[08] The present specification discloses solid solution pharmaceutical compositions. The pharmaceutical compositions disclosed herein are formulated in a manner that essentially produces a lipid-adjuvant delivery system that enables a therapeutic compound having an activity that modulates lipid and/or lipoprotein levels to be delivered in a manner that more effectively treats a cardiovascular disease.

SUMMARY

[09] Aspects of the present specification disclose, in part, a solid solution pharmaceutical composition comprising a therapeutic compound, one or more room temperature solid lipids. The solid solution pharmaceutical composition disclosed herein may further comprise one or more room temperature liquid lipids, one or more stabilizing agents, one or more neutralizing agents, or any combination thereof. A therapeutic compound may have an activity that normalizes lipid levels.

[09a] In one aspect, there is provided a solid solution pharmaceutical composition comprising:

a) one or more statins in an amount of about 1% to about 30% by weight of the pharmaceutical composition;

b) one or more pharmaceutically-acceptable hard fats, wherein the one or more hard fats include one or more triglycerides in an amount of about 30% to about 75% by weight of the pharmaceutical composition, the one or more triglycerides comprising a triglyceride with one saturated or unsaturated fatty acid having a carbon length of C12-C24, two saturated or unsaturated fatty acids each having a carbon length of C12-C24, or three saturated or unsaturated fatty acids each having a carbon length of C12-C24;

c) one or more pharmaceutically-acceptable monoglycerides or acetylated monoglycerides that is liquid at room temperature in an amount of about 8% to about 40% by weight of the pharmaceutical composition, wherein the monoglyceride or the acetylated monoglyceride has a fatty acid of at least 12 carbons,

wherein the solid solution pharmaceutical composition does not comprise a surfactant; and

wherein the solid solution pharmaceutical composition is formulated to be a solid at a temperature of about 15°C or lower and has a melting point of 30°C or higher.~~a solution pharmaceutical composition comprising:~~

~~a) one or more statins in an amount of about 1% to about 30% by weight of the pharmaceutical composition;~~

~~b) one or more pharmaceutically-acceptable hard fats in an amount of about 30% to about 75% by weight of the pharmaceutical composition;~~

~~c) one or more pharmaceutically-acceptable monoglycerides or acetylated monoglycerides that is liquid at room temperature in an amount of about 8% to about 40% by weight of the pharmaceutical composition,~~

~~wherein the solid solution pharmaceutical composition is formulated to be a solid at a temperature of about 15°C or lower.~~

[09b] In one aspect, there is provided of a pharmaceutical composition as defined herein in the manufacture of a medicament for the treatment of a cardiovascular disease

[010] Other aspects of the present specification disclose, in part, a method of preparing a solid solution pharmaceutical composition disclosed herein. A method disclosed herein comprises the steps of a) contacting a therapeutic compound disclosed herein with one or more room temperature liquid lipids under conditions which allow the therapeutic compound to dissolve in the lipids; and b) contacting the compound/lipid solution with one or more room temperature solid lipids under conditions which allow the formation of a solid solution composition. In aspects of this method, heat is applied to dissolve the therapeutic compound into the one or more room temperature liquid lipids to create a solution. In other aspects of this method, step (a) comprises contacting a therapeutic compound disclosed herein with one or more room temperature liquid lipids and/or one or more stabilizing agents, and/or one or more neutralizing agents under conditions which allow the therapeutic compound to dissolve in the lipids.

[011] Other aspects of the present specification disclose a method of treating an individual with a cardiovascular disease, the method comprising the step of administering to the individual in need thereof a solid solution pharmaceutical composition disclosed herein, wherein administration results in a reduction in a symptom associated with the cardiovascular disease, thereby treating the individual.

CLAIMS

1. A solid solution pharmaceutical composition comprising:

   a) one or more statins in an amount of about 1% to about 30% by weight of the pharmaceutical composition;

   b) one or more pharmaceutically-acceptable hard fats in an amount of about 30% to about 75% by weight of the pharmaceutical composition;

   c) one or more pharmaceutically-acceptable monoglycerides or acetylated monoglycerides that is liquid at room temperature in an amount of about 8% to about 40% by weight of the pharmaceutical composition,

   wherein the solid solution pharmaceutical composition is formulated to be a solid at a temperature of about 15°C or lower.

2. The solid solution pharmaceutical composition according to Claim 1, wherein the amount of the one or more statins is about 1% to about 15% by weight of the pharmaceutical composition.

3. The pharmaceutical composition according to Claim 1 or Claim 2, wherein the one or more statins comprises Atorvastatin, Fluvastatin, Lovastatin, Pitavastatin, Pravastatin, Rosuvastatin, and Simvastatin.

4. The solid solution pharmaceutical composition according to any one of Claims 1-3, wherein the amount of the one or more pharmaceutically-acceptable hard fats is at least 55% by weight of the pharmaceutical composition.

5. The solid solution pharmaceutical composition according to any one of Claims 1-4, wherein the one or more pharmaceutically-acceptable hard fats have a melting point of about 40°C to about 50°C.

6. The solid solution pharmaceutical composition according to Claim 5, wherein the one or more pharmaceutically-acceptable hard fats comprise one or more glycerolipids.

7. The solid solution pharmaceutical composition according to Claim 6, wherein the one or more glycerolipids comprise a triglyceride with one saturated or unsaturated fatty acid having a carbon length of C_{12}-C_{24}, two saturated or unsaturated fatty acids each having a carbon length of C_{12}-C_{24}, or three saturated or unsaturated fatty acids each having a carbon length of C_{12}-C_{24}.

8. The solid solution pharmaceutical composition according to Claim 6, wherein the one or more glycerolipids comprise a mixture of saturated C_{10}-C_{18} triglycerides having a melting point range of about 41°C to 45°C.

9. The solid solution pharmaceutical composition according to Claim 8, wherein the one or more glycerolipids comprise a mixture of saturated C_{10}-C_{18} triglycerides having a melting point range of about 43°C.

10. The solid solution pharmaceutical composition according to any one of Claims 1-9, wherein the amount of the one or more pharmaceutically-acceptable monoglycerides or acetylated monoglycerides is less than 35% by weight of the pharmaceutical composition.

11. The solid solution pharmaceutical composition according to any one of Claims 1-10, wherein the one or more pharmaceutically-acceptable monoglycerides or an acetylated monoglycerides comprise glycerol monomyristoleate, glycerol monopalmitoleate, glycerol monosapienate, glycerol monooleate, glycerol monoelaidate, glycerol monovaccenate, glycerol monolinoleate, glycerol monolinoelaidate, glycerol monolinolenate, glycerol monostearidonate, glycerol monoeicosenoate, glycerol monomeadate, glycerol monoarachidonate, glycerol monoeicosapentaenoate, glycerol monoerucate, glycerol monodocosahexaenoate, or glycerol mononervonate.

12. The solid solution pharmaceutical composition according to Claims 11, wherein the one or more pharmaceutically-acceptable monoglycerides or acetylated monoglycerides comprise glycerol monolinoleate.

13. Use of a pharmaceutical composition as defined in any one of Claims 1-12 in the manufacture of a medicament for the treatment of a cardiovascular disease.

14. The use according to Claim 13, wherein the cardiovascular disease is associated with a hyperlipidemia, a coronary heart disease, an atherosclerosis, a peripheral vascular disease, a vascular occlusive disease, a cardiomyopathy, a vasculitis, an inflammatory heart disease, an ischemic heart disease, a congestive heart failure, a hypertensive heart disease, a valvular heart disease, a hypertension, myocardial infarction, a diabetic cardiac conditions, an aneurysm; an embolism, a dissection, a pseudoaneurysm, a vascular malformation, a vascular nevus, a thrombosis, a varicose vein, or a stroke.

CLAIMS

1. A solid solution pharmaceutical composition comprising:

   a) one or more statins in an amount of about 1% to about 30% by weight of the pharmaceutical composition;

   b) one or more pharmaceutically-acceptable hard fats, wherein the one or more hard fats include one or more triglycerides in an amount of about 30% to about 75% by weight of the pharmaceutical composition, the one or more triglycerides comprising a triglyceride with one saturated or unsaturated fatty acid having a carbon length of C_{12}-C_{24}, two saturated or unsaturated fatty acids each having a carbon length of C_{12}-C_{24}, or three saturated or unsaturated fatty acids each having a carbon length of C_{12}-C_{24};

   c) one or more pharmaceutically-acceptable monoglycerides or acetylated monoglycerides that is liquid at room temperature in an amount of about 8% to about 40% by weight of the pharmaceutical composition, wherein the monoglyceride or the acetylated monoglyceride has a fatty acid of at least 12 carbons,

   wherein the solid solution pharmaceutical composition does not comprise a surfactant; and

   wherein the solid solution pharmaceutical composition is formulated to be a solid at a temperature of about 15°C or lower and has a melting point of 30°C or higher.

2. The solid solution pharmaceutical composition according to Claim 1, wherein the amount of the one or more statins is about 1% to about 15% by weight of the pharmaceutical composition.

3. The pharmaceutical composition according to Claim 1 or Claim 2, wherein the one or more statins comprises Atorvastatin, Fluvastatin, Lovastatin, Pitavastatin, Pravastatin, Rosuvastatin, and Simvastatin.

4. The solid solution pharmaceutical composition according to any one of Claims 1-3, wherein the amount of the one or more pharmaceutically-acceptable hard fats is at least 55% by weight of the pharmaceutical composition.

5. The solid solution pharmaceutical composition according to any one of Claims 1-4, wherein the one or more pharmaceutically-acceptable hard fats have a melting point of about 40°C to about 50°C.

6. The solid solution pharmaceutical composition according to any one of Claims 1-5, wherein the one or more triglycerides comprise a mixture of saturated C_{10}-C_{18} triglycerides having a melting point range of about 41°C to 45°C.

7. The solid solution pharmaceutical composition according to Claim 6, wherein the one or more triglycerides comprise a mixture of saturated C_{10}-C_{18} triglycerides having a melting point range of about 43°C.

8. The solid solution pharmaceutical composition according to any one of Claims 1-7, wherein the amount of the one or more pharmaceutically-acceptable monoglycerides or acetylated monoglycerides is less than 35% by weight of the pharmaceutical composition.

9. The solid solution pharmaceutical composition according to any one of Claims 1-8, wherein the one or more pharmaceutically-acceptable monoglycerides or an acetylated monoglycerides comprise glycerol monomyristoleate, glycerol monopalmitoleate, glycerol monosapienate, glycerol monooleate, glycerol monoelaidate, glycerol monovaccenate, glycerol monolinoleate, glycerol monolinoelaidate, glycerol monolinolenate, glycerol monostearidonate, glycerol monoeicosenoate, glycerol monomeadate, glycerol monoarachidonate, glycerol monoeicosapentaenoate, glycerol monoerucate, glycerol monodocosahexaenoate, or glycerol mononervonate.

10. The solid solution pharmaceutical composition according to Claims 9, wherein the one or more pharmaceutically-acceptable monoglycerides or acetylated monoglycerides comprise glycerol monolinoleate.

11. The solid solution composition according to any one of Claims 1-10, wherein the one or more statins have a logP of about 3.0 or greater.

12. Use of a pharmaceutical composition as defined in any one of Claims 1-10 in the manufacture of a medicament for the treatment of a cardiovascular disease.

13. The use according to Claim 11, wherein the cardiovascular disease is associated with a hyperlipidemia, a coronary heart disease, an atherosclerosis, a peripheral vascular disease, a vascular occlusive disease, a cardiomyopathy, a vasculitis, an inflammatory heart disease, an ischemic heart disease, a congestive heart failure, a hypertensive heart disease, a valvular heart disease, a hypertension, myocardial infarction, a diabetic cardiac conditions, an aneurysm; an embolism, a dissection, a pseudoaneurysm, a vascular malformation, a vascular nevus, a thrombosis, a varicose vein, or a stroke.