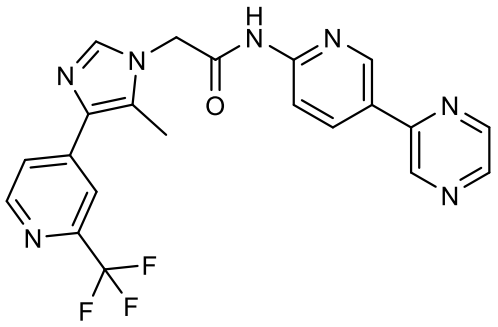
(iii) loading the molten blend into a capsule shell.

[0013c] In yet another aspect of the present disclosure, there is provided the pharmaceutical formulation as disclosed herein for use as a medicament.

[0013d] In a further aspect of the present disclosure, there is provided a use of the pharmaceutical formulation as disclosed herein, in the manufacture of a medicament for the treatment of cancer.

[0014] In accordance with a first example of the present disclosure there is provided a semi-solid pharmaceutical formulation comprising:

Compound I;



Compound I

distributed in a semi-solid diluent.

[0015] By combining Compound I with a semi-solid diluent, the inventors discovered that it was possible to achieve the desired homogeneity of the API in the formulation. The resulting formulation can be encapsulated in a capsule. For example, a gelatin capsule may be used. The capsule can then be administered to a patient in need thereof.

[0016] The semi-solid diluent may be an amphiphilic substance in which a polyalkylene glycol, e.g. a polyethylene glycol, is conjugated to a lipophilic or hydrophobic molecular entity. The polyethylene glycol chain may comprise from 3 to 70 alkylene glycol (e.g. ethylene glycol) units. Semi-solid formulations formed with these diluents are particularly beneficial in achieving a stable formulation.

[0017] The melting point of the semi-solid diluent may range from 40 °C to 55 °C e.g. from 42 °C to 51 °C. The theoretical HLB ((Hydrophilic Lipophilic balance, i.e. the degree to which the component is hydrophilic or lipophilic) of the semi-solid diluent may range from 10 to 20 e.g. from 12 to 17.

[0018] In some examples, the semi-solid formulation comprises a Gelucire® component. Following the name Gelucire®, there is a set of two figures: the first (e.g. 44) indicates the melting point in degrees Celsius, the second (e.g. 14) indicates the theoretical HLB (Hydrophilic Lipophilic balance) i.e. the degree to which the component is hydrophilic or lipophilic. The melting point of the Gelucire® component may range from 40 °C to 55 °C e.g. e.g. from 42 °C to 51 °C , e.g. 44 °C, 48 °C or 50 °C. The theoretical HLB may range from 1 to 20, e.g. from 12 to 17, e.g. 01, 13, 14 or 16.

[0019] In some examples, the semi-solid diluent is selected from the group comprising polyethylene glycol e.g. PEG (e.g. PEG1000 or higher Mw variants), a water soluble surfactant e.g. Gelucire® 48/16, a water dispersible surfactant e.g. Gelucire® 44/14 or Gelucire® 50/13, or a hard fat e.g. Gelucire® 43/01, Vitamin E polyethylene glycol succinate (TPGS), polyoxyl 35 castor oil e.g. Kolliphor EL, polyoxyl 40 castor oil e.g. Kolliphor RH40, Solutol HS15 (polyoxyethylene esters of 12-monohydroxy stearic acid), glyceryl stearate (Imwitor 900), glyceryl caprate/caprylate ester such as Capmul MCM. In some examples, the semi-solid diluent is selected from the group comprising a water soluble surfactant, a water dispersible surfactant, a hard fat, Vitamin E polyethylene glycol succinate, medium chain triglycerides, polyoxyl 35 castor oil.

[0020] In some examples, the semi-solid diluent is selected from the group comprising Vitamin E polyethylene glycol succinate and lauroyl macrogol-32 glycerides. Thus, in some examples, the semi-solid diluent is Vitamin E polyethylene glycol succinate. Thus, in some examples, the semi-solid diluent is a pegylated lipid, for example Gelucire® 44/14 (lauroyl macrogol-32 glycerides). In some examples, the semi-solid diluent is Gelucire® 48/16, (macrogol-32 stearate) Gelucire® 50/13 (stearoyl macrogol-32 glycerides) or Gelucire® 43/01 (hard fat). Gelucire® 48/16 is a polyethylene glycol monostearate (type I) NF and consists of PEG-32 (MW 1500) esters of palmitic (C16) and stearic (C18) acids. It is a solid at ambient temperature. Gelucire® 44/14 is a lauroyl polyoxyl/macrogol 32 glycerides NF/EP and consists of a small fraction of mono, di- and triglycerides and mainly PEG-32 (MW 1500) mono- and diesters of lauric acid (C12). Gelucire® 50/13 is a stearoyl polyoxyl/macrogol 32 glycerides NF/EP and consists of mono, di- and triglycerides and PEG-32 (MW 1500) mono- and diesters of palmitic (C16) and stearic (C18) acids. Gelucire® 43/01 is composed of mono-, di- and triglyceride esters of fatty acids (C8 to C18), the triester fraction being predominant.

[0021] Compound I is particularly compatible with Vitamin E polyethylene glycol succinate and with Gelucire® 44/14, a polyethylene glycol glyceride.

[0022] In some examples, the semi-solid pharmaceutical formulation further comprises an anti-oxidant. In some examples, the anti-oxidant may be selected from butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT).

[0023] In some examples, the semi-solid pharmaceutical formulation further comprises a pharmaceutically acceptable excipient selected from the group comprising sodium lauryl sulphate, poloxamer and other surfactants. In some examples, the semi-solid pharmaceutical formulation further comprises a polymer agent, e.g a polymer agent which can inhibit precipitation of Compound I. In some examples, the polymer agent is selected from the group comprising polyvinylpyrrolidone (PVP), hydroxypropyl methylcellulose (HPMC), methylcellulose and copovidone.

[0024] In some examples, the semi-solid pharmaceutical formulation comprises Compound I in an amount of from 0.1%w/w to about 10%w/w. In some examples, the semi-solid pharmaceutical formulation comprises Compound I in an amount of from 0.5%w/w to about 5%w/w. In some examples, the semi-solid pharmaceutical formulation comprises Compound I in an amount of about 0.5%w/w, about 1%w/w, about 1.5%w/w, about 2%w/w, about 2.5%w/w, about 3%w/w, about 3.5%w/w, about 4%w/w, about 4.5%w/w or about 5%w/w. In some examples, the semi-solid pharmaceutical formulation comprises Compound I in an amount of from 0.5 %w/w to about 3 %w/w. In some examples, the semi-solid pharmaceutical formulation comprises Compound I in an amount of from 1.5 %w/w to about 2.5 %w/w. In some examples, the semi-solid pharmaceutical formulation comprises Compound I in an amount of from 1%w/w to about 2%w/w.

[0025] In some examples, the semi-solid pharmaceutical formulation comprises Compound I in a total dose of from about 0.05 mg to about 5 mg. In some examples, the semi-solid pharmaceutical formulation comprises Compound I in a total dose of from about 0.25 mg to about 2.5 mg. In some examples, the semi-solid pharmaceutical formulation comprises Compound I in a total dose of from

about 0.25 mg to about 1.5 mg. In some examples, the semi-solid pharmaceutical formulation comprises Compound I in a total dose of about 0.25 mg, about 0.5 mg, about 0.75 mg, about 1.0 mg, about 1.25 mg, about 1.5 mg, about 1.75 mg, about 2.0 mg, about 2.25 mg or about 2.5 mg. In some examples, the semi-solid pharmaceutical formulation comprises Compound I in a total dose of from about 0.5 mg to about 1 mg.

[0026] In an example, the semi-solid pharmaceutical formulation comprises: Compound I present in an amount of from 0.5%w/w to 3%w/w; and Vitamin E polyethylene glycol succinate in an amount of from 97%w/w to 99.5%w/w. In an example, the semi-solid pharmaceutical formulation comprises: Compound I present in an amount of from 1%w/w to 2%w/w; and Vitamin E polyethylene glycol succinate in an amount of from 98%w/w to 99%w/w.

[0027] In some examples, the semi-solid pharmaceutical formulation is encapsulated in a capsule. In some examples, the capsule is a gelatin capsule. In some examples, the capsule is a vegetable-derived capsule e.g. HPMC. In some examples, the semi-solid pharmaceutical formulation is encapsulated in a gelatin capsule, such as a white opaque gelatin capsule (gelatin and titanium dioxide).

[0028] In an example, the semi-solid pharmaceutical formulation comprises a total dose of between about 0.5 mg and 2 mg of Compound I and between about 48.0 mg and about 49.5 mg of vitamin E polyethylene glycol succinate. In an example, the semi-solid pharmaceutical formulation comprises a total dose of between about 0.5 mg and 2 mg of Compound I and between about 48 mg and about 49.5 mg of vitamin E polyethylene glycol succinate encapsulated in a gelatin capsule.

[0029] In an example, the semi-solid pharmaceutical formulation comprises a total dose of between about 0.75 mg and 1.25 mg of Compound I and between about 48.75 mg and about 49.25 mg of vitamin E polyethylene glycol succinate. In an example, the semi-solid pharmaceutical formulation comprises a total dose of between about 0.75 mg and 1.25 mg of Compound I and between about 48.75 mg and about 49.25 mg of vitamin E polyethylene glycol succinate encapsulated in a gelatin capsule.

[0030] In an example, the semi-solid pharmaceutical formulation comprises a total dose of between about 0.25 mg and about 0.75 mg of Compound I and between about 49.25 mg and about 49.75 mg of vitamin E polyethylene glycol succinate. In an example, the semi-solid pharmaceutical formulation comprises a total dose of between about 0.25 mg and about 0.75 mg of Compound I and between about 49.25 mg and about 49.75 mg of vitamin E polyethylene glycol succinate encapsulated in a gelatin capsule.

[0031] In an example, the semi-solid pharmaceutical formulation comprises a total dose of about 1 mg of Compound I and about 49 mg of vitamin E polyethylene glycol succinate. In an example, the semi-solid pharmaceutical formulation comprises a total dose of about 1 mg of Compound I and about 49 mg of vitamin E polyethylene glycol succinate encapsulated in a gelatin capsule.

[0032] In an example, the semi-solid pharmaceutical formulation comprises a total dose of about 0.5 mg of Compound I and about 49.5 mg of vitamin E polyethylene glycol succinate. In an example, the semi-solid pharmaceutical formulation comprises a total dose of about 0.5 mg of Compound I and about 49.5 mg of vitamin E polyethylene glycol succinate encapsulated in a gelatin capsule.

[0033] The semi-solid pharmaceutical formulation of the present disclosure may be for medical use.

[0034] The semi-solid pharmaceutical formulation of the present disclosure may be for use in the treatment of cancer.

[0035] The present disclosure also provides a method of treating cancer, the method comprising administering to a subject in need thereof a therapeutically acceptable amount of the semi-solid formulation of the first example.

[0036] The cancer may be selected from sarcoma, melanoma, skin cancer, haematological tumors, lymphoma, carcinoma, adenoma and leukemia. Specific cancer, sarcoma, melanoma, skin cancer, haematological tumors, lymphoma, carcinoma, and leukemia that may be treated by the compound of the present disclosure may be selected from: esophageal squamous cell carcinoma, gastric cancer, glioblastomas, astrocytomas; retinoblastoma, osteosarcoma, chondosarcoma, Ewing's sarcoma, rabdomysarcoma, Wilm's tumor, basal cell carcinoma, non-small cell lung cancer, brain tumour, hormone refractory prostate cancer, prostate cancer, metastatic breast cancer, breast cancer, metastatic pancreatic cancer, pancreatic cancer, colorectal cancer, biliary cancer e.g. cholangiocarcinoma, thymus cancer, cervical cancer, head and neck squamous cell carcinoma and cancer of the head and neck.

[0037] The cancer may be a solid tumour. The cancer may be selected from gastric cancer, pancreatic cancer, colorectal cancer, thymus cancer, and biliary cancer e.g cholangiocarcinoma. The cancer may be selected from colorectal cancer, thymus cancer and biliary cancer e.g cholangiocarcinoma. The cancer may be selected from colorectal cancer, pancreatic cancer and biliary cancer e.g cholangiocarcinoma. The cancer may be biliary tract cancer, e,g, cholangiocarcinoma. The cancer may be thymus cancer. The cancer may be colorectal cancer. The cancer may be pancreatic cancer.

[0038] The semi-solid pharmaceutical formulation of the present disclosure may be for treatment of a condition which is modulated by Porcn.

[0039] The present disclosure also provides a method of treating a condition which is modulated by Porcn, the method comprising administering to a subject in need thereof a therapeutically acceptable amount of the semi-solid formulation of the first example.

[0040] The condition which is modulated by Porcn may be cancer.

[0041] The condition which is modulated by Porcn may be selected from: skin fibrosis, idiopathic pulmonary fibrosis, renal interstitial fibrosis, liver fibrosis, proteinuria, kidney graft rejection,

osteoarthritis, Parkinsons's disease, cystoid macular edema, uveitis associated cystoid macular edema, retinopathy, diabetic retinopathy and retinopathy of prematurity.

[0042] The semi-solid pharmaceutical formulation of the present disclosure may be for use in the treatment of a condition selected from: skin fibrosis, idiopathic pulmonary fibrosis, renal interstitial fibrosis, liver fibrosis, proteinuria, kidney graft rejection, osteoarthritis, Parkinsons's disease, cystoid macular edema, uveitis associated cystoid macular edema, retinopathy, diabetic retinopathy and retinopathy of prematurity.

[0043] The present disclosure also provides a method of treating a condition selected from: skin fibrosis, idiopathic pulmonary fibrosis, renal interstitial fibrosis, liver fibrosis, proteinuria, kidney graft rejection, osteoarthritis, Parkinsons's disease, cystoid macular edema, uveitis associated cystoid macular edema, retinopathy, diabetic retinopathy and retinopathy of prematurity, the method comprising administering to a subject in need thereof a therapeutically acceptable amount of the semi-solid formulation of the first example.

[0044] In accordance with a second example of the present disclosure there is provided a method of making a semi-solid pharmaceutical formulation, the method comprising the steps of:

(i) melting a semi-solid diluent;

(ii) distributing Compound I in the molten semi-solid diluent to form a molten blend;

(iii) loading the molten blend into a capsule shell.

[0045] In some examples, the method of the second example may be used to provide the semi-solid pharmaceutical formulation of the first example and related examples.

[0046] In some examples, step (ii) comprises dissolving Compound I in the semi-solid diluent. In some examples, step (ii) further comprises mixing Compound I with the melted semi-solid diluent of step (i).

[0047] In some examples, the method may further comprise the step of passing Compound I through a screen to remove any lumps prior to the step of dissolving Compound I in the diluent.

[0048] In some examples, Compound I and the molten diluent are continuously mixed together using a suitable mixer to produce a uniform solution.

[0049] Capsule filling may be undertaken using conventional capsule filling methods and equipment suitable for use with molten semisolid formulations. Capsules can be filled using a range of methods in which a fixed volume of formulation is dispensed into an empty capsule shell. This may include methods of hand filling using positive displacement pipettes or using automated capsule filling machines. In an illustrative filling process, the body of the capsule and its cap are separated, with the body immobilised using a capsule holder. When filling by hand, a pipette is used to measure and dispense a known volume and weight of the formulation into the capsule body. Once filling is complete, the cap is returned

and fixed onto the capsule body by hand. When filling using automated systems, commercially available machines are used, which achieve the same functions as filling by hand.

[0050] In some examples, the step of melting the semi-solid diluent is performed at a temperature of between about 30 °C and about 90 °C. In some examples, the step of melting the semi-solid diluent is performed at a temperature of between about 40 °C and about 80 °C. In some examples, the step of melting the semi-solid diluent is performed at a temperature of about 40 °C, 45 °C, 50 °C, 55 °C , 60 °C , 65 °C, 70 °C, 75 °C or about 80 °C. In some examples, the step of melting the semi-solid diluent is performed at a temperature of between about 45 °C and about 80 °C. In some examples, the step of melting the semi-solid diluent is performed at a temperature of about 50 °C to about 60 °C. In some examples, the step of melting the semi-solid diluent is performed at a temperature of about 55 °C.

DETAILED DESCRIPTION

[0051] Throughout the description and claims of this specification, the words “comprise” and “contain” and variations of them mean “including but not limited to”, and they are not intended to (and do not) exclude other moieties, additives, components, integers or steps. Throughout the description and claims of this specification, the singular encompasses the plural unless the context otherwise requires. In particular, where the indefinite article is used, the specification is to be understood as contemplating plurality as well as singularity, unless the context requires otherwise.

[0052] Features, integers, characteristics, compounds, chemical moieties or groups described in conjunction with a particular aspect, embodiment or example of the invention are to be understood to be applicable to any other aspect, embodiment or example described herein unless incompatible therewith. All of the features disclosed in this specification (including any accompanying claims, abstract and drawings), and/or all of the steps of any method or process so disclosed, may be combined in any combination, except combinations where at least some of such features and/or steps are mutually exclusive. The invention is not restricted to the details of any foregoing embodiments. The invention extends to any novel one, or any novel combination, of the features disclosed in this specification (including any accompanying claims, abstract and drawings), or to any novel one, or any novel combination, of the steps of any method or process so disclosed.

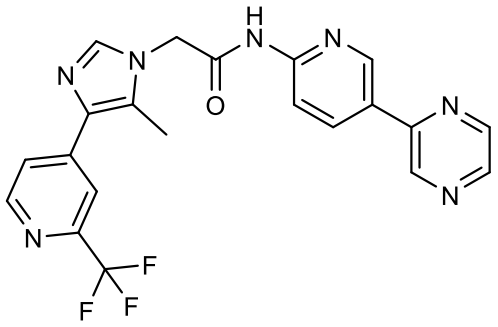
[0053] The term “semi-solid” refers to a substance having both liquid and solid properties at room temperature i.e. having a viscosity and rigidity intermediate between that of a solid and a liquid. At lower temperatures, the substance may display solid properties. At higher temperatures, the substance may display liquid properties. The term “semi-solid” may refer to a waxy solid which is a wax at room temperature but which softens and/or melts at elevated temperatures.

[0054] The term “stable” refers to both chemical and physical stability. The term “stable” may refer to chemical and/or physical stability of a compound or composition over a period of time (e.g. 6 months) at about 20 °C to about 40 °C and about 50% RH to about 80% RH. For example, the compound or composition may be chemically and/or physically stable over a period of 24 hours. The compound or composition may be chemically and/or physically stable over a period of up to 6 months. The compound

CLAIMS

1. A semi-solid pharmaceutical formulation comprising:

Compound I;



Compound I

distributed in a semi-solid diluent.

2. The semi-solid pharmaceutical formulation of claim 1, wherein the semi-solid diluent is selected from the group comprising polyethylene glycol, a water soluble surfactant, a water dispersible surfactant, a hard fat, Vitamin E polyethylene glycol succinate, a polyoxyl 35 castor oil, a polyoxyl 40 castor oil, a glyceryl stearate, a glyceryl caprate/caprylate ester and medium chain triglycerides.

3. The semi-solid pharmaceutical formulation of claim 1 or claim 2, wherein the semi-solid diluent is selected from the group comprising PEG, PEG1000, Gelucire® 48/16, Gelucire® 44/14, Gelucire® 50/13, Gelucire® 43/01, Vitamin E polyethylene glycol succinate, polyoxyl 35 castor oil e.g. Kolliphor EL, polyoxyl 40 castor oil e.g. Kolliphor RH40, Solutol HS15 (polyoxyethylene esters of 12-monohydroxy stearic acid), glyceryl stearate (Imwitor 900), glyceryl caprate/caprylate ester e.g. Capmul MCM.

4. The semi-solid pharmaceutical formulation of any preceding claim, wherein the diluent is Vitamin E polyethylene glycol succinate.

5. The semi-solid pharmaceutical formulation of any preceding claim, wherein Compound I is present in an amount of from about 0.1%w/w to about 10%w/w.

6. The semi-solid pharmaceutical formulation of preceding claim, wherein Compound I is present in an amount of from about 0.5%w/w to about 5%w/w.

7. The semi-solid pharmaceutical formulation of preceding claim, wherein Compound I is present in an amount of from about 0.5%w/w to about 3%w/w.

8. The semi-solid pharmaceutical formulation of any preceding claim, wherein Compound I is present in an amount of from about 0.05 mg to about 5 mg.

9. The semi-solid pharmaceutical formulation of any preceding claim, wherein Compound I is present in an amount of from about 0.25 mg to about 2.5 mg.

10. The semi-solid pharmaceutical formulation of any preceding claim, wherein Compound I is present in an amount of from about 0.5mg to about 1 mg.

11. The semi-solid pharmaceutical formulation of any preceding claim, wherein the formulation comprises:

Compound I present in an amount of from 0.5%w/w to 3%w/w; and

Vitamin E polyethylene glycol succinate in an amount of from 97%w/w to 99.5%w/w.

12. The semi-solid pharmaceutical formulation of any preceding claim, wherein the semi-solid pharmaceutical formulation is encapsulated in a gelatin capsule.

13. A method of making a semi-solid pharmaceutical formulation, the method comprising the steps of:

(i) melting a semi-solid diluent;

(ii) distributing Compound I in the molten semi-solid diluent to form a molten blend;

(iii) loading the molten blend into a capsule shell.

14. The method of claim 13, wherein the distributing comprises dissolving Compound I in the molten semi-solid diluent.

15. The method of claim 13 or claim 14, wherein the capsule is a gelatin capsule.

16. The method of claim 13 or claim 14, wherein step (i) is performed at a temperature of between about 45 °C and about 80 °C.

17. The method of any of claims 13 to 16, wherein the semi-solid diluent is selected from the group comprising polyethylene glycol, a water soluble surfactant, a water dispersible surfactant, a hard fat, Vitamin E polyethylene glycol succinate, a polyoxyl 35 castor oil, a polyoxyl 40 castor oil, a glyceryl stearate, a glyceryl caprate/caprylate ester and medium chain triglycerides.

18. The method of any of claims 13 to 16, wherein the semi-solid diluent is selected from the group comprising PEG, PEG1000, Gelucire® 48/16, Gelucire® 44/14, Gelucire® 50/13, Gelucire® 43/01, Vitamin E polyethylene glycol succinate, polyoxyl 35 castor oil e.g. Kolliphor EL, polyoxyl 40 castor oil e.g. Kolliphor RH40, Solutol HS15 (polyoxyethylene esters of 12-monohydroxy stearic acid), glyceryl stearate (Imwitor 900), glyceryl caprate/caprylate ester e.g. Capmul MCM.

19. The method of any of claims 13 to 16, wherein the semi-solid diluent is selected from Vitamin E polyethylene glycol succinate and Gelucire® 44/14.

20. The method of any of claims 13 to 19, wherein Compound I is present in an amount of from 0.1%w/w to 10%w/w.

21. The method of claim 20, wherein Compound I is present in an amount of from 0.5%w/w to 3%w/w.

22. The method of claim 20, wherein Compound I is present in an amount of from 1%w/w to 2%w/w.

23. The method of any of claims 13 to 22, wherein Compound I is present in an amount of from about 0.05 mg to about 5 mg.

24. The method of claim 23, wherein Compound I is present in an amount of from about 0.25 mg to about 2.5 mg.

25. The method of any one of claims 13 to 15, wherein step (i) is performed at a temperature in the range from about 45 °C and about 80 °C and the diluent is Vitamin E polyethylene glycol succinate; and

Compound I is dissolved at an amount of from 0.5%w/w to 3%w/w.

26. The pharmaceutical formulation of any of claims 1 to 12 for use as a medicament.

27. Use of the pharmaceutical formulation of any of claims 1 to 12, in the manufacture of a medicament for the treatment of cancer.

28. The use of claim 27, wherein the cancer is a solid tumour.

29. The use of claim 27, wherein the cancer is selected from gastric cancer, thymus cancer, pancreatic cancer, and biliary cancer.