CLAIMS

1. A pharmaceutical composition for topical wound treatment comprising:

- one or more nitrogenous heterocyclic compound of 5 or 6 atoms with imide group;
- one or more deoxyribonuclease enzyme with activity pH between 4.5 and 6.5; and
- one or more carboxylic acid.

2. The pharmaceutical composition according to claim 1, wherein the nitrogenous heterocyclic compound of 5 or 6 atoms with imide group comprises a nitrogenous heterocyclic compound of 5 or 6 atoms with imide group selected from the group consisting of ethosuximide, barbituric acid, phenobarbital, 5,5-diethyl barbituric acid, 5-Ethyl-5- (1-methylbutyl) barbituric acid, pentobarbitone, pentobarbital, Nembutal, 5-Ethyl-5- (1-methylpropyl) barbituric acid, Butobarbital, butisol, 5-Allyl-5- (1-methylbutyl) -barbituric acid, secobarbital, Seconal, Phenytoin, Hydantoin and, and a mixture thereof.

3. The pharmaceutical composition according to claim 1, wherein the deoxyribonuclease enzyme comprises a deoxyribonuclease enzyme selected from the group consisting of DNase, rh-dornase alfa, bovine pancreatic DNase I, DNase II, prokaryotic DNase II or eukaryotic DNase II, DNase II alfa, DNase II beta, porcine spleen DNase II, and a mixture thereof.

4. The pharmaceutical composition according to claim 1, wherein the carboxylic acid comprises an carboxylic acid selected from the group consisting of citric acid, lactic acid, acetic acid, formic acid, malic acid, tartaric acid, salicylic acid, oxalic acid, benzoic acid, propionic acid, and a mixture thereof.

5. The pharmaceutical composition according to claim 1, comprising:

- from about 0.5 to about 50 mg/ml one or more nitrogenous heterocyclic compound of 5 or 6 atoms with imide group;
- from about 0.5 to about 4000 μg/ml one or more deoxyribonuclease enzyme;
- from about 1 to about 15 mg/ml one or more carboxylic acid.

6. The pharmaceutical composition according to claim 1, further comprising one or more tensioactive agent selected from the group consisting of polysorbate 20, polysorbate 80, polysorbate 60, sorbitan triestearate, sorbitan monostearate, octoxynol-9, nonoxynol-9, and a mixture thereof.

7. The pharmaceutical composition according to claim 6, comprising about 5 mg/ml or less of said tensioactive agents.

8. The pharmaceutical composition according to claim 1, further comprising one or more complex forming acid selected from the group consisting of ethylene glycol tetra acetic acid, ethylenediaminetetraacetic acid, dimercaptosuccinic acid, 2,3-Dimercapto-1-propanesulfonic acid, lipoic acid (1,2-dithiol-3-valeric acid), oxalic acid, and a mixture thereof.

9. The pharmaceutical composition according to claim 8, comprising about 1 mg/ml or less of said complex forming acid.

10. The pharmaceutical composition according to claim 1, further comprising one or more hydrophilic reducing acid selected from the group consisting of uric acid, ascorbic acid, lipoic acid and a mixture thereof.

11. The pharmaceutical composition according to claim 10, comprising about 3 mg/ml or less of said hydrophilic reducing acid.

12. The pharmaceutical composition according to claim 1, further comprising one or more gelling agent selected from the group consisting of cellulose, nano-crystalline cellulose, bacterial cellulose, hydroxyethyl cellulose, hydroxypropyl cellulose, microcrystalline cellulose, carboxymethyl cellulose, carbopol and a mixture thereof.

13. The pharmaceutical composition according to claim 12, comprising about 25 mg/ml or less one of said gelling agent.

14. The pharmaceutical composition according to claim 1, further comprising a solution selected from the group consisting of acetic acid 0.2M / sodium acetate 0.2M: Ratio 2.78 to 0.66 %(v/v) pH = 4.2 to 4.8; acetic acid 0.10 M / sodium acetate 0.01 M: Ratio 1.05 to 10.05 %(v/v) pH = 5,6; monobasic potassium phosphate 0.05M pH = 4.5; monobasic potassium phosphate 0.36 M/disodium phosphate 0.07M: Ratio 4.92 to 0.98 %(p/v) pH = 5,7; monobasic potassium phosphate 0.36 M/disodium phosphate 0.10M: Ratio 4.92 to 1.49 %(p/v) pH = 6,0; citric acid 0.31 M/disodium phosphate 0.20 M: Ratio 2.99 to 1.42 %(p/v) pH = 5.8; citric acid 0.10 M/sodium citrate 0.03 M: Ratio 1.92 a 0.77 %(p/v) pH = 5,8; Sørensen's phosphate buffer:

sodium monobasic phosphate 0.2M/Disodium phosphate 2.3 M: Ratio 1.2 to 16.33 %(p/v) pH = 5,8; Hank's balanced salt solution (HBSS): sodium chloride 0.14 M (0.800%), potassium chloride 5 mM (0.040%), Calcium chloride 1 mM (0.014%), Magnesium sulphate heptahydrate 0.4 mM (0.010%), Magnesium chloride hexahydrate 0.5 mM (0.010%), Disodium phosphate dihydrate 0.3 mM (0.006%), Potassium monobasic phosphate 0.4 mM (0.006%), Glucose 6 mM (0.100%), Sodium bicarbonate 4 mM (0.035%): pH = 5.7; 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid (HEPES) 1M (pH = 6.5); 2-(N-Morpholino)ethanesulfonic acid sodium salt,4-Morpholineethanesulfonic acid (MES sodium salt) 0.5 M (pH 5.5 – 6.7); N,N-Bis(2-hydroxyethyl)-2-aminoethanesulfonic acid sodium salt (BES) 0.5 M (pH = 6.0); N-(2-Acetamido)-2-aminoethanesulfonic acid (ACES) 0.5 M (pH = 6.0); 2,2'-[(2-Amino-2-oxoethyl)imino]diacetic acid (ADA) 0.2 M (pH = 6.0); piperazine-N,N'-bis(2-ethanesulfonic acid) (PIPES) 0.5 M (pH = 6.0 – 6.8); 3-Morpholino-2-hydroxypropanesulfonic acid (MOPSO) 0.2 M (pH = 6.0); saline solution (0.9%) / MgCL2 (5 mM). pH 5.5; 1M NaHCO3 solution and combinations thereof.

15. The pharmaceutical composition according to claim 1, wherein:

the one or more nitrogenous heterocyclic compound of 5 or 6 atoms with imide group comprises ethosuximide;

the one or more deoxyribonuclease enzyme with activity pH between 4.5 and 6.5 comprises recombinant human Dornase-Alpha;

the one or more carboxylic acid comprises lactic acid.

16. The pharmaceutical composition according to claim 15, further comprising:

one or more hydrophilic reducing acid;

one or more tensioactive agent;

one or more complex forming acid;

one or more gelling agent; and

a solution.

17. The pharmaceutical composition according to claim 1, wherein:

the nitrogenous heterocyclic compound of 5 or 6 atoms with imide group comprises ethosuximide;

the deoxyribonuclease enzyme comprises recombinant human Dornase-Alpha;

the carboxylic acid comprises lactic acid,

and further comprising:

ascorbic acid;

polysorbate-80;

ethylenediaminetetraacetic acid;

hydroxyethyl cellulose; and

a solution comprising saline solution 0.9% and $MgCl_2$ 5 mM at pH 5.5.

18. The pharmaceutical composition according to claim 1, having a pH between 4.5 and 6.8.

19. The pharmaceutical composition according to claim 1, comprising an aqueous solution of :

from about 0.5 to about 30 mg/ml ethosuximide;

from about 1 to about 4 µg/ml recombinant human Dornase-alpha;

from about 1 to about 9 mg/ml lactic acid,

and wherein the pharmaceutical composition further comprises:

about 2.5 mg/ml or less ascorbic acid;

about 3 mg/ml or less polysorbate-80;

about 0.75 mg/ml or less ethylenediaminetetraacetic acid;

about 17 mg/ml or less hydroxyethyl cellulose.

20. The pharmaceutical composition according to claim 1, comprising:

from about 0.5 to about 3 mg/ml ethosuximide;

from about 0.97 to about 3.9 µg/ml recombinant human Dornase-alpha;

from about 1.6 to about 8.7 mg/ml lactic acid,

and wherein the pharmaceutical composition further comprises:

about 2.5 mg/ml or less ascorbic acid;

about 3 mg/ml or less polysorbate-80;

about 0.75 mg/ml or less ethylenediaminetetraacetic acid;

about 17 mg/ml or less hydroxyethyl cellulose.

21. A pharmaceutical formulation kit for topical wound treatment comprising a first composition and a second composition for mixing before use to obtain a pharmaceutical composition, wherein:

a. the first composition is solid and comprises a deoxyribonuclease enzyme and a gelling agent powder; and

b. the second composition is an aqueous liquid comprising at least one nitrogenous heterocyclic compound of 5 or 6 atoms with imide group and at least one carboxylic acid; and

c. the second composition has a pH between 4.5 and 6.8.

22. A pharmaceutical formulation kit for topical wound treatment comprising a first composition, a second composition, and a third composition for mixing before use to obtain a pharmaceutical composition, wherein:

a. the first composition is solid and comprises a gelling agent powder;

b. the second composition is solid and comprises a deoxyribonuclease enzyme; and

c. the third composition is an aqueous liquid comprising an at least one nitrogenous heterocyclic compound of 5 or 6 atoms with imide group and an at least one carboxylic acid; and

d. the third composition has a pH between 4.5 and 6.8.

23. The pharmaceutical formulation kit according to claim 21, wherein each one of the first composition, the second composition, and the third composition is contained in a hermetic and separate container.

24. The pharmaceutical formulation according to claims 22, wherein each one of the first composition, the second composition, and the third composition is contained in a hermetic and separate container.

25. A process for preparing the pharmaceutical formulation according to claim 21 comprising:

a. putting into contact the first composition with the second composition;

b. mixing and shaking to obtain a gel pharmaceutical composition.

26. A process for preparing the composition of claim 12 from a pharmaceutical formulation comprising a first composition, a second composition, and a third composition that are mixed before use, wherein the first composition is solid and comprises a gelling agent powder; the second composition is solid and comprises a deoxyribonuclease enzyme; and the third composition is an aqueous liquid comprising at least one nitrogenous heterocyclic compound of 5 or 6 atoms with imide group and at least one carboxylic acid; and the third composition has a pH between 4.5 and 6.8. comprising:

a. putting in contact the third composition with the second composition;

b. mixing and shaking the third composition with the second composition to form a mixture (b);

c. putting in contact the first composition with the mixture (b) to form a mixture (c);

d. mixing and shaking to obtain a gel pharmaceutical composition

27. The use of the pharmaceutical composition according to claim 1 for the manufacture of a medicament for the therapeutic treatment of wound of a mammal comprising the formulation to be applied to the wound at least once a day.

28. The use of the pharmaceutical formulation according to claim 21 for the manufacture of a medicament for the therapeutic treatment of wound of a mammal comprising the formulation to be applied to the wound at least once a day.

29. The use of the pharmaceutical formulation according to claim 22 for the manufacture of a medicament for the therapeutic treatment of wound of a mammal comprising the formulation to be applied to the wound at least once a day.

30. The use according to claim 27, wherein the wound is a wound selected from the group consisting of a diabetic foot ulcer, a venous ulcer, an arterial ulcer, a pressure ulcers, a mechanical wound characterized by a superinfection with a biofilm-forming bacteria, a post-surgical wound characterized by a superinfection with a biofilm-forming bacteria, and a combination thereof.

31. The use according to claims 28 and 29, wherein the wound is a wound selected from the group consisting of a diabetic foot ulcer, a venous ulcer, an arterial ulcer, a pressure ulcer, a mechanical wound characterized by a superinfection with a biofilm-forming bacteria, or a post-surgical wound characterized by a superinfection with a biofilm-forming bacteria, and a combination thereof.

32. A device comprising the pharmaceutical formulation kit according to claim 21, comprising:

a first container comprising a first composition; and

a second container comprising a second composition,

wherein the first container and the second container are separated by a collapsible membrane capable of keeping the first composition and the second composition isolated.

33. A device comprising the pharmaceutical formulation kit according to claim 22, comprising:

a first container comprising a first composition;

a second container comprising a second composition; and

a third container comprising a third composition,

wherein:

the first container and the second container are separated by a first collapsible membrane capable of keeping the first composition and the second composition isolated; and

the second container and the third container are separated by a second collapsible membrane capable of keeping the second composition and the third composition isolated.

34. A process for producing the pharmaceutical composition according to claim 1 comprising:

a. mixing in a solution a nitrogenous heterocyclic compound of 5 or 6 atoms with imide group, a deoxyribonuclease enzyme, and carboxylic acid, thereby forming a mixture;

b. adding an alkaline solution dropwise to the mixture until the pH of the mixture is between 4.50 and 6.50, thereby forming a pH-adjusted mixture; and

c. sterilizing the pH-adjusted mixture.

35. The process according to claim 34 further comprising the steps:

d. adding a gelling agent.

36. The process according to claim 34 further comprising the steps:

e. adding a complex forming acid, tensioactive agent and hydrophilic reducing acid.