In one aspect, the present disclosure provides a use of a photosensitive antibiotic in the manufacture of a medicament for use in combinatorial therapy for treating microbial infection, wherein said medicament is to be administered in combination with photodynamic therapy, comprising that

- said photosensitive antibiotic is to be systemically administered to a subject having a microbial infection in a target tissue to provide a blood plasma concentration of said antibiotic in said subject; and
- the target tissue is to be subjected to photodynamic therapy in order to enhance the antimicrobial action of the antibiotic in the target tissue,

wherein the antibiotic is selected from the group of macrolides, including levofloxacin, ofloxacin, 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 metronidatzole; and in particular azithromycin, doxycycline, minocycline or colchicine or metronidatzole, or any of their combinations.

In another aspect, the present disclosure provides 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 systemically administered antibiotic, wherein the antibiotic is selected from the group of macrolides, including levofloxacin, ofloxacin, 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 metronidatzole; and in particular azithromycin, doxycycline, minocycline or colchicine or metronidatzole, or any of their combinations.

In yet another aspect, the present disclosure provides a use of a systemically administered antibiotic in the manufacture of a medicament for use in combinatorial therapy for treating

local microbial infections, wherein said medicament is to be administered in combination with antimicrobial photodynamic therapy, wherein the antibiotic is selected from the group of macrolides, including levofloxacin, ofloxacin, 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 metronidatzole; and in particular azithromycin, doxycycline, minocycline or colchicine or metronidatzole, or any of their combinations.

Claims:

1. Use of a photosensitive antibiotic in the manufacture of a medicament for use in combinatorial therapy for treating microbial infection, wherein said medicament is to be administered in combination with photodynamic therapy, comprising that

- said photosensitive antibiotic is to be systemically administered to a subject having a microbial infection in a target tissue to provide a blood plasma concentration of said antibiotic in said subject; and
- the target tissue is to be subjected to photodynamic therapy in order to enhance the antimicrobial action of the antibiotic in the target tissue,

wherein the antibiotic is selected from the group of macrolides, including levofloxacin, ofloxacin, 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 metronidatzole; and in particular azithromycin, doxycycline, minocycline or colchicine or metronidatzole, or any of their combinations.

2. The use according to claim 1, wherein the microbial infection is caused by virus, bacteria or fungus.

3. The use 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 species, such as *Streptococcus mutans* or *Staphylococcus aureaus*, 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, Porphyromonas* and *Chloroflexi*.

4. The use 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, Reoviruses, Picornaviruses, Togaviruses, Orthomyxoviruses, Rhabdoviruses, Retroviruses, Papillomavirus and Hepadnaviruses

5. The use according to any of the preceding claims, comprising that the antibiotic is to be administered orally or parenterally.

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

7. The use according to any of the preceding claims, comprising raising the antibiotic concentration in the Gingival Precrevicular Fluid.

8. The use 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 %, in particular 20 to 100 %, of the administered antibiotics' maximum plasma concentration before the target tissue is to be subjected to photodynamic therapy.

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

10. The use 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.

11. The use according to any of the preceding claims, wherein the microbial infection of the target tissue comprises a gumline bacterial biofilm.

12. The use according to any of claims 1 to 8, wherein the target tissue comprises tissue in the throat, in the nose or in the ears.

13. The use according to claim 12, wherein the microbial infection of the target tissue comprises pharyngitis or otitis.

14. The use according to any of the preceding claims, wherein the target tissue is to be topically subjected to photodynamic therapy.

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

16. The use according to any of the preceding claims, wherein the photodynamic therapy comprises that the target tissue is to be subjected to electromagnetic radiation in the form of light of either or two of the following energy levels: a first light with high energy photons having a majority energy in the range from 3.5 eV to 2.8 eV, and a second light with low energy 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.

17. The use according to any of the preceding claims, wherein

- 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 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.

18. The use according to any of the preceding claims, wherein the photodynamic therapy comprises that the target tissue is to be subjected to a light having a wavelength in the range of 350 to 450 nm, for example 370 to 410 nm, to light having a wavelength in the range of 500 to 1000 nm, for example 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).

19. The use according to any of the preceding claims, wherein the photodynamic therapy comprises that the target tissue is to be subjected to a first light having a wavelength of 405 nm ±10 nm and second light having a wavelength of 810 nm ±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).

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

21. The use according to any of claims 16 to 20, wherein the light is combined with at least one photosensitive substance for treating the target tissue using photodynamic therapy.

22. The use according to claim 21, wherein the photosensitive substance is selected from the group of Hypericin, curcumin, phenalenone derivatives, Cercosporin, psoralen, xanthotoxin, Angelicin, alpha-Terthienyl, Phenylthepatriyne, Cannabidiol (CBD). Synthetic photosensitizers include the following: RB (Rose Bengal), Porphyrin derivatives, Curcumin derivatives, Methylene Blue, Indocyanine Green, Erythosine, Phenalenone derivatives, Fullerene derivatives, Xanthene derivates and combinations thereof.

23. The use according to claim 16, 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.

24. The use according to claim 23, wherein the photosensitizer is provided for topical treatment of mammalian tissues, wherein said sensitizer is to be applied to a superficial part of the tissue, such as on mammalian skin or on a mucous membrane and the part thus

treated is to be subsequently or simultaneously subjected to light at two different wavelengths.

25. The use according to claim 23, wherein the photosensitizer is to be 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.

26. The use according to any of the preceding claims, wherein the area of the target 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.

27. The use according to any of the preceding claims, comprising that an antibiotic is to be topically administered to the target tissue.

28. 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 systemically administered antibiotic,
wherein the antibiotic is selected from the group of macrolides, including levofloxacin, ofloxacin, 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 metronidatzole; and in particular azithromycin, doxycycline, minocycline or colchicine or metronidatzole, or any of their combinations.

29. Use of a systemically administered antibiotic in the manufacture of a medicament for use in combinatorial therapy for treating local microbial infections, wherein said medicament is to be administered in combination with antimicrobial photodynamic therapy, wherein the antibiotic is selected from the group of macrolides, including levofloxacin, ofloxacin, 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 metronidatzole; and in particular azithromycin, doxycycline, minocycline or colchicine or metronidatzole, or any of their combinations.

30. The use according to claim 29, wherein the photodynamic therapy is to be carried out for treatment of oral diseases, such as periodontal diseases.

31. The use according to claim 29 or 30, wherein the photodynamic therapy is to be carried out for treatment of bacterial biofilm, such as gumline bacterial biofilm.

32. The use according to any of claims 29 to 31, wherein the systemic antibiotic is selected from the group of photosensitive antibiotics of the group of azithromycin, tetracycline, macrolide, and combinations thereof.

33. The use according to any of claims 29 to 32, comprising that a cyclic photoactive antibiotic is to be used to inhibit collagenase 2 enzyme.

34. The use according to claim 33, wherein the cyclic photoactive antibiotic is doxycycline or minocycline.