(93%) and statins (95%) were randomly assigned colchicine 0.5 mg/day or no colchicine and followed for a median of 3 years (Nidorf *et al.*, *JACC*, 2013, 61 (4), 404-410). This study showed that colchicine 0.5 mg/day administered in addition to statins and other standard secondary prevention therapies appeared effective for the prevention of cardiovascular events in patients with stable coronary disease.

[0011] For the treatment of gout, the recommended dose of colchcine (COLCRYS®) is 1.8 mg/day in one or multiple doses in one hour For adults with gout, treatment is initiated with a dose of 1.2 mg at the first sign of symptoms followed by 0.6 mg one hour later. (Physician's Desk Reference, 68th ed., (2014)).

[0012] COLCRYS® is an immediate release formulation. Adverse effects associated with the administration of COLCRYS® include, but are not limited to, nausea, vomiting, abdominal pain, diarrhea, hair loss, weakness, nerve irritation, severe anemia, low white blood counts, and low platelets (Physician's Desk Reference, 68th ed., (2014)).

[0013] The instant invention addresses these and other needs by providing a modified formulation of colchicine characterized by a sustained release of an active ingredient. This invention additionally provides an effective, once-daily dosage form of colchicine or salts thereof, which may improve patient compliance and also may reduce some of the side effects of colchicine compared to the current or higher daily doses of immediate release colchicine formulations.

~~BRIEF~~ SUMMARY ~~OF THE INVENTION~~

[0014] According to aspects of the invention illustrated herein, there is provided a sustained release formulation of colchicine ~~as an active ingredient, the formulation~~ comprising: granules comprising colchicine or a pharmaceutically acceptable salt thereof in an amount of not more than about 0.6 mg; a release retarding agent admixed with said granules in an amount of about 20% to about 40% w/w of the formulation, said release retarding agent being approximately equal portions of hypromellose and lactose monohydrate, and said release retarding agent having a viscosity of 4000 mPa*s; and at least one pharmaceutically acceptable excipient admixed with said granules.

[0015] According to an example illustrated herein, there is provided a method for treating and/or preventing a cardiovascular disease in a subject, comprising administering to the subject a therapeutically effective amount of a sustained release formulation of colchicine. In one other aspect, the present invention refers to the use of a sustained release formulation of colchicine according to the present invention in the manufacture of a medicament for treating and/or preventing a cardiovascular disease in a subject.

to the subject a therapeutically effective amount of a sustained release formulation of colchicine. In another aspect, the present invention refers to the use of a sustained release formulation of colchicine according to the present invention in the manufacture of a medicament for treating and/or preventing an inflammatory disease in a subject.

[0017] According to aspects of the invention illustrated herein, there is provided a process of preparing a colchicine-sustained release tablet comprising forming a granulating agent by dissolving 0.25% weight to about -0.75 % weight of the total composition of colchicine in an acceptable solvent, and; adding a binder and a filling agent ~~and a binder~~ to Step A, and forming a wet granulate~~ion;~~, wherein the binder comprises hypromellose having a viscosity rating of 6 mPa*s; drying the wet granulation of Step B; blending the dried granulation from Step C with a retarding agent, a filling agent, a glidant and a lubricant~~;~~, wherein the retarding agent is approximately equal portions of hypromellose and lactose monohydrate having a viscosity of 4000 mPa*s; and compressing the final granulation from step D into a tablet or pill form.

[0018] According to ~~aspects~~examples of the present ~~invention~~disclosure ~~illustrated herein~~, there is provided a shaped and compressed sustained release therapeutic composition comprising colchicine and excipients combined into a matrix, characterized by a long-lasting, slow and relatively regular incremental release of the colchicine upon administration, wherein the excipients include Hypromellose, and wherein the total amount of excipients is effective to bind the colchicine in a sustained release solid matrix and is no less than 99 percent of the weight of said shaped and compressed composition.

[0019] According to aspects of the invention illustrated herein, there is provided a shaped and compressed colchicine ~~sustained release~~ tablet ~~made~~produced by wet granulating a sufficient amount of colchicine to comprise from about 0.25 percent weight to about 0.75 percent weight of the total ~~composition~~tablet with the excipients wherein the excipients comprise the following: lactose monohydrate from about 10 to about 80 percent of the total composition, pregelatinized starch from about 5 to about 50 percent of the total composition, Hypromellose 6mPa*s from about 1 to about 30 percent of the total composition, purified water (q.s.), Retalac from about 5 to about 40 percent of the total composition, talc from about 0.5 to about 5 percent of the total composition, and stearic acid from about 0.5 to about 5 percent of the total composition. In still another aspect, the present invention refers to the use of about 0.5 mg to about 0.6 mg colchicine in the manufacture of a medicament for treating a patient having a cardiovascular disease, wherein the medicament is to be administered orallyto a human patient, wherein the use provides a maximum colchicine blood plasma concentration (Cmax) in a range of about 0.5 ng/mL to 5 ng/mL, and a time after the first administration at

which Cmax is reached (Tmax) of about 1.5 hr to 8 hr. In ~~another aspect~~one example, the present ~~invention~~disclosure refers to the use of an adjusted daily dosage amount of colchicine in the manufacture of a medicament for treating a patient with a cardiovascular disease, wherein the use comprises administration to the patient the adjusted daily dosage amount of colchicine, wherein the adjusted dialy dosage amount of colchicine is based on the weight of the patient, wherein the adjusted daily dosage amount of colchicine is about 50% to about 300% of 0.5 mg per day, which is suitable for the patient if the patient weighs about 70kg.

BRIEF DESCRIPTION OF THE DRAWINGS/FIGURES

[0020] The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawings will be provided by the Office upon request and payment of the necessary fee.

WHAT IS CLAIMED IS:

1. A sustained release formulation of colchicine comprising:

(a) granules comprising colchicine or a pharmaceutically acceptable salt thereof in an amount of not more than about 0.6 mg;

(b) a release retarding agent admixed with said granules in an amount of about 20% to about 40% w/w of the formulation, said release retarding agent being approximately equal portions of hypromellose and lactose monohydrate, and said release retarding agent having a viscosity of 4000 mPa*s; and

(c) at least one pharmaceutically acceptable excipient admixed with said granules.

2. The formulation of claim 1, wherein said release retarding agent admixed with said granules in an amount of about 30% to about 40% w/w of the formulation, and wherein less than 70% of colchicine is released *in vitro* from said formulation within 2 hours at 37°C.

3. The formulation of claim 2, wherein the formulation releases no more than about 30% of the colchicine *in vitro* within the first 30 minutes.

4. The formulation of any one of claims 1-3, wherein the retarding agent further comprises one or more cellulose ethers, cellulose esters, acrylic acid copolymers, waxes, gums, glyceryl fatty acid esters, or sucrose fatty acid esters.

5. The formulation of any one of claims 1-4, wherein the pharmaceutically acceptable excipient is one or more of a binder, a filling agent, a glidant, or a lubricant.

6. The formulation of any one of claims 1-5, wherein the pharmaceutically acceptable excipient is one or more binders including starches, gelatin, polyvinylpyrrolidone, cellulose derivatives, or polyvinyl alcohol.

7. The formulation of claim 6, wherein the cellulose derivative is selected from a group consisting of hydroxypropyl methylcellulose (HPMC) and hydroxypropyl cellulose (HPC).

8. The formulation of claim 6 or claim 7, wherein the cellulose derivative forms a hydrophilic matrix.

9. The formulation of any one of claims 1-8, wherein the pharmaceutically acceptable excipient is one or more filling agents including sucrose, lactose, in particular lactose monohydrate, trehalose, maltose, mannitol and sorbitol, croscarmellose sodium, crospovidone, alginic acid, sodium alginate, methacrylic acid DVB, cross-linked PVP, microcrystalline cellulose, polacrilin potassium, sodium starch glycolate, starch, or pregelatinized starch.

10. The formulation of any one of claims 1-9, wherein the total amount of filling agent in the formulation is between about 5.0 wt % and 90.0 wt % of the formulation.

11. The formulation of any one of claims 1-10, wherein the pharmaceutically acceptable excipient is one or more glidants including colloidal silicon dioxide, magnesium trisilicate, powdered cellulose, talc, or tribasic calcium phosphate

12. The formulation of any one of claims 1-11, wherein total amount of glidant in the formulation is between about 0.5 wt % to about 5 wt % of the formulation.

13. The formulation of any one of claims 1-12, wherein the pharmaceutically acceptable excipient is one or more lubricants including glyceryl behenate, stearic acid, hydrogenated vegetable oils, stearyl alcohol, leucine, polyethylene glycol, magnesium stearate, glyceryl monostearate, polyethylene glycol, ethylene oxide polymers, sodium lauryl sulfate, magnesium lauryl sulfate, sodium oleate, sodium stearyl fumarate, DL-leucine, or colloidal silica.

14. The formulation of any one of claims 1-4, wherein the lubricant is included in an amount between about 0.5 wt % to about 5 wt % of the formulation.

15. The formulation of any one of claims 1-14, wherein the formulation is in the form of a tablet, a pill, a capsule, a caplet, a suppository, a dermal patch, a cream, a sublingual formulation, an eye drop, a gel, an ointment, a troche, a pouch, sprinkles, or in fixed combination with a surgically insertable medical device.

16. The formulation of any one of claims 1-15, wherein the dosage form is a tablet.

17. The formulation of claim 16, wherein the compression strength of the tablet is between about 30N and about 130N.

18. The formulation of any one of claims 1-17, wherein the total amount of colchicine in the formulation is between about 0.25 wt % and about 0.75 wt % of the formulation.

19. The formulation of any one of claims 1-18 for use in preventing and/or treating a cardiovascular disease.

20. The formulation of any one of claims 1-19, wherein the cardiovascular disease is one or more of acute pericarditis, recurrent pericarditis, post-pericardiotomy syndrome (PPS) or cardiovascular events in patients with stable coronary disease.

21. The formulation of any one of claims 1-20, for use in combination with conventional therapy for the long-term prevention of an acute cardiovascular event in patients with established stable coronary disease.

22. The formulation of any one of claims 1-21, wherein said acute cardiovascular event is acute coronary syndrome, out-of-hospital cardiac arrest or noncardioembolic ischemic stroke.

23. The formulation of any one of claims 1-22, wherein the conventional therapy includes the administration of a colchicine-compatible statin.

24. The formulation of any one of claims 1-23, wherein the colchicine-compatible statin is administered in a fixed or unfixed combination with colchicine.

25. The formulation of any one of claims 1-24, wherein the colchicine-compatible statin is one or more of atorvastatin, rosuvastatin, simvastatin and pravastatin, a derivative or a salt thereof.

26. The formulation of any one of claims 1-18 for use in preventing and/or treating an inflammatory disease.

27. The formulation of any one of claims 1-18 and 26, wherein the inflammatory disease is gout, familial Mediterranean fever, Behcet´s disease, Age-related macular degeneration, or Alzheimer´s disease.

28. The formulation according to any one of claims 1-18 and 26-27, wherein the total daily dose of colchicine administered to a subject is no more than about 0.75mg.

29. Use of a sustained release formulation of colchicine according to any one of claims 1-18 in the manufacture of a medicament for treating and/or preventing a cardiovascular disease in a subject.

30. The use of claim 29, wherein the cardiovascular disease is acute pericarditis, recurrent pericarditis, post-pericardiotomy syndrome (PPS), or cardiovascular events in patients with stable coronary disease.

31. The use of any one of claims 29-30, wherein the total daily dose of colchicine to be administered to the subject is no more than about 0.75mg.

32. The use of any one of claims 29-31, further comprising administration to the subject a conventional therapy for the long-term prevention of an acute cardiovascular event in patients with established stable coronary disease.

33. The use of any one of claims 29-32, wherein the acute cardiovascular event is acute coronary syndrome, out-of-hospital cardiac arrest or noncardioembolic ischemic stroke.

34. The use of any one of claims 29-33, wherein the conventional therapy includes the administration of a colchicine-compatible statin.

35. The use of any one of claims 29-34, wherein the colchicine-compatible statin is one or more of atorvastatin, rosuvastatin, simvastatin, pravastatin, a derivative, or a salt thereof.

36. Use of a sustained release formulation of colchicine according to any one of claims 1-18 in the manufacture of a medicament for treating and/or preventing an inflammatory disease in a subject.

37. The use of claim 36, wherein the inflammatory disease is gout, familial Mediterranean fever, Behcet's disease, Age-related macular degeneration, or Alzheimer's disease.

38. The use of any one of claims 36-37, wherein the total daily dose of colchicine to be administered to the subject is no more than about 0.75mg.

39. A process of preparing a colchicine-sustained release tablet comprising:

(A) forming a granulate by dissolving about 0.25 % weight to about 0.75 % weight of the total composition of colchicine in an acceptable solvent, and

(B) adding a binder and a filling agent to Step A, and forming a wet granulate, wherein the binder comprises hypromellose having a viscosity rating of 6 mPa*s;

(C) drying the wet granulate of Step B;

(D) blending the dried granulate from Step C with a retarding agent, a filling agent, a glidant and a lubricant, wherein the retarding agent is approximately equal portions of hypromellose and lactose monohydrate having a viscosity of 4000 mPa*s; and

(E) compressing the final granulation from step D into a tablet or pill form.

40. The process of claim 39 wherein:

in Step B the filling agent is lactose monohydrate and pregelatinized starch; and

in Step D the filing agent is lactose monohydrate, the glidant is talc, and the lubricant is stearic acid.

41. The process of claim 39 or claim 40, wherein the tablet or pill comprises:

Ingredient	**mg / Tablet**	**Tablet %**
Colchicine	0.500	0.5
Lactose monohydrate	59.00	59.0
Pregelatinized Starch	7.50	7.5
Hypromellose 6mPa*s	1.000	1.0
Purified water[1]	q.s.	q.s.
Retalac (Compound of Lactose monohydrate and Hypromellose 4000mPa*s 50/50 w/w %)	5.0 - 40.00	5.0 - 40.0
Talc	1.00	1.0
Stearic acid 50	1.00	1.0
Total tablet weight [mg]:	**100.00**	

42. A shaped and compressed colchicine tablet produced by wet granulating a sufficient amount of colchicine to comprise from about 0.25 percent weight to about 0.75 percent weight of the total tablet with the excipients, wherein the excipients comprise the following:

Ingredient	**% Range**
Lactose monohydrate	10-80
Pregelatinized Starch	5-50
Hypromellose 6mPa*s	1-30
Purified water[1]	q.s.
Retalac (Compound of Lactose monohydrate and Hypromellose 4000mPa*s 50/50 w/w %)	5-40
Talc	0.5-5
Stearic acid 50	0.5-5

43. The composition of claim 42 wherein the total amount of excipients is at least 99 percent of the total weight of said shaped and compressed composition.

44. Use of about 0.5 mg to about 0.6 mg colchicine in the manufacture of a medicament for treating a patient having a cardiovascular disease, wherein the medicament is to be administered orallyto a human patient, wherein the use provides a maximum colchicine blood plasma concentration (Cmax) in a range of about 0.5 ng/mL to 5 ng/mL, and a time after the first administration at which Cmax is reached (Tmax) of about 1.5 hr to 8 hr.

45. The use of claim 44, wherein the use further provides an area under the curve of colchicine plasma concentration versus time from time 0 to time t (AUC0-t), wherein t is the last time point with a measurable colchicine plasma concentration, in a range of from about 4 ng-hr/mL to 20 ng-hr/mL.

46. The use of claims 44 and 45, wherein the use further provides an area under the curve of colchicine plasma concentration versus time from time 0 to time infinity (AUC0-∞) in a range of from 4 ng-hr/mL to 20 ng-hr/mL.

47. The use of any one of claims 44-46, wherein the use further provides an area under the curve of colchicine plasma concentration versus time from time 0 to time t (AUC0-t), wherein t is the last time point with a measurable colchicine plasma concentration, in a range of about 4 ng-hr/mL to 20 ng-hr/mL and an area under the curve of colchicine plasma concentration versus time from time 0 to time infinity (AUC0-∞) in a range of from about 4 ng-hr/mL to 20 ng-hr/mL.

48. The use of any one of claims 44-47, wherein in each said oral administration one or more dosage forms each containing about 0.5 mg colchicine are to be administered.

49. The use of any one of claims 44-48, wherein the dosage form is a tablet.

WHAT IS CLAIMED IS:

1. A sustained release formulation of colchicine as an active ingredient, the formulation comprising:

(a) colchicine or a pharmaceutically acceptable salt thereof;

(b) a retarding agent; and

(c) at least one pharmaceutically acceptable excipient.

2. The formulation of claim 1, wherein the formulation releases at least about 80% of the colchicine in vitro within 24 hours, within 16 hours, within 12 hours, within 8 hours, within 6 hours, within 4 hours, within 3.5 hours, or within 1.5 hours.

3. The formulation of claims 1 or 2, wherein the formulation releases at least about 20% of the colchicine in vitro within the first 30 minutes.

4. The formulation of any one of claims 1-3, wherein the retarding agent is selected from a group consisting of cellulose ethers, cellulose esters, acrylic acid copolymers, waxes, gums, glyceryl fatty acid esters and sucrose fatty acid esters.

5. The formulation of any one of claims 1-4, wherein the retarding agent contains hypromellose.

6. The formulation of any one of claims 1-5, wherein the retarding agent is included in an amount between about 5 wt % and about 40 wt % of the formulation

7. The formulation of any one of claims 1-6, wherein the pharmaceutically acceptable excipient is selected from a group consisting of a binder, a filling agent, a glidant, and a lubricant, or a combination thereof.

8. The formulation of any one of claims 1-7, wherein the pharmaceutically acceptable excipient is a binder selected from the group consisting of starches, gelatin, polyvinylpyrrolidone, cellulose derivatives, polyvinyl alcohol and mixtures thereof.

9. The formulation of any one of claims 1-8, wherein the cellulose derivative is selected from a group consisting of hydroxypropyl methylcellulose (HPMC) and hydroxypropyl cellulose (HPC).

10. The formulation of any one of claims 1-9, wherein the cellulose derivative forms a hydrophilic matrix.

11. The formulation of any one of claims 1-10, wherein the pharmaceutically acceptable excipients is a filling agent selected from the group consisting of sucrose, lactose, in particular lactose monohydrate, trehalose, maltose, mannitol and sorbitol, croscarmellose sodium, crospovidone, alginic acid, sodium alginate, methacrylic acid DVB, cross-linked PVP, microcrystalline cellulose, polacrilin potassium, sodium starch glycolate, starch, pregelatinized starch, and combinations thereof.

12. The formulation of any one of claims 1-11, wherein the total amount of filling agent in the formulation is between about 5.0 wt % and 90.0 wt % of the formulation.

13. The formulation of any one of claims 1-12, wherein the pharmaceutically acceptable excipient is a glidant selected from the group consisting of colloidal silicon dioxide, magnesium trisilicate, powdered cellulose, talc, and tribasic calcium phosphate

14. The formulation of any one of claims 1-13, wherein total amount of glidant in the formulation is between about 0.5 wt % to about 5 wt % of the formulation.

15. The formulation of any one of claims 1-14, wherein the pharmaceutically acceptable excipient is a lubricant selected from the group consisting of glyceryl behenate, stearic acid, hydrogenated vegetable oils, stearyl alcohol, leucine, polyethylene glycol, magnesium stearate, glyceryl monostearate, polyethylene glycol, ethylene oxide polymers, sodium lauryl

sulfate, magnesium lauryl sulfate, sodium oleate, sodium stearyl fumarate, DL-leucine, and colloidal silica.

16. The formulation of any one of claims 1-15, wherein the lubricant is included in an amount between about 0.5 wt % to about 5 wt % of the formulation.

17. The formulation of any one of claims 1-16, wherein the formulation is in a dosage form selected from the group consisting of a tablet, a pill, a capsule, a caplet, a suppository, a dermal patch, a cream, sublingual formulation, eye drops, gel, ointment, a troche, a pouch, sprinkles, or in fixed combination with a surgically insertable medical device.

18. The formulation of any one of claims 1-17, wherein the dosage form is a tablet.

19. The formulation of any one of claims 1-18, wherein the compression strength of the tablet is between about 30N and about 130N.

20. The formulation of any one of claims 1-19, wherein the total amount of colchicine in the formulation is from about 0.1 to about 5.0mg per dose.

21. The formulation of any one of claims 1-20, wherein the amount of colchicine per dose is between 0.1 mg to 2.0 mg, 0.1 mg to 1.75 mg, 0.1 mg to 1.5 mg, 0.1 mg to 1.25 mg, 0.1 mg to 1.0 mg, 0.1 mg to 0.75 mg, 0.1mg to 0.6mg, 0.1 mg to 0.5 mg or more than 0.25 mg and less than 0.5 mg.

22. The formulation of any one of claims 1-21, wherein the total amount of colchicine in the formulation is between about 0.25 wt % and about 0.75 wt % of the formulation.

23. The formulation of any one of claims 1-22 for use in preventing and/or treating a cardiovascular disease.

24. The formulation of any one of claims 1-23, wherein the cardiovascular disease is selected from the group consisting of acute pericarditis, recurrent pericarditis, post-

pericardiotomy syndrome (PPS) and cardiovascular events in patients with stable coronary disease.

25. The formulation of any one of claims 1-24, for use in combination with conventional therapy for the long-term prevention of an acute cardiovascular event in patients with established stable coronary disease.

26. The formulation of any one of claims 1-25, wherein said acute cardiovascular event is acute coronary syndrome, out-of-hospital cardiac arrest or noncardioembolic ischemic stroke.

27. The formulation of any one of claims 1-26, wherein the conventional therapy includes the administration of a colchicine-compatible statin.

28. The formulation of any one of claims 1-27, wherein the colchicine-compatible statin is administered in a fixed or unfixed combination with colchicine.

29. The formulation of any one of claims 1-28, wherein the colchicine-compatible statin is selected from the group consisting of atorvastatin, rosuvastatin, simvastatin and pravastatin, a derivative or a salt thereof.

30. The formulation of any one of claims 1-22 for use in preventing and/or treating an inflammatory disease.

31. The formulation of any one of claims 1-22 and 30, wherein the inflammatory disease is selected from the group consisting of gout, familial Mediterranean fever, Behcet's disease, Age-related macular degeneration and Alzheimer's disease.

32. The formulation according to any one of claims 1-22 and 30-31, wherein the total daily dose of colchicine administered to a subject is no more than about 0.75mg.

33. Use of a sustained release formulation of colchicine according to any one of claims 1-22 in the manufacture of a medicament for treating and/or preventing a cardiovascular disease in a subject.

34. The use of claim 33, wherein the cardiovascular disease is selected from the group consisting of acute pericarditis, recurrent pericarditis, post-pericardiotomy syndrome (PPS) and cardiovascular events in patients with stable coronary disease.

35. The use of claims 33 and 34, wherein the total amount of colchicine in the formulation is from about 0.1 to about 5.0mg per dose.

36. The use of any one of claims 33-35, wherein the amount of colchicine per dose is between 0.1 mg to 2.0 mg, 0.1 mg to 1.75 mg, 0.1 mg to 1.5 mg, 0.1 mg to 1.25 mg, 0.1 mg to 1.0 mg, 0.1 mg to 0.75 mg, 0.1mg to 0.6mg, 0.1 mg to 0.5 mg or more than 0.25 mg and less than 0.5 mg.

37. The use of any one of claims 33-36, wherein the total daily dose of colchicine to be administered to the subject is no more than about 0.75mg.

38. The use of any one of claims 33-37, further comprising administration to the subject a conventional therapy for the long-term prevention of an acute cardiovascular event in patients with established stable coronary disease.

39. The use of any one of claims 33-38, wherein the acute cardiovascular event is acute coronary syndrome, out-of-hospital cardiac arrest or noncardioembolic ischemic stroke.

40. The use of any one of claims 33-39, wherein the conventional therapy includes the administration of a colchicine-compatible statin.

41. The use of any one of claims 33-40, wherein the colchicine-compatible statin is selected from the group consisting of atorvastatin, rosuvastatin, simvastatin and pravastatin, a derivative or a salt thereof.

42. Use of a sustained release formulation of colchicine according to any one of claims 1-22 in the manufacture of a medicament for treating and/or preventing an inflammatory disease in a subject.

43. The use of claim 42, wherein the inflammatory disease is selected from the group consisting of gout, familial Mediterranean fever, Behcet's disease, Age-related macular degeneration and Alzheimer's disease.

44. The use of claims 42 and 43, wherein the total amount of colchicine in the formulation is from about 0.1 to about 5.0mg per dose.

45. The use of any one of claims 42-44, wherein the amount of colchicine per dose is between 0.1 mg to 2.0 mg, 0.1 mg to 1.75 mg, 0.1 mg to 1.5 mg, 0.1 mg to 1.25 mg, 0.1 mg to 1.0 mg, 0.1 mg to 0.75 mg, 0.1mg to 0.6mg, 0.1 mg to 0.5 mg or more than 0.25 mg and less than 0.5 mg..

46. The use of any one of claims 42-45, wherein the total daily dose of colchicine to be administered to the subject is no more than about 0.75mg.

47. A process of preparing a colchicine-sustained release tablet comprising:

(A) forming a granuate by dissolving about 0.25 to about 0.75 % weight of the total composition of colchicine in an acceptable solvent, water and

(B) adding a binder and a filling agent to Step A, and forming a wet granulate;

(C) drying the wet granulate of Step B;

(D) blending the dried granulate from Step C with a retarding agent, a filling agent, a glidant and a lubricant; and

(E) compressing the final granulation from step D into a tablet.

48. The process of claim 47 wherein:

in Step A the binder is Hypromellose;

in Step B the filling agent used is lactose monohydrate and Pregelatinized Starch; and

in Step D the retarding agent used is Retalac; the filing agent used is lactose monohydrate, the glidant used is Talc, and the lubricant used is Stearic acid.

49. The process of claims 47 and 48, wherein the specific ingredients and amounts used are:

Ingredient	mg / Tablet	Tablet %
Colchicine	0.500	0.5
Lactose monohydrate	59.00	59.0
Pregelatinized Starch	7.50	7.5
Hypromellose 6mPa*s	1.000	1.0
Purified water	q.s.	q.s.
Retalac (Compound of Lactose monohydrate and Hypromellose 4000mPa*s 50/50 w/w %)	5.0 - 40.00	5.0 - 40.0
Talc	1.00	1.0
Stearic acid 50	1.00	1.0
Total tablet weight [mg]:	100.00	

50. A shaped and compressed sustained release therapeutic composition comprising colchicine and excipients combined into a matrix, wherein the excipients comprise Hypromellose, and wherein the total amount of excipients is effective to bind the colchicine in a sustained release solid matrix and is at least about 99 percent of the weight of said shaped and compressed composition.

51. The sustained release therapeutic composition of claim 50, wherein the composition releases at least about 80% of the colchicine in vitro within 24 hours, within 16 hours, within 12 hours, within 8 hours, within 6 hours, within 4 hours, within 3.5 hours, or within 1.5 hours.

52. The sustained release therapeutic composition of claims 50 and 51, wherein the composition releases at least about 20% of the colchicine in vitro within the first 30 minutes.

53. A shaped and compressed colchicine sustained release tablet made by wet granulating a sufficient amount of colchicine to comprise from about 0.25 to about 0.75 percent weight of the total composition with the excipients wherein the excipients comprise the following:

Ingredient	**% Range**
Lactose monohydrate	10-80
Pregelatinized Starch	5-50
Hypromellose 6mPa*s	1-30
Purified water[1]	q.s.
Retalac (Compound of Lactose monohydrate and Hypromellose 4000mPa*s 50/50 w/w %)	5-40
Talc	0.5-5
Stearic acid 50	0.5-5

54. A composition of claim 53 wherein the total amount of excipients is at least about 99 percent of the total weight of said shaped and compressed composition.

55. Use of 0.5 mg colchicine in the manufacture of a medicament for treating a patient having a cardiovascular disease, wherein the medicament is to be administered orallyto a human patient, wherein the use provides a maximum colchicine blood plasma concentration (Cmax) in a range of about 0.5 to 5 ng/mL, and a time after the first administration at which Cmax is reached (Tmax) of about 1.5 to 8 hr.

56. The use of claim 55, the use further provides an area under the curve of colchicine plasma concentration versus time from time 0 to time t (AUC0-t), where t is the last time point with a measurable colchicine plasma concentration, in a range of about 4 to 20 ng-hr/mL.

57. The use of claims 55 and 56, the use further provides an area under the curve of colchicine plasma concentration versus time from time 0 to time infinity (AUC0-∞) in a range of 4 to 20 ng-hr/mL.

58. The use of any one of claims 55-57, the use further provides an area under the curve of colchicine plasma concentration versus time from time 0 to time t (AUC0-t), where t is the last time point with a measurable colchicine plasma concentration, in a range of about 4 to 20 ng-hr/mL and an area under the curve of colchicine plasma concentration versus time from time 0 to time infinity (AUC0-∞) in a range of about 4 to 20 ng-hr/mL.

59. The use of any one of claims 55-58, wherein each said oral administration comprises that one or more dosage forms each containing 0.5 mg colchicine are to be adminstered.

60. The use of any one of claims 55-59, wherein the dosage form is a tablet.

61. The use of any one of claims 55-60, wherein the tablet is a sustained release tablet.

62. Use of an adjusted daily dosage amount of colchicine in the manufacture of a medicament for treating a patient with a cardiovascular disease, wherein the use comprises administration to the patient the adjusted daily dosage amount of colchicine, wherein the adjusted dialy dosage amount of colchicine is based on the weight of the patient, wherein the adjusted daily dosage amount of colchicine is about 50% to about 300% of 0.5 mg per day, which is suitable for the patient if the patient weighs about 70kg.

63. The formulation of claims 1 or 2, wherein the formulation releases at least about 80% of the colchicine in vitro in between about 1.5 and about 3.5 hours.