

SUMMARY

[0012] Examples described herein provide unique and effective microbial growth inhibiting solutions (e.g., locking solutions) that include effective amounts of a carboxylate antimicrobial agent, such as a C₄-C₉ carboxylate antimicrobial agent or antifungal agent, and a chelating agent. In one aspect, the present invention refers to a microbial growth inhibiting solution comprising a C₄-C₉ carboxylate antimicrobial agent, a chelating agent and a buffer, wherein the C₄-C₉ carboxylate antimicrobial agent comprises sodium caprylate and is present in an amount ranging from 0.05 mg/mL to 5 mg/mL, the chelating agent comprises disodium ethylenediaminetetraacetic acid and is present in an amount ranging from 0.01 mg/mL to 2 mg/mL, and the buffer comprises citrate ~~In a first aspect one example, the present invention refers to a disclosure describes to~~ a microbial growth inhibiting solution comprising a C₄-C₉ carboxylate antimicrobial agent, a chelating agent and a buffer, wherein the C₄-C₉ carboxylate antimicrobial agent comprises sodium caprylate, the chelating agent comprises disodium ethylenediaminetetraacetic acid and is present in an amount ranging from about 0.01 mg/mL to about 2 mg/mL, and the buffer comprises citrate. In one example, the chelating agent is EDTA and the C₄-C₉ carboxylate antimicrobial agent is n-octanoic acid. In other embodiments, the microbial growth inhibiting solutions comprise a C₄-C₉ carboxylate antimicrobial agent and a chelating agent other than EDTA. A preferred combination includes a C₄-C₉ carboxylate antimicrobial agent and a calcium chelating agent, such as EGTA. Chelating agents that may be used in conjunction with the present invention include, but are not limited to, EDTA, EGTA, DTPA, dimercaptosuccinic acid ("DMSA"), deferoxamine, dimercaprol, triethylene tetramine dihydrochloride, zinc citrate, combination of bismuth and citrate, penicillamine, etidronate and pharmaceutically acceptable salts thereof. Preferred chelating agents include those that chelate divalent metal cations such as Ca, Mg, Mn, Fe and Zn.

[0013] It has been surprisingly found that a C₄-C₉ carboxylate antimicrobial agent in combination with a chelating agent present in an amount of about 2 mg/mL, 1 mg/mL or lower can effectively inhibit microbial or fungal growth in a catheter. In any of the examples described herein, the microbial growth inhibiting solutions can include a combination of a chelating agent and a C₄-C₉ carboxylate antimicrobial agent, wherein the concentration of the chelating agent is present in an amount ranging from about 0.01 to about 2 mg/mL in the solution and the concentration of the antimicrobial agent is present in an amount ranging from about 0.05 mg/ml to about 5 mg/ml in the solution. In a preferred example, the combination includes about 0.5 mg/ml of the chelating agent and about 1.15 mg/ml of the C₄-C₉ carboxylate antimicrobial agent.

[0014] Where n-octanoic acid is the antimicrobial agent of choice, it can be reconstituted to an appropriate concentration from a vial of n-octanoic acid and then

CLAIMS

The invention is claimed as follows:

1. A microbial growth inhibiting solution comprising a C₄-C₉ carboxylate antimicrobial agent, a chelating agent and a buffer, wherein the C₄-C₉ carboxylate antimicrobial agent comprises sodium caprylate and is present in an amount ranging from 0.05 mg/mL to 5 mg/mL, the chelating agent comprises disodium ethylenediaminetetraacetic acid and is present in an amount ranging from 0.01 mg/mL to 2 mg/mL, and the buffer comprises citrate.

~~2. The microbial growth inhibiting solution of claim 1, wherein the C₄-C₉ carboxylate antimicrobial agent is present in an amount ranging from 0.05 mg/mL to 5 mg/mL.~~

~~3.2.~~ The microbial growth inhibiting solution of claim 1, wherein the chelating agent is present in an amount ranging from 0.1 mg/mL to 1 mg/mL.

~~4.3.~~ The microbial growth inhibiting solution of claim 1, wherein the chelating agent is present in an amount ranging from 0.25 mg/mL to 0.5 mg/mL.

~~5.4.~~ The microbial growth inhibiting solution of claim 1 further comprising a pharmacologically acceptable carrier solution.

~~6.5.~~ The microbial growth inhibiting solution of claim ~~54~~, wherein the pharmacologically acceptable carrier solution comprises saline, Ringer's solution, or water pH adjusted to 5.2 or less.

~~7.6.~~ The microbial growth inhibiting solution of claim 1 wherein the buffer is present in an amount ranging from 1.5 to 24 mM, wherein the C₄-C₉ carboxylate antimicrobial agent is present in an amount ranging from 0.071 mg/mL to 1.15 mg/mL, and the chelating agent is present in an amount ranging from 0.0625 mg/mL to 1 mg/mL.

~~8.7.~~ The use of a C₄-C₉ carboxylate antimicrobial agent and a chelating agent for the preparation of a microbial growth inhibiting solution for the disinfection of a lumen of an implanted catheter from bacteria and fungi, wherein the microbial growth inhibiting solution comprises a C₄-C₉ carboxylate antimicrobial agent, a chelating agent and a buffer, wherein the C₄-C₉ carboxylate antimicrobial agent comprises sodium caprylate and is present in an amount ranging from 0.05 mg/mL to 5 mg/mL, the chelating agent comprises disodium

ethylenediaminetetraacetic acid and is present in an amount ranging from 0.01 mg/mL to 2 mg/mL, and the buffer comprises citrate.

~~9-8.~~ The use of claim ~~87~~, wherein at least a portion of the catheter is sufficiently porous to permit diffusion of the solution outwardly from the lumen to the outer surface of the catheter and into tissues or the bloodstream surrounding the catheter to inhibit infection.

~~10-9.~~ The use of claim ~~87~~, wherein the chelating agent is present in an amount ranging from 0.1 mg/mL to 1 mg/mL.

~~11-10.~~ The use of claim ~~87~~, wherein the chelating agent is present in an amount ranging from 0.25 mg/mL to 0.5 mg/mL.

~~12-11.~~ The use of claim ~~87~~, wherein the buffer is present in an amount ranging from 1.5 to 24 mM, wherein the C₄-C₉ carboxylate antimicrobial agent is present in an amount ranging from 0.071 mg/mL to 1.15 mg/mL, and the chelating agent is present in an amount ranging from 0.0625 mg/mL to 1 mg/mL.

~~13-12.~~ A method for coating a medical device, the method comprising:
exposing the medical device to a microbial growth inhibiting solution for a sufficient amount of time to provide a coating on the exposed surface of the device, wherein the microbial growth inhibiting solution comprises a C₄-C₉ carboxylate antimicrobial agent, a chelating agent and a buffer, wherein the C₄-C₉ carboxylate antimicrobial agent comprises sodium caprylate and is present in an amount ranging from 0.05 mg/mL to 5 mg/mL, the chelating agent comprises disodium ethylenediaminetetraacetic acid and is present in an amount ranging from 0.01 mg/mL to 2 mg/mL, and the buffer comprises citrate.

~~14-13.~~ The method of claim ~~13-12~~ further comprising treating the device with a surfactant before exposing the device to the microbial growth inhibiting solution.

~~15-14.~~ The method of claim ~~14-13~~, wherein the surfactant is selected from the group of surfactant consisting of tridodecylmethyl ammonium chloride, benzalkonium chloride and combinations thereof.

~~16-15.~~ The method of claim ~~13-12~~, wherein the chelating agent is present in an amount ranging from 0.1 mg/mL to 1 mg/mL.

~~17-16.~~ The method of claim ~~13~~12, wherein the chelating agent is present in an amount ranging from 0.25 mg/mL to 0.5 mg/mL.

~~18-17.~~ The method of claim ~~13~~12, wherein the buffer is present in an amount ranging from 1.5 to 24 mM, wherein the C₄-C₉ carboxylate antimicrobial agent is present in an amount ranging from 0.071 mg/mL to 1.15 mg/mL, and the chelating agent is present in an amount ranging from 0.0625 mg/mL to 1 mg/mL.

~~19-18.~~ A medical device coated with a microbial growth inhibiting solution comprising a C₄-C₉ carboxylate antimicrobial agent, a chelating agent and a buffer, wherein the C₄-C₉ carboxylate antimicrobial agent comprises sodium caprylate and is present in an amount ranging from 0.05 mg/mL to 5 mg/mL, the chelating agent comprises disodium ethylenediaminetetraacetic acid and is present in an amount ranging from 0.01 mg/mL to 2 mg/mL, and the buffer comprises citrate.

~~20-19.~~ The medical device of claim ~~19~~18, wherein the medical device is selected from the group of devices consisting of a central venous catheter, a peripheral intravenous catheter, an arterial catheter, a Swant-Ganz catheter, a hemodialysis catheter, an umbilical catheter, a percutaneous nontunneled silicone catheter, a cuffed tunneled central venous catheter and a subcutaneous central venous pert.

~~21-20.~~ The medical device of claim ~~19~~18, wherein the chelating agent is present in an amount ranging from 0.1 mg/mL to 1 mg/mL.

~~22-21.~~ The medical device of claim ~~19~~18, wherein the chelating agent is present in an amount ranging from 0.25 mg/mL to 0.5 mg/mL.

~~23-22.~~ The medical device of claim ~~19~~18, wherein the buffer is present in an amount ranging from 1.5 to 24 mM, wherein the C₄-C₉ carboxylate antimicrobial agent is present in an amount ranging from 0.071 mg/mL to 1.15 mg/mL, and the chelating agent is present in an amount ranging from 0.0625 mg/mL to 1 mg/mL.

~~24-23.~~ The use of a C₄-C₉ carboxylate antimicrobial agent, a chelating agent and a buffer for the preparation of a microbial growth inhibiting solution for the locking and/or flushing a lumen of an implanted catheter from bacteria and fungi, wherein the lumen of the implanted catheter open to a body lumen, and wherein the C₄-C₉ carboxylate antimicrobial agent comprises sodium caprylate and is present in an amount ranging from 0.05 mg/mL to 5

mg/mL, the chelating agent comprises disodium ethylenediaminetetraacetic acid and is present in an amount ranging from 0.01 mg/mL to 2 mg/mL, and the buffer comprises citrate.

~~25-24.~~ The use of claim ~~2423~~, wherein the chelating agent is present in an amount ranging from 0.1 mg/mL to 1 mg/mL.

~~26-25.~~ The use of claim ~~2423~~, wherein the chelating agent is present in an amount ranging from 0.25 mg/mL to 0.5 mg/mL.

~~27-26.~~ The use of claim ~~2423~~, wherein the buffer is present in an amount ranging from 1.5 to 24 mM, wherein the C₄-C₉ carboxylate antimicrobial agent is present in an amount ranging from 0.071 mg/mL to 1.15 mg/mL, and the chelating agent is present in an amount ranging from 0.0625 mg/mL to 1 mg/mL.

~~28-27.~~ A kit for locking and/or flushing an implanted catheter, the kit comprising:
a container holding a volume of a microbial growth inhibiting solution comprising a C₄-C₉ carboxylate antimicrobial agent, a chelating agent and a buffer, wherein the C₄-C₉ carboxylate antimicrobial agent comprises sodium caprylate and is present in an amount ranging from 0.05 mg/mL to 5 mg/mL, the chelating agent comprises disodium ethylenediaminetetraacetic acid and is present in an amount ranging from 0.01 mg/mL to 2 mg/mL, and the buffer comprises citrate; and
an implantable catheter lumen that receives the microbial growth inhibiting solution.

~~29-28.~~ The kit of claim ~~2827~~, wherein the container comprises a syringe.

~~30-29.~~ The kit of claim ~~2827~~, wherein the chelating agent is present in an amount ranging from 0.1 mg/mL to 1 mg/mL.

~~34-30.~~ The kit of claim ~~2827~~, wherein the chelating agent is present in an amount ranging from 0.25 mg/mL to 0.5 mg/mL.

~~32-31.~~ The kit of claim ~~2827~~, wherein the buffer is present in an amount ranging from 1.5 to 24 mM, wherein the C₄-C₉ carboxylate antimicrobial agent is present in an amount ranging from 0.5 mM to 8 mM, and the chelating agent is present in an amount ranging from 0.0625 mg/mL to 1 mg/mL.

~~33-32.~~ A kit for locking and/or flushing an implanted catheter, the kit comprising:

a container having a first compartment holding a C₄-C₉ carboxylate antimicrobial agent and a chelating agent in powder form and a second compartment holding a pharmacologically acceptable carrier solution, wherein the C₄-C₉ carboxylate antimicrobial agent comprises sodium caprylate and is present in an amount ranging from 0.05 mg/mL to 5 mg/mL, the chelating agent comprises disodium ethylenediaminetetraacetic acid and is present in an amount ranging from 0.01 mg/mL to 2 mg/mL when mixed with the pharmacologically acceptable carrier solution, and wherein the first or second compartment further comprises a buffer comprising citrate.

~~34-33.~~ The kit of claim ~~3332~~, wherein the container comprises an implantable catheter lumen.

~~35-34.~~ The kit of claim ~~3332~~, wherein the container comprises a syringe.

~~36-35.~~ The kit of claim ~~3332~~, wherein the chelating agent is present in an amount ranging from 0.1 mg/mL to 1 mg/mL when mixed with the pharmacologically acceptable carrier solution.

~~37-36.~~ The kit of claim ~~3332~~, wherein the chelating agent is present in an amount ranging from 0.25 mg/mL to 0.5 mg/mL when mixed with the pharmacologically acceptable carrier solution.

~~38-37.~~ The kit of claim ~~3332~~, wherein the buffer is present in an amount ranging from 1.5 to 24 mM, wherein the C₄-C₉ carboxylate antimicrobial agent is present in an amount ranging from 0.071 mg/mL to 1.15 mg/mL, and the chelating agent is present in an amount ranging from 0.0625 mg/mL to 1 mg/mL when mixed with the pharmacologically acceptable carrier solution.