surgical site.

SUMMARY

The present disclosure provides methods for preventing, inhibiting or treating a surgical site infection associated with a surgical operation comprising the step of applying to the surgical site a biocompatible, biodegradable substrate being impregnated and/or having its surface coated fully or partially with a matrix composition which provides local controlled and prolonged release of at least one pharmaceutically active agent at the surgical site. Specifically, the matrix composition comprises (a) a biocompatible polymer, (b) a first lipid component comprising a sterol, (c) a second lipid component comprising at least one phospholipid having fatty acid moieties of at least 12 carbons; and (d) a pharmaceutically active agent selected from the group consisting of an antibiotic agent, antiseptic agent, an anti-inflammatory agent, anti-fungal agent and any combination thereof. In one aspect, the present disclosure provides a use of a biodegradable mineral substrate in the manufacture of a medicament for the treatment or prophylaxis of a soft tissue incision site infection associated with a surgical operation, wherein the biodegradable mineral substrate shaped in the form of particles is to be administered directly to the soft-tissue incision site, wherein the mineral substrate is impregnated or has its surface coated fully or partially with a matrix composition, wherein the matrix composition comprises: (a) a biodegradable polyester, (b) a first lipid component comprising at least one sterol, wherein the at least one sterol is non-covalently associated with the biodegradable polyester; (c) a second lipid component comprising at least one phospholipid having fatty acid moieties of at least 12 carbons; and (d) an antibiotic agent selected from the group consisting of: doxycycline and doxycycline hyclate.

The substrate being impregnated and/or having its surface coated fully or partially with a matrix composition described herein is intended for local administration to soft tissues and solid organs during surgical procedures and provides localized infection prevention and treatment by reducing the overall infection rate post-surgery and by reducing or eradicating soft tissue infections that may exist prior to surgery. According to some examples, the drug coated substrate described herein prevents or inhibits the formation of biofilm that may form at the surgical site and its vicinity, thereby preventing or inhibiting surgical site infections. Inhibition of biofilm formation at the surgical site refers

to inhibition of biofilm formation on surfaces such as biological tissues and/or materials or devices that may be used during surgery (e.g. wound tissue, necrotic cells, biomaterials and surgical implants (e.g. sutures and hard ware-stainless steel wires)). According to some examples, the drug coated substrate disclosed herein is capable of eradicating an existing biofilm.

Following its application to the surgical site, the substrate being impregnated and/or having its surface coated fully or partially with a matrix composition described herein provides local controlled release of the drug at the surgical site and its surrounding over a predetermined, prolonged period of time, preferably between several days to

CLAIMS:

1. Use of a biodegradable mineral substrate in the manufacture of a medicament for the treatment or prophylaxis of a soft tissue incision site infection associated with a surgical operation, wherein the biodegradable mineral substrate shaped in the form of particles is to be administered directly to the soft-tissue incision site, wherein the mineral substrate is impregnated or has its surface coated fully or partially with a matrix composition, wherein the matrix composition comprises: (a) a biodegradable polyester, (b) a first lipid component comprising at least one sterol, wherein the at least one sterol is non-covalently associated with the biodegradable polyester; (c) a second lipid component comprising at least one phospholipid having fatty acid moieties of at least 12 carbons; and (d) an antibiotic agent selected from the group consisting of: doxycycline and doxycycline hyclate.

2. The use according to claim 1, wherein the soft tissue incision is associated with a surgical operation selected from the group consisting of orthopedic surgical operations, spine surgical operations, operations on a digestive system organ, gastric ulcer procedures, gastric cancer procedures, open gastric bypass, appendectomy, colectomy, cholecystectomy, vagotomy, open biliary tract procedures, small intestine procedures, colorectal procedures, cardiac procedures, hernia repair, vascular procedures, caesarian, prostatectomy, obstetric and gynecologic surgical operations, head and neck cancer surgery, transplantation surgeries, neurosurgery and plastic surgeries.

3. The use according to claim 2, wherein the surgical operation is a surgical operation on a digestive system organ.

4. The use of claim 3, wherein the digestive organ is selected from the group consisting of: esophagus, stomach, small intestine, large intestine, rectum, colon, appendix, liver, pancreas, gallbladder, and any combination thereof.

5. The use of claim 2, wherein the surgical operation on a digestive system organ includes a procedure selected from the group consisting of open gastric bypass, appendectomy, colectomy, cholecystectomy, vagotomy, open biliary tract procedures, small intestine procedures, colorectal procedures, and any combination thereof.

6. The use according to claim 2, wherein the soft tissue incision is associated with cardiac surgery procedures.

7. The use according to claim 1, wherein the mineral substrate is selected from the group consisting of hydroxyapatite, fluorapatite, oxyapatite, wollastonite, apatite/wollastonite glass ceramics, anorthite, calcium fluoride, calcium sulfate, calcium carbonate, tetracalcium phosphate, α-tricalcium phosphate (α-TCP), β-tricalcium phosphate (β-TCP), amorphous calcium phosphate, dicalcium phosphate, agrellite, devitrite, canasite, phlogopite, monetite, brushite, octocalcium

phosphate, whitlockite, cordierite, berlinite, combeite, phosphoric acid crystals, disodium hydrogen phosphate, and any combination thereof.

8. The use according to claim 7, wherein the mineral substrate is β-TCP.

9. The use according to claim 1, wherein the mineral substrate comprises particles having an average particle size of less than about 200 microns (μm).

10. The use according to claim 9, wherein the average particle size is from 50 to 150 μm.

11. The use according to claim 1, wherein a majority of the particles are spherical, spheroidal, or any combination thereof.

12. The use according to claim 1, wherein the matrix composition comprises a phospholipid selected from a phosphatidylcholine or a combination of phosphatidylcholines having fatty acid moieties having at least 14 carbons.

13. The use according to claim 12, wherein the phospholipid is a phosphatidylcholine or a combination of phosphatidylcholines having fatty acid moieties having 14 — 18 carbons.

14. The use according to claim 1, wherein the biodegradable polyester is selected from the group consisting of PLA (polylactic acid), PGA (poly glycolic acid) and PLGA (Poly (lactic co glycolic acid).

15. The use according to claim 1, wherein the matrix composition further comprises a pharmaceutically active agent selected from the group consisting of: an antibiotic agent, an antiseptic agent, an anti-inflammatory agent, anti-fungal agent and any combination thereof.

16. The use according to claim 1, wherein the at least one sterol in the matrix composition comprises a cholesterol.

17. The use according to claim 1, wherein when the coated or impregnated mineral substrate is maintained in an aqueous environment, the matrix composition provides sustained release of said antibiotic agent, wherein at least 30% of the antibiotic agent is released from the composition at zero-order kinetics.

18. The use according to claim 1, wherein the matrix composition comprises:
(a) 10-30% w/w of a biodegradable polyester by weight of the matrix composition;
(b) 5-30% w/w of a first lipid component by weight of the matrix composition;
(c) 40-75% w/w of a second lipid component by weight of the matrix composition; and
(d) 1-20% w/w of doxycycline or doxycycline hyclate, by weight of the matrix composition.

19. The use according to claim 1, wherein the coated biodegradable mineral substrate comprises between about 60-90% (w/w) of biodegradable mineral substrate and 10-40% (w/w) of the matrix composition.

20. The use of claim 1, wherein the infection is caused by hospital acquired resistant bacteria.

21. The use of claim 20, wherein the hospital acquired resistant bacteria include Methicillin-resistant S. aureus (MRSA).

22. The use according to claim 1, wherein the coated mineral substrate is formulated as a paste prior to application of the coated mineral substrate to the soft-tissue incision site.