

Claims:

1. Method of enhancing the antimicrobial action of an antibiotic, comprising
 - systemically administering a photosensitive antibiotic to a subject having a
 - 5 microbial infection in a target tissue to provide a blood plasma concentration of said antibiotic in said subject; and
 - subjecting the target tissue to photodynamic therapy in order to enhance the antimicrobial action of the antibiotic in the target tissue.
- 10 2. The method according to claim 1, wherein the microbial infection is caused by virus, bacteria or fungus.
3. The method according to claim 1 or 2, wherein the microbial infection to be treated is caused by gram-positive bacteria, such as bacteria of the streptococci or staphylococci
- 15 species, such as *Streptococcus mutans* or *Staphylococcus aureus*, or *Corynebacterium*, *Clostridium*, *Mycobacterium*, *Nocardia*, *Listeria*, *Bacillus*, or gram-negative bacteria, in particular selected from the group of *Proteobacteria*, *Aquificae*, *Chlamydiae*, *Bacteroidetes*, *Chlorobi*, *Cyanobacteria*, *Fibrobacteres*, *Verrucomicrobia*, *Planctomycetes*, *Spirochetes*, *Acidobacteria*, *Actinobacteria*, *Firmicutes*, *Thermotogae*,
- 20 *Porphyromonas* and *Chloroflexi*.
4. The method according to claim 1 or 2, wherein the antibiotic action is enhanced to provide for antiviral action and the microbial infection to be treated is caused by virus selected from the group of Adenoviruses, Herpesviruses, Poxviruses, Parvoviruses,
- 25 Reoviruses, Picornaviruses, Togaviruses, Orthomyxoviruses, Rhabdoviruses, Retroviruses, Papillomavirus and Hepadnaviruses
5. The method according to any of the preceding claims, comprising administering an antibiotic selected from the group of macrolides, including levofloxacin, ofloxacin,
- 30 ciprofloxacin, clarithromycin, erythromycin, roxithromycin, or azithromycin; tetracyclines including doxycycline, ionocycline, tetracycline, chlortetracycline, demeclocycline, lymecycline, meclocycline, methacycline, rolitetracycline, tigecycline, eravacycline, sarecycline, omacycline, sarecycline, eravacycline, omadacycline, oxytetracycline; other antibiotics such as colchicine, trimethoprim or metronidazole; and in particular

azithromycin, doxycycline, minocycline or colchicine or metronidazole, or any of their combinations.

5 6. The method according to any of the preceding claims, comprising administering the antibiotic orally or parenterally.

7. The method according to any of the preceding claims, comprising raising the tissue concentration of the antibiotic by oral mucosal delivery.

10 8. The method according to any of the preceding claims, comprising raising the antibiotic concentration in the Gingival Precrevicular Fluid.

9. The method according to any of the preceding claims, comprising allowing the plasma concentration of the antibiotic increase to a predetermined level, in particular to at least 10
15 %, in particular 20 to 100 %, of the administered antibiotics' maximum plasma concentration before subjecting the target tissue to photodynamic therapy.

10. The method according to any of the preceding claims, wherein the target tissue comprises soft tissues, biofilms, saliva, skin, plaque and teeth surfaces and mucous
20 membranes.

11. The method according to any of the preceding claims, wherein the target tissue comprises oral tissue, such as tissue in the oral cavity, including gum and oral mucosa as well as underlying tissue.
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12. The method according to any of the preceding claims, wherein the microbial infection of the target tissue comprises a gumline bacterial biofilm.

13. The method according to any of claims 1 to 9, wherein the target tissue comprises
30 tissue in the throat, in the nose or in the ears.

14. The method according to claim 13, wherein the microbial infection of the target tissue comprises pharyngitis or otitis.

15. The method according to any of the preceding claims, wherein the target tissue is topically subjected to photodynamic therapy.

16. The method according to any of the preceding claims, wherein the antibiotic is
5 photoactivated in order to eliminate pathogens inside tissue and host cells.

17. The method according to any of the preceding claims, wherein the photodynamic therapy comprises subjecting the target tissue to electromagnetic radiation in the form of light of either or two of the following energy levels: a first light with photons having a
10 majority energy in the range from 3.5 eV to 2.8 eV, and a second light with photons having a majority energy in the range from 1.24 eV to 2.48 eV, wherein photons of the first light and the second light are simultaneously directed against the target tissue.

18. The method according to any of the preceding claims, wherein
15 – non-coherent radiant light energy is generated at one first energy level, or preferably at least two different energy levels, a first and a second energy level;
– from the non-coherent radiant light energy there is provided first light having a wavelength corresponding to the majority energy of the first energy level, and optionally a second light having a wavelength corresponding to the majority energy
20 of the second energy level; and
– the first and optionally the second light are then simultaneously directed against the target tissue, in particular against the surface of the target tissue.

19. The method according to any of the preceding claims, wherein the photodynamic
25 therapy comprises subjecting the target tissue to a light having a wavelength in the range of about 350 to 450 nm, for example about 370 to 410 nm, to light having a wavelength in the range of about 500 to 1000 nm, for example about 780 to 830 nm, or to a combination thereof, said light preferably comprising non-coherent light, for example produced by optoelectronic devices, such as light emitting diodes (LEDs).

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20. The method according to any of the preceding claims, wherein the photodynamic therapy comprises subjecting the target tissue to a first light having a wavelength of 405 nm $\pm$ 10 nm and second light having a wavelength of 810 nm $\pm$ 15 nm is used, both the first

and the second lights comprising non-coherent light, for example produced by optoelectronic devices, such as light emitting diodes (LEDs).

21. The method according to any of the preceding claims, wherein the target tissue is
5 subjected to endogenous and exogenous excitement, in particular so as to generate reactive oxygen singlets or reactive oxygen species or both.

22. The method according to any of the preceding claims, wherein the light is combined
10 with at least one photosensitive substance for treating the target tissue using photodynamic therapy.

23. The method according to claim 22, wherein the photosensitive substance is selected from the group of Hypericin, curcumin, phenalenone derivatives, Cercosporin, psoralen, xanthotoxin, Angelicin, alpha-Terthienyl, Phenylthepatriyne, THC, Cannabidiol (CBD).
15 Synthetic photosensitizers include the following: RB (Rose Bengal), MB, Porphyrin derivatives, Curcumin derivatives, Methylene Blue, Indocyanine Green, Erythrosine, Phenalenone derivatives, Fullerene derivatives, Xanthene derivatives and combinations thereof.

20 24. The method according to any of claims 17 to 23, wherein the high energy photons and low energy photons are applied in conjugation with at least one exogeneous photosensitizer, which can be activated with the low energy photons.

25 25. The method according to any of claims 17 to 24, wherein a photosensitizer is provided for use in topical treatment of mammalian tissues, wherein said sensitizer is applied to a superficial part of the tissue, such as on mammalian skin or on a mucous membrane and the part thus treated is subsequently or simultaneously subjected to light at two different wavelengths.

30 26. The method according to any of the preceding claims, wherein a photosensitizer is contacted with micro-organisms, such as bacteria, virus and fungus, in the target tissue, such as in biofilm, saliva, skin, plaque and on teeth surfaces or mucous membranes, by applying it on the target in the form of an aqueous solution, an alcohol containing solution,

a hydrophilic gel, a hydrophobic gel, a hydrophilic polymer, a hydrophobic polymer or a paste, lotion, tape, tablet, plaster or band-aid.

27. The method according to any of the preceding claims, wherein the area of the target
5 tissue subjected to photodynamic therapy is less than 100 cm^2 , such as less than 50 cm^2 , in particular less than 40 cm^2 , for example 1 to 30 cm^2 .

28. The method according to any of the preceding claims, comprising topically
administering to the target tissue an antibiotic.

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29. A kit for treating local microbial infections, comprising an optoelectronic device
capable of simultaneously emitting a first light consisting of high energy and a second light
consisting of low energy photons, said first and said second light amounting to at least 50
% of all light emitted from the optoelectronic component or device, and at least one
15 systemically administered antibiotic.

30. The kit according to claim 29, comprising an optoelectronic device capable of emitting
high energy photons with majority energy between 2.8 eV and 3.5 eV and low energy
photons with majority energy between 1.24 eV and 1.65 eV.

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31. The kit according to claim 29 or 30 comprising an optoelectronic device having a light
emitting component that has two or more light emitting surfaces (EPIs), together with a
photosensitizer or a plurality of photosensitizers.

25 32. The kit according to any of claims 29 to 31, wherein the systemically administered
antibiotic is capable of achieving antimicrobial action in a target tissue of a subject.

33. The kit according to any of claims 29 to 32, wherein the antibiotic is selected from the
group of macrolides, including levofloxacin, ofloxacin, ciprofloxacin, clarithromycin,
30 erythromycin, roxithromycin, or azithromycin; tetracyclines including doxycycline,
ionocycline, tetracycline, chlortetracycline, demeclocycline, lymecycline, meclocycline,
methacycline, rolitetracycline, tigecycline, eravacycline, sarecycline, omacycline,
sarecycline, eravacycline, omadacycline, oxytetracycline; other antibiotics such as

colchicine, trimethoprim or metronidazole; and in particular azithromycin, doxycycline, minocycline or colchicine or metronidazole, or any of their combinations.

34. The kit according to any of claims 29 to 33, comprising a pharmaceutically acceptable
5 composition of the antibiotic suitable for administration orally, parenterally or transdermally.

35. The kit according to any of claims 29 to 34, comprising a photosensitizer.

10 36. The kit according to any of claims 29 to 35, comprising a photosensitizer that can be activated by at least either of the high energy and low energy photons, preferably both.

37. The kit according to any of claims 29 to 36, comprising a photosensitizer selected from the group of Hypericin, curcumin, phenalenone derivatives, Cercosporin, psoralen,
15 xanthotoxin, Angelicin, alpha-Terthienyl, Phenylthepatriyne, THC, Cannabidiol (CBD). Synthetic photosensitizers include the following: RB (Rose Bengal), MB, Porphyrin derivatives, Curcumin derivatives, Methylene Blue, Indocyanine Green, Erythosine, Phenalenone derivatives, Fullerene derivatives, and Xanthene derivatives and combinations thereof.

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38. The kit according to any of claims 29 to 37, comprising a photosensitizer capable of being topically applied to a target tissue of a subject.

39. Systemically administered antibiotic for use in antimicrobial photodynamic therapy of
25 local microbial infections.

40. The systemically administered antibiotic for use in antimicrobial photodynamic therapy according to claim 39, wherein the photodynamic therapy is carried out for treatment of oral diseases, such as periodontal diseases.

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41. The systemically administered antibiotic for use in antimicrobial photodynamic therapy according to claim 39 or 40, wherein the photodynamic therapy is carried out for treatment bacterial biofilm, such as gumline bacterial biofilm.

42. The systemically administered antibiotic for use in antimicrobial photodynamic therapy according to any of claims 39 to 41, wherein the systemic antibiotic is selected from the group of photosensitive antibiotics of the group of azithromycin, tetracycline, macrolide, and combinations thereof.
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43. The systemically administered antibiotic for use in antimicrobial photodynamic therapy according to any of claims 39 to 42, wherein a cyclic photoactive antibiotic is used to inhibit collagenase 2 enzyme.
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44. The systemically administered antibiotic for use in antimicrobial photodynamic therapy according to claim 43, wherein the cyclic photoactive antibiotic is doxycycline or minocycline.
45. Method of enhancing the enzyme inhibition action of a pharmaceutical substance
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- having a antimicrobial activity, comprising
- systemically administering a photosensitive pharmaceutical substance to a subject having a microbial infection in a target tissue to provide a plasma concentration of said substance in said subject;
 - optionally allowing the plasma concentration of the antibiotic increase to a
 - 20 predetermined level; and
 - subjecting the target tissue to photodynamic therapy in order to increase the enzyme inhibition action of the substance in the target tissue.
46. The method according to claim 45, comprising the use of cyclic photoactive antibiotics
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- for inhibition of collagenase enzyme activity.
47. The method according to claim 45 or 46, wherein the cyclic photoactive antibiotic is used to inhibit MMP-8, MMP-9, MMP-13 or MMP-1 action or their gene expression or any of their combinations.
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48. The method according to claim 46 or 47, wherein the cyclic photoactive antibiotic is doxycycline or minocycline.

49. Method of enhancing the enzyme inhibition action of a cyclic photoactive antibiotic for inhibition of collagenase enzyme activity, comprising

- systemically administering a photosensitive pharmaceutical substance to a subject having a microbial infection in a target tissue to provide a plasma concentration of said antibiotic in said subject;
- optionally allowing the plasma concentration of the substance increase to a predetermined level; and
- subjecting the target tissue to photodynamic therapy in order to increase the enzyme inhibition action of the substance in the target tissue.