[0006] However, many of these treatments are recommended for acute conditions and do not address or provide for a long-term reduction in cardiovascular events in patients with clinically stable atherosclerotic vascular disease.

[0007] It is against this background that the present invention has been developed.

[0008] The present invention seeks to overcome, or at least ameliorate, one or more of the deficiencies of the prior art mentioned above, or to provide the consumer with a useful or commercial choice.

SUMMARY

[0009] In one aspect, there is provided use of a therapeutically effective amount of a composition comprising about 0.6 total mg of (i) colchicine, (ii) a known colchicine derivative, (iii) a salt of (i) or (ii), or any combination of (i)-(iii), in the manufacture of a medicament for treating and/or preventing a cardiovascular event in a subject.

[0009a]In another aspect, there is provided use of a therapeutically effective amount of a composition comprising no more than about 0.6 total mg of (i) colchicine, (ii) a known colchicine derivative, (iii) a salt of (i) or (ii), or any combination of (i)-(iii), in the manufacture of a medicament for treating and/or preventing inflammation in a subject having, or having a previous history of, atherosclerotic vascular disease.

[0009b] In yet another aspect, there is provided use of a therapeutically effective amount of a composition comprising no more than about 0.6 total mg of (i) colchicine, (ii) a known colchicine derivative, (iii) a salt of (i) or (ii), or any combination of (i)-(iii), in the manufacture of a medicament for treating and/or preventing atherosclerotic vascular disease.

[0009c] In a further aspect, there is provided use of a therapeutically effective amount of a composition comprising no more than about 0.6 total mg of (i) colchicine, (ii) a known colchicine derivative, (iii) a salt of (i) or (ii), or any combination of (i)-(iii), in the manufacture of a medicament for treating and/or preventing a cardiovascular event in a patient undergoing co-administration of a second agent for the treatment and/or prevention of an atherosclerotic vascular disease.

[0009d]The present disclosure also provides a method for the treatment or prevention of a cardiovascular event in a subject comprising the step of:

administering a therapeutically effective amount of a compound of formula (I), a known colchicine derivative and/or a salt thereof.

[0010] The present disclosure also provides a method for the treatment or prevention of a cardiovascular event in a subject with atherosclerotic vascular disease comprising the step of:

administering a therapeutically effective amount of a compound of formula (I), a known colchicine derivative and/or a salt thereof.

[0011] The present disclosure further provides a method for the treatment or prevention of a cardiovascular event in a subject with atherosclerotic vascular disease comprising the step of:

administering a therapeutically effective amount of a compound of formula (I), a known colchicine derivative and/or a salt thereof and one or more additional agents selected from the list comprising: a statin and/or an anti-platelet agent.

[0012] In one example, the atherosclerotic vascular disease is a coronary disease. The coronary disease may be stable or unstable.

[0013] The present disclosure further provides a method for the treatment or prevention of a cardiovascular event in a subject comprising the step of:

administering a therapeutically effective amount of a compound of formula (I), a known colchicine derivative and/or a salt thereof

wherein the subject has coronary disease prior to administration of the therapeutically effective amount of a compound of formula (I), a known colchicine derivative and/or a salt thereof. Preferably the coronary disease is a stable coronary disease.

[0014] The present disclosurefurther provides a method for reducing or preventing cholesterol crystal induced inflammation within atherosclerotic plaques in a subject, comprising the step of

administering a dosage of 0.5 mg or 0.6 mg of a compound of formula (I), a known colchicine derivative and/or a salt thereof.

[0015] The present disclosure also provides for the use of a compound of formula (I), a known colchicine derivative and/or a salt thereof in the preparation of a medicament for the treatment or prevention of a cardiovascular event.

[0016] In addition, the disclosure provides a composition for the prevention or treatment of a cardiovascular event in a subject, the composition comprising a therapeutically effective amount of a compound of formula (I), a known colchicine derivative and/or a salt thereof and one or more pharmaceutically acceptable additives, excipients carriers and/or diluents.

[0017] In one example, the composition comprises 0.5 mg or 0.6 mg of a compound of formula (I), a known colchicine derivative and/or a salt thereof.

[0018] In another example, the composition further comprises one or more additional agents selected from the list comprising: a statin and/or an anti-platelet agent.

[0019] The present disclosurealso provides a regimen for the treatment or prevention of a cardiovascular event in a subject, the regimen comprising the step of:

> administering a dosage of 0.5 mg or 0.6 mg of a compound of formula (I), a known colchicine derivative and/or a salt thereof once per day.

[0020] The present disclosure also provides a regimen for reducing or preventing cholesterol crystal induced inflammation within atherosclerotic plaques in a subject, the regimen comprising the step of:

> administering a dosage of 0.5 mg or 0.6 mg of a compound of formula (I), a known colchicine derivative and/or a salt thereof once or more times per day.

[0021] In one example, the subject being administered the regimen has atherosclerotic vascular disease, more preferably a coronary disease which may be a stable or unstable coronary disease.

FIGURES

[0022] Figure 1 is a flow chart of the subject enrolment process for Example 1.

[0023] Figure 2 is a graph of the time to first clinical event in each group by treatment.

[0024] Figure 3 is a table of the first time to clinical event across subgroups examined.

[0025] Figure 4 is series of graphs of the time to first clinical event in each group by treatment broken down into specific events.

DETAILED DESCRIPTION OF THE INVENTION

General

[0026] Those skilled in the art will appreciate that the invention described herein is susceptible to variations and modifications other than those specifically described. The invention includes all such variation and modifications. The invention also includes all of the steps, features, formulations and compounds referred to or indicated in the specification, individually or collectively and any and all combinations or any two or more of the steps or features.

CLAIMS

1. Use of a therapeutically effective amount of a composition comprising about 0.6 total mg of (i) colchicine, (ii) a known colchicine derivative, (iii) a salt of (i) or (ii), or any combination of (i)-(iii), in the manufacture of a medicament for treating and/or preventing a cardiovascular event in a subject.

2. The use of claim 1, wherein the subject has atherosclerotic vascular disease.

3. The use of claim 1 or 2, wherein the cardiovascular event is acute coronary syndrome, out-of-hospital cardiac arrest, or noncardioembolic ischemic stroke.

4. The use of any one of claims 1 to 3, wherein the treatment and/or prevention of the cardiovascular event further comprises a second agent to be co-administered for the treatment and/or prevention of the cardiovascular event in the subject.

5. Use of a therapeutically effective amount of a composition comprising no more than about 0.6 total mg of (i) colchicine, (ii) a known colchicine derivative, (iii) a salt of (i) or (ii), or any combination of (i)-(iii), in the manufacture of a medicament for treating and/or preventing inflammation in a subject having, or having a previous history of, atherosclerotic vascular disease.

6. The use of claim 5, wherein the composition reduces or prevents cholesterol crystal induced inflammation within atherosclerotic plaques.

7. Use of a therapeutically effective amount of a composition comprising no more than about 0.6 total mg of (i) colchicine, (ii) a known colchicine derivative, (iii) a salt of (i) or (ii), or any combination of (i)-(iii), in the manufacture of a medicament for treating and/or preventing atherosclerotic vascular disease.

8. The use of any one of claims 2-7, wherein the atherosclerotic vascular disease is a coronary disease.

9. The use of claim 8, wherein the coronary disease is a clinically stable coronary disease.

10. The use of any one of claims 1 to 9, wherein the composition is to be administered once per day.

11. The use of any one of claims 1 to 10, wherein the composition is to be administered orally, topically, parenterally, intraorbitally, ophthalmically, intraventricularly, intracranially, intracapsularly, intraspinally, intracisternally, intraperitoneally, buccally, rectally, vaginally, intranasally, or by aerosol administration, and/or inhalation spray, or via an implanted reservoir.

12. The use of any one of claims 1 to 11, wherein the composition is to be administered in the form of a tablet, capsule, liquid dose, gel, or powder.

13. Use of a therapeutically effective amount of a composition comprising no more than about 0.6 total mg of (i) colchicine, (ii) a known colchicine derivative, (iii) a salt of (i) or (ii), or any combination of (i)-(iii), in the manufacture of a medicament for treating and/or preventing a cardiovascular event in a patient undergoing co-administration of a second agent for the treatment and/or prevention of an atherosclerotic vascular disease.

14. The use of claim 13, wherein the cardiovascular event is acute coronary syndrome, out-of-hospital cardiac arrest, or noncardioembolic ischemic stroke.

15. The use of any one of claims 4 and 8 to 14, wherein the second agent is a statin.

16. The use of claim 15, wherein the statin is selected from the group consisting of atorvastatin, rosuvastatin, simvastatin, fluvastatin, lovastatin, pitavastatin, rosuvastatin and pravastatin, a derivative, or a salt thereof.

17. The use of any one of claims 4 and 8-16, wherein the second agent is an anti-platelet agent.

18. The use of claim 17, wherein the anti-platelet agent is selected from the group consisting of irreversible cyclooxygenase inhibitors; adenosine diphosphate (ADP) receptor inhibitors; phosphodiesterase inhibitors; glycoprotein IIB/IIIA inhibitors; adenosine reuptake inhibitors; thromboxane inhibitors; and Thromboxane receptor antagonists.

19. The use of any one of claims 1 to 18, wherein the composition comprises a pharmaceutically acceptable carrier, diluent, or excipient.