



(51) International Patent Classification:

C09D 5/16 (2006.01) A61L 2/16 (2006.01)

(21) International Application Number:

PCT/US2023/074697

(22) International Filing Date:

20 September 2023 (20.09.2023)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

63/408,704 21 September 2022 (21.09.2022) US

(71) Applicant: **HERCULES LLC** [US/US]; 500 Hercules Road, Wilmington, Delaware 19808 (US).(72) Inventors: **ZERMEÑO-PÉREZ, David**; 213 The Grove, Petitswood Manor, Mullingar, Co., Westmeath, N91A6D6 (IE). **CHOUIRFA, Hamza**; 14 Saunders Court, Mullingar, Co., Westmeath, N91A262 (IE). **DUFFY, Patrick**; Teach Mhuire, Naas Road, Newbridge, Co., Kildare, W12VY96 (IE). **MCMAHON, Sean**; 12 Tobarkeel, Drumcliffe Road, Ennis, Co., Clare, V95K8NW (IE). **GREISER, Udo**; Keoltown, Ballinea, Mullingar, Co., Westmeath, N91D2Y1 (IE).(74) Agent: **DAVIS, William** et al.; 1005 U.S. 202/206, Bridge-water, 08807 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CV, CZ, DE, DJ, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IQ, IR, IS, IT, JM, JO, JP, KE, KG, KH, KN, KP, KR, KW, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, MG, MK, MN, MU, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, WS, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, CV, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SC, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, ME, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— of inventorship (Rule 4.17(iv))

(54) Title: COATING COMPOSITION COMPRISING A BIORESORBABLE COPOLYMER AND AN ANTI-MICROBIAL AGENT

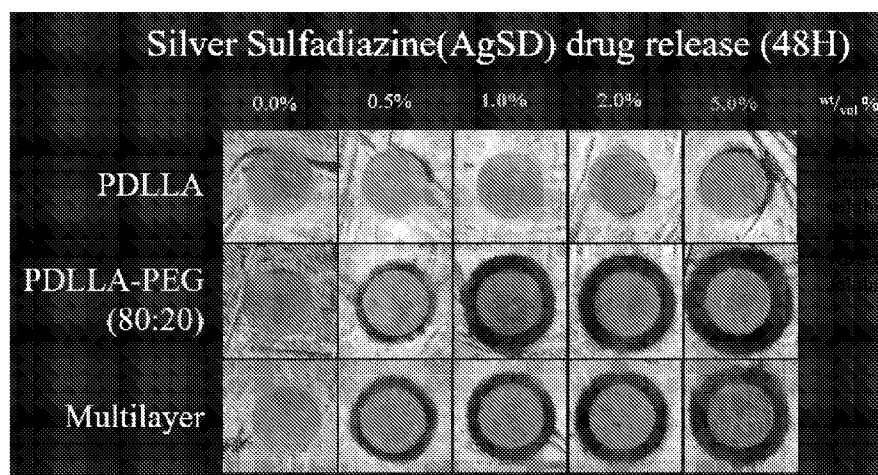


FIG. 1

(57) Abstract: Present application relates to a coating composition comprising (A) a copolymer of (a) methyl ether polyethylene glycol, and (b) at least one component selected from poly(D,L-lactide), poly(lactic-co-glycolic acid), or poly(ϵ -caprolactone); or (ii) silver sulfadiazine; or (B) a silver sulfadiazine functionalized copolymer of (a) polyethylene glycol, and (b) at least one component selected from poly(D,L-lactide), poly(lactic-co-glycolic acid), or poly(ϵ -caprolactone); or (C) a mixture of A and B. Also discloses the process for preparing the claimed copolymers and its use thereof.



Published:

- *without international search report and to be republished
upon receipt of that report (Rule 48.2(g))*

**COATING COMPOSITION COMPRISING A BIORESORBABLE COPOLYMER AND
AN ANTI-MICROBIAL AGENT**

FIELD OF THE INVENTION

[0001] Present application relates to an antimicrobial coating composition and particularly, relates to a bioresorbable anti-microbial and anti-fouling coating composition comprising at least one polyethylene glycol based copolymer and a silver based anti-microbial agent.

BACKGROUND OF THE INVENTION

[0002] Healthcare-Associated Infections (nosocomial infections) remains to be one of the main clinical and economic challenges now a days, and a marginal number of patients contract infection worldwide in association with their hospital care. A majority of such nosocomial infections spread through various devices such as biomedical implants, hospital equipments, diagnostic equipments, surgery equipments/tools, laboratory equipments, and other contact surfaces including furniture, building walls, floor, etc. Implant associated infections caused by biofilm-forming bacteria are another important class of Healthcare-Associated Infections and ends up in 70% implant rejections and became highly problematic for the patients and to the healthcare system.

[0003] Infectious microorganisms such as bacteria, fungi, etc. that are capable of growing on various living and non-living surfaces, are identified as the root cause for such infections. Colonization of these microorganisms on the surfaces of the implants can cause serious medical complications and often arises a need for removal and/or replacement of the implanted device to avoid secondary infective conditions. A considerable amount of research has been conducted in this technology area that aim to prevent such colonization of microorganisms and prevent nosocomial infections.

[0004] U.S. Pat. No. 7,794,490 filed by SCIMED Life Systems Inc, discloses a composite vascular graft, which incorporates bioactive agents that can be controllably delivered to the implantation site to deliver therapeutic materials and/or to reduce infection of the implant.

[0005] U.S. Publication. No. 2016/0000725 filed by Northeastern University discloses polymersomes for co-delivery of hydrophobic metallic nanoparticles, pharmaceutical agents/suspensions of such polymersomes, and methods of using such polymersomes to treat diseases or conditions.

[0006] New Zealand Pat. No. 548,940 filed by Angiotech Pharm Inc & Univ British Columbia AG discloses, a composition, comprising a therapeutic agent and a diblock copolymer of a polyethylene glycol and a lactide, lactic acid, glycolide, glycolic acid, or lactone.

[0007] U.S. Publication. No. 2021/0178025 filed by Covidien LP discloses antimicrobial coating formulations for medical devices comprising at least one water permeable polymer with at least one antimicrobial agent.

[0008] U.S. Publication. No. 2011/0287080 filed by Smith and Nephew PLC discloses a bioresorbable coating composition for an implantable medical device, wherein the composition comprises a co-polymer of a lactide, a glycolide and ϵ -caprolactone and at least one drug and/or bioactive agent.

[0009] U.S. Publication. No. 20100215716 filed by Biomet Manufacturing LLC discloses an orthopedic implant comprising a metal substrate and a coating on a surface of the substrate comprising a resorbable polymer impregnated with an admixture of antibiotic agents.

[0010] U.S. Pat. No. 5,616,338 filed by Columbia University, discloses a method for preparing a medical article comprising forming a layer of a polymeric material containing an anti-infective agent selected from a biguanide and silver sulfadiazine bulk distributed therein onto a surface of a preformed hydrophilic polymeric article.

[0011] However, a strong need still exists to formulate an anti-fouling and anti-bacterial bioresorbable polymer coating composition that effectively prevents the formation of biofilms and inhibits the adherence and proliferation of infectious microorganisms on the coated surfaces.

[0012] The foregoing and other objects and features of the invention will be made apparent from the following description.

SUMMARY OF THE INVENTION

[0013] The primary objective the present application is to provide a coating composition comprising: (A) a mixture of (i) about 0.01 wt. % to about 99.99 wt. % at least one copolymer comprising: (a) methyl ether polyethylene glycol (mPEG), a first component; and (b) at least one second component comprises poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); and (ii) about 0.01 wt. % to about 10 wt. % silver sulfadiazine (AgSD), an antimicrobial agent; or (B) about 0.01 wt. % to about 99.99 wt. % at least one silver sulfadiazine (AgSD) functionalized copolymer, wherein, the copolymer comprises (a) polyethylene glycol (PEG), a first component; and (b) at least one second component selected from

poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); or, (C) about 0.01 wt. % to about 99.99 wt. % mixture of A and B.

[0014] In another aspect of the present application, the antimicrobial agent further comprises silver iodide, silver benzoate, silver oxide, silver nitrite, silver laurate, silver acetate, silver palmitate, silver lactate, silver iodate, silver carbonate, and combinations thereof.

[0015] In another aspect of the present application, the weight average molecular weight of the copolymer is ranging from about 10,000 Daltons to about 400,000 Daltons.

[0016] In another aspect of the present application, the weight average molecular weight of the silver sulfadiazine functionalized copolymer is ranging from about 10,000 Daltons to about 400,000 Daltons.

[0017] In another aspect of the present application, the coating composition used to prevent the coated surfaces from adherence and proliferation of microorganisms selected from the group consisting of *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, and combinations thereof.

[0018] In another aspect of the present application, the composition is coated on surfaces using various techniques selected from solvent casting, spin coating, dip coating, spray coating, slot die coating, brushing, doctor blade coating, roller coating, screen printing, nozzle printing, 3D-printing, extrusion coating, curtain coating, and combinations thereof.

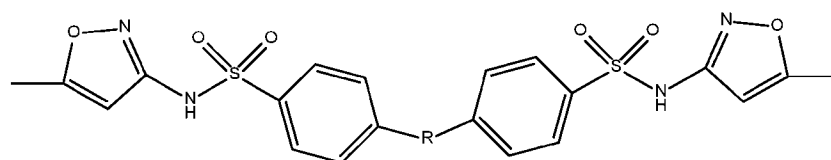
[0019] In another aspect of the present application, the coating composition is applied as a multilayer coating comprising up to five layers.

[0020] Another aspect of the present application discloses a process for preparing the copolymer of the coating composition comprising copolymerizing: about 0.01 wt.% to about 60 wt.% methyl ether polyethylene glycol (mPEG), a first component; and (b) about 40 wt.% to about 99.99 wt.% at least one second component comprises poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); wherein, the polymerization is carried out using a Tin based catalyst, in presence of an inert gas and at a temperature ranging from about 100° C to about 200° C.

[0021] Another aspect of the present application discloses a process for preparing the silver sulfadiazine functionalized copolymer of the coating composition comprising the steps of: (i) reacting polyethylene glycol (PEG) with succinic anhydride at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one solvent to obtain carboxylic acid-

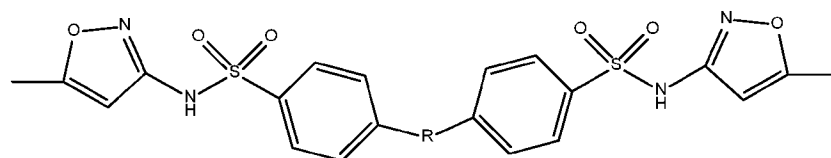
PEG-carboxylic acid; (ii) reacting carboxylic acid-PEG-carboxylic acid of step (i) and at least one polymer selected from acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ϵ -caprolactone), at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one carbodiimide to obtain a copolymer; and (iii) reacting the copolymer of step (ii) and silver sulfadiazine at a molar ratio ranging from about 1:15 to about 15:1 in presence of at least one solvent and at least one catalyst to obtain the silver sulfadiazine functionalized copolymer.

[0022] Another important aspect of the present application discloses a silver sulfadiazine functionalized copolymer having formula:



wherein, R is a copolymer of: (a) polyethylene glycol (PEG), a first component; and (b) at least one second component selected from poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL).

[0023] Another aspect of the present application discloses a process for preparing the silver sulfadiazine functionalized copolymer having formula:



wherein the process comprising the steps of: (i) reacting polyethylene glycol (PEG) with succinic anhydride at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one solvent to obtain carboxylic acid-PEG-carboxylic acid; (ii) reacting carboxylic acid-PEG-carboxylic acid of step (i) and at least one polymer selected from acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ϵ -caprolactone), at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one carbodiimide to obtain a copolymer; and (iii) reacting the copolymer of step (ii) and silver sulfadiazine at a molar ratio ranging from about 1:15 to about 15:1 in presence of at least one solvent and at least one catalyst to obtain the silver sulfadiazine functionalized copolymer.

BRIEF DESCRIPTION OF THE DRAWINGS

[0024] Illustrative embodiments of the present invention are described in detail below with reference to the attached drawing figures, which are incorporated by reference herein and wherein:

[0025] **FIG. 1** illustrates the drug diffusion behavior of PDLLA, PDLLA-PEG (80:20) and multilayer (PDLLA + PDLLA-PEG (80:20) + PDLLA-PEG (60:40)) polymers containing Silver sulfadiazine from 0 to 5%, finding a minimum effective dosage at 1% against *Staphylococcus Aureus* (132-GFP).

[0026] **FIG. 1A** illustrates images of Fluorescent microscopy of halo assay discs at 48 hours to corroborate presence of staphylococcus aureus labelled with Green Fluorescent Protein (GFP) and qualitatively analyze the viability.

[0027] **FIG. 2** illustrates antifouling effect of PEGylated polymer formulations against *Staphylococcus Aureus* (SH1000) bacteria.

[0028] **FIG. 3** illustrates antifouling effect of PEGylated polymer formulations against *Pseudomonas Aeruginosa* (PA01) bacteria.

[0029] **FIG. 4** illustrates Atomic Force Microscopy (AFM) topographical analysis of Titanium+ Aluminium+ Vanadium (Ti6Al4V) substrate.

[0030] **FIG. 5** illustrates Atomic Force Microscopy (AFM) topographical analysis of Titanium+ Aluminium+ Vanadium (Ti6Al4V) substrate incubated with *Staphylococcus Aureus* bacteria.

[0031] **FIG. 6** illustrates Atomic Force Microscopy (AFM) topographical analysis of Titanium+ Aluminium+ Vanadium (Ti6Al4V) substrate incubated with *Staphylococcus Aureus* - a zoom in section with bacteria in 10x10 microns area.

[0032] **FIG. 7** illustrates biological adherence analysis on substrates comprising bare Titanium, and titanium coated with PDLLA-PEG5000 at 10, 20 and 30 wt.% solutions.

[0033] **FIG. 8** illustrates average (n=3) contact angle behavior of bare Titanium and Titanium coated substrates with the polymers at 10% concentration by spin coating.

[0034] **FIG. 9** illustrates contact angle behavior of bare Titanium and titanium coated with polymer samples including PDLLA, PDLLA-PEG (80:20), PDLLA-PEG (60:40) and mPEG5000.

[0035] **FIG. 10** illustrates Fluorescent microscopy images of substrates coated with polymer compositions PDLLA, PDLLA-PEG (80:20), and PDLLA-PEG (60:40) using *Staphylococcus Aureus* strain.

[0036] **FIG. 11** illustrates Fluorescent microscopy images of substrates coated with polymer compositions PDLLA, PDLLA-PEG (20%), and PDLLA-PEG (40%) using *Pseudomonas Aeruginosa* strain.

[0037] **FIG. 12** illustrates Confocal microscopy to analyze 3D structure of biofilm and the antifouling effect of PEGylated polymer coatings in comparison to Ti6Al4V.

[0038] **FIG. 13** illustrates Confocal microscopy on THP-1 cells in contact with Ti6Al4V and polymer coatings.

[0039] **FIG. 14** illustrates total cell count adhered to the samples and Lactate Dehydrogenase (LDH) activity of cells.

[0040] **FIG. 15** illustrates Scanning Electron Microscopy of half coated sample to analyze homogeneity and quality of the coating. Energy dispersive X-ray spectroscopy (EDS) was performed to detect presence of the titanium and polymer.

[0041] **Fig. 15A** illustrates cross section of coated Ti6Al4V disc, where it is possible to observe the polymer filling the pores in the topography of the bare Ti6Al4V sample working as physical anchoring points for the coating.

[0042] **FIG. 16** illustrates Scanning Electron Microscopy of sample coated with polymer loaded with Silver Sulfadiazine, intentional scarrings were made on the sample to be able to perform EDS and detect Titanium under the coating.

DETAILED DESCRIPTION OF THE INVENTION

[0044] Before explaining at least one aspect of the disclosed and/or claimed inventive concept(s) in detail, it is to be understood that the disclosed and/or claimed inventive concept(s) is not limited in its application to the details of construction and the arrangement of the components or steps or methodologies set forth in the following description or illustrated in the drawings. The disclosed and/or claimed inventive concept(s) is capable of other aspects or of being practiced or carried out in several ways. Also, it is to be understood that the phraseology and terminology employed herein is for the purpose of description and should not be regarded as limiting.

[0045] As utilized in accordance with the disclosure, the following terms, unless otherwise indicated, shall be understood to have the following meanings.

[0046] Unless otherwise defined herein, technical terms used in connection with the disclosed and/or claimed inventive concept(s) shall have the meanings that are commonly understood by those of ordinary skill in the art. Further, unless otherwise required by context, singular terms shall include pluralities and plural terms shall include the singular.

[0047] The singular forms "a," "an," and "the" include plural forms unless the context clearly dictates otherwise specified or clearly implied to the contrary by the context in which the reference is made. The term "Comprising" and "Comprises of" includes the more restrictive claims such as "Consisting essentially of" and "Consisting of."

[0048] For purposes of the following detailed description, other than in any operating examples, or where otherwise indicated, numbers that express, for example, quantities of ingredients used in the specification and claims are to be understood as being modified in all instances by the term "about". The numerical parameters set forth in the specification and attached claims are approximations that may vary depending upon the desired properties to be obtained in carrying out the invention.

[0049] All percentages, parts, proportions, and ratios as used herein, are by weight of the total composition, unless otherwise specified. All such weights as they pertain to listed ingredients are based on the active level and, therefore; do not include solvents or by-products that may be included in commercially available materials, unless otherwise specified.

[0050] All publications, articles, papers, patents, patent publications, and other references cited herein are hereby incorporated herein in their entirety for all purposes to the extent consistent with the disclosure herein.

[0051] The use of the term “at least one” will be understood to include one as well as any quantity more than one, including but not limited to, 1, 2, 3, 4, 5, 10, 15, 20, 30, 40, 50, 100, etc. The term “at least one” may extend up to 100 or 1000 or more depending on the term to which it is attached. In addition, the quantities of 100/1000 are not to be considered limiting as lower or higher limits may also produce satisfactory results.

[0052] As used herein, the words “comprising” (and any form of comprising, such as “comprise” and “comprises”), “having” (and any form of having, such as “have” and “has”), “including” (and any form of including, such as “includes” and “include”) or “containing” (and any form of containing, such as “contains” and “contain”) are inclusive or open-ended and do not exclude additional, unrecited elements or method steps.

[0053] The term “each independently selected from the group consisting of” means when a group appears more than once in a structure, that group may be selected independently each time it appears.

[0054] A “coating” as described herein can include one or more coated layer applied on to a surface of the substrate wherein, each coated layer includes one or more coating components of the invention.

[0055] As used herein, the term “multilayer” refers to two or more layers of coated compositions of sufficient dimensions (for example, thickness and area) for its intended use over the entire, or less than the entire, portion of an article surface.

[0056] As used herein, the term "copolymer" refers to a polymer comprising more than one different polymeric repeating units.

[0057] As used herein, the term “mixture” refers to a composition comprising a blend of two or more individual components for example, a blend of a copolymer and an antimicrobial agent.

[0058] As used herein, the term “bioresorbable” refers to the breakdown of a compound into a simpler substance or substances that are eliminated by the body. For example, in the case of a “bioresorbable copolymer”, the macromolecule is cleaved into low molecular mass by-products, which are then eliminated from the body by biological pathways.

[0059] As used herein, the term “antifouling” refers to the effect of preventing, reducing and/or eliminating the fouling behavior.

[0060] As used herein, the term "antimicrobial " or "antibacterial" refer to the property of a copolymer, a composition, or coating thereof, to suppress, kill or inhibit the growth, proliferation, and/or colonization of microorganisms such as bacteria, fungus, or virus.

[0061] The present disclosure is directed to a coating composition comprising: (A) a mixture of (i) about 0.01 wt. % to about 99.99 wt. % at least one copolymer comprising: (a) methyl ether polyethylene glycol (mPEG), a first component; and (b) at least one second component comprises poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); and (ii) about 0.01 wt. % to about 10 wt. % silver sulfadiazine (AgSD), an antimicrobial agent; or (B) about 0.01 wt. % to about 99.99 wt. % at least one silver sulfadiazine (AgSD) functionalized copolymer, wherein, the copolymer comprises (a) polyethylene glycol (PEG), a first component; and (b) at least one second component selected from poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); or, (C) about 0.01 wt. % to about 99.99 wt. % mixture of A and B.

[0062] According to another aspect of the invention, aforesaid mixture (C) of A and B comprises in the ratio of about 1:10 to about 10:1; or about 1:9 to about 9:1; or about 1:8 to about 8:1; or about 1:7 to about 7:1; or about 1:6 to about 6:1; or about 1:5 to about 5:1; or about 1:4 to about 4:1; or about 1:3 to about 3:1; or about 1:2 to about 2:1; or about 10:1 to about 1:10; or about 9:1 to about 1:9; or about 8:1 to about 1:8; or about 7:1 to about 1:7; or about 6:1 to about 1:6; or about 5:1 to about 1:5; or about 4:1 to about 1:4; or about 3:1 to about 1:3; or about 2:1 to about 1:2; or about 1:1.

[0063] According to one embodiment, the methyl ether polyethylene glycol (mPEG) of the present application has a molecular weight ranging from about 1,000 Daltons to about 2,000 Daltons; or about 2,000 Daltons to about 3,000 Daltons; or about 3,000 Daltons to about 4,000 Daltons; or about 4,000 Daltons to about 5,000 Daltons; or about 5,000 Daltons to about 6,000 Daltons; or about 6,000 Daltons to about 7,000 Daltons; or about 7,000 Daltons to about 8,000 Daltons; or about 8,000 Daltons to about 9,000 Daltons; or about 9,000 Daltons to about 10,000 Daltons; or about 10,000 Daltons to about 11,000 Daltons; or about 11,000 Daltons to about 12,000 Daltons; or about 12,000 Daltons to about 13,000 Daltons; or about 13,000 Daltons to about 14,000 Daltons; or about 14,000 Daltons to about 15,000 Daltons.

[0064] According to one embodiment, the polyethylene glycol (PEG) of the present application has a molecular weight ranging from about 1,000 Daltons to about 2,000 Daltons; or about 2,000

Daltons to about 3,000 Daltons; or about 3,000 Daltons to about 4,000 Daltons; or about 4,000 Daltons to about 5,000 Daltons; or about 5,000 Daltons to about 6,000 Daltons; or about 6,000 Daltons to about 7,000 Daltons; or about 7,000 Daltons to about 8,000 Daltons; or about 8,000 Daltons to about 9,000 Daltons; or about or about 9,000 Daltons to about 10,000 Daltons; or about 10,000 Daltons to about 11,000 Daltons; or about 11,000 Daltons to about 12,000 Daltons; or about 12,000 Daltons to about 13,000 Daltons; or about 13,000 Daltons to about 14,000 Daltons; or about 14,000 Daltons to about 15,000 Daltons.

[0065] According to another aspect of the invention, the methyl ether polyethylene glycol (mPEG) of the present application is ranging from about 0.01 wt.% to about 5 wt.%; or about 5 wt.% to about 10 wt.%; or from about 10 wt.% to about 15 wt.%; or from about 15 wt.% to about 20 wt.%; or from about 20 wt.% to about 25 wt.%; or from about 25 wt.% to about 30 wt.%; or from about 30 wt.% to about 35 wt.%; or from about 35 wt.% to about 40 wt.%; or from about 40 wt.% to about 45 wt.%; or from about 45 wt.% to about 50 wt.%; or from about 50 wt.% to about 55 wt.%; or from about 55 wt.% to about 60 wt.%; or from about 60 wt.% to about 65 wt.%; of the total weight of the copolymer.

[0066] According to another aspect of the invention, the polyethylene glycol (PEG) of the present application is ranging from about 0.01 wt.% to about 5 wt.%; or about 5 wt.% to about 10 wt.%; or from about 10 wt.% to about 15 wt.%; or from about 15 wt.% to about 20 wt.%; or from about 20 wt.% to about 25 wt.%; or from about 25 wt.% to about 30 wt.%; or from about 30 wt.% to about 35 wt.%; or from about 35 wt.% to about 40 wt.%; or from about 40 wt.% to about 45 wt.%; or from about 45 wt.% to about 50 wt.%; or from about 50 wt.% to about 55 wt.%; or from about 55 wt.% to about 60 wt.%; or from about 60 wt.% to about 65 wt.%; of the total weight of the silver sulfadiazine functionalized copolymer.

[0067] According to another aspect of the invention, the poly(D,L-lactide) (PDLLA) has a molecular weight ranging from about 5,000 Daltons to about 10,000 Daltons; or about 10,000 Daltons to about 20,000 Daltons; or about 20,000 Daltons to about 30,000 Daltons; or about 30,000 Daltons to about 40,000 Daltons; or about 40,000 Daltons to about 50,000 Daltons; or about 50,000 Daltons to about 60,000 Daltons; or about 60,000 Daltons to about 70,000 Daltons; or about 70,000 Daltons to about 80,000 Daltons; or about 80,000 Daltons to about 90,000 Daltons; or about 90,000 Daltons to about 100,000 Daltons.

[0068] According to another aspect of the invention, the poly(lactic-co-glycolic acid) (PLGA) has a molecular weight ranging from about 5,000 Daltons to about 10,000 Daltons; or about 10,000 Daltons to about 20,000 Daltons; or about 20,000 Daltons to about 30,000 Daltons; or about 30,000 Daltons to about 40,000 Daltons; or about 40,000 Daltons to about 50,000 Daltons; or about 50,000 Daltons to about 60,000 Daltons; or about 60,000 Daltons to about 70,000 Daltons; or about 70,000 Daltons to about 80,000 Daltons; or about 80,000 Daltons to about 90,000 Daltons; or about 90,000 Daltons to about 100,000 Daltons.

[0069] According to another aspect of the invention, the poly(lactic-co-glycolic acid) (PLGA) comprises lactic acid and glycolic acid comonomers in the ratio of about 1:10 to about 10:1; or about 1:9 to about 9:1; or about 1:8 to about 8:1; or about 1:7 to about 7:1; or about 1:6 to about 6:1; or about 1:5 to about 5:1; or about 1:4 to about 4:1; or about 1:3 to about 3:1; or about 1:2 to about 2:1; or about 10:1 to about 1:10; or about 9:1 to about 1:9; or about 8:1 to about 1:8; or about 7:1 to about 1:7; or about 6:1 to about 1:6; or about 5:1 to about 1:5; or about 4:1 to about 1:4; or about 3:1 to about 1:3; or about 2:1 to about 1:2; or about 1:1.

[0070] According to another aspect of the invention, the poly(ϵ -caprolactone) (PCL) has a molecular weight ranging from about 5,000 Daltons to about 20,000 Daltons; or about 20,000 Daltons to about 40,000 Daltons; or about 40,000 Daltons to about 60,000 Daltons; or about 60,000 Daltons to about 80,000 Daltons; or about 80,000 Daltons to about 100,000 Daltons; or about 100,000 Daltons to about 120,000 Daltons; or 120,000 Daltons to about 140,000 Daltons; or 140,000 Daltons to about 160,000 Daltons; or 160,000 Daltons to about 180,000 Daltons; or 180,000 Daltons to about 200,000 Daltons; or 200,000 Daltons to about 220,000 Daltons; or 220,000 Daltons to about 240,000 Daltons or 240,000 Daltons to about 260,000 Daltons; or 260,000 Daltons to about 280,000 Daltons; or 280,000 Daltons to about 300,000 Daltons.

[0071] According to another aspect of the invention, the amount of second component is ranging from about 35 wt.% to about 40 wt.%; or from about 40 wt.% to about 45 wt.%; or from about 45 wt.% to about 50 wt.%; or from about 50 wt.% to about 55 wt.%; or from about 55 wt.% to about 60 wt.%; or from about 60 wt.% to about 65 wt.%; or from about 65 wt.% to about 70 wt.%; or from about 70 wt.% to about 75 wt.%; or from about 75 wt.% to about 80 wt.%; or from about 80 wt.% to about 85 wt.%; or from about 85 wt.% to about 90 wt.%; or from about 90 wt.% to about 95 wt.%; or from about 95 wt.% to about 99.99 wt.%; of the total weight of the copolymer.

[0072] According to yet another embodiment, the antimicrobial agent further includes, but not limited to, silver iodide, silver benzoate, silver oxide, silver nitrite, silver laurate, silver acetate, silver palmitate, silver lactate, silver iodate, silver carbonate, and combinations thereof.

[0073] According to another aspect of the invention, the degradation time of the copolymer is ranging from about 5 days to about 50 days; or 50 days to about 100 days; or 100 days to about 150 days; or 150 days to about 200 days; or 200 days to about 250 days; or 250 days to about 300 days; or 300 days to about 350 days; or 350 days to about 400 days; or 400 days to about 450 days; or 450 days to about 500 days; or 500 days to about 550 days; or 550 days to about 600 days; or 600 days to about 650 days;

[0074] According to another aspect of the invention, the degradation time of the silver sulfadiazine functionalized copolymer is ranging from about 5 days to about 50 days; or 50 days to about 100 days; or 100 days to about 150 days; or 150 days to about 200 days; or 200 days to about 250 days; or 250 days to about 300 days; or 300 days to about 350 days; or 350 days to about 400 days; or 400 days to about 450 days; or 450 days to about 500 days; or 500 days to about 550 days; or 550 days to about 600 days; or 600 days to about 650 days;

[0075] According to another aspect of the invention, the weight average molecular weight of the copolymer is ranging from about 10,000 Daltons to about 25,000 Daltons; or from about 25,000 Daltons to about 50,000 Daltons; or from about 50,000 Daltons to about 75,000 Daltons; or from about 75,000 Daltons to about 100,000 Daltons; or from about 100,000 Daltons to about 125,000 Daltons; or from about 125,000 Daltons to about 150,000 Daltons; or from about 150,000 Daltons to about 175,000 Daltons; or from about 175,000 Daltons to about 200,000 Daltons; or from about 200,000 Daltons to about 225,000 Daltons; or from about 225,000 Daltons to about 250,000 Daltons; or from about 250,000 Daltons to about 275,000 Daltons; or from about 275,000 Daltons to about 300,000 Daltons; or from about 300,000 Daltons to about 325,000 Daltons; or from about 325,000 Daltons to about 350,000 Daltons; or from about 350,000 Daltons to about 375,000 Daltons; or from about 375,000 Daltons to about 400,000 Daltons.

[0076] According to another aspect of the invention, the weight average molecular weight of the silver sulfadiazine functionalized copolymer is ranging from about 10,000 Daltons to about 25,000 Daltons; or from about 25,000 Daltons to about 50,000 Daltons; or from about 50,000 Daltons to about 75,000 Daltons; or from about 75,000 Daltons to about 100,000 Daltons; or from about

100,000 Daltons to about 125,000 Daltons; or from about 125,000 Daltons to about 150,000 Daltons; or from about 150,000 Daltons to about 175,000 Daltons; or from about 150,000 Daltons to about 175,000 Daltons; or from about 175,000 Daltons to about 200,000 Daltons; or from about 200,000 Daltons to about 225,000 Daltons; or from about 225,000 Daltons to about 250,000 Daltons; or from about 250,000 Daltons to about 275,000 Daltons; or from about 275,000 Daltons to about 300,000 Daltons; or from about 300,000 Daltons to about 325,000 Daltons; or from about 325,000 Daltons to about 350,000 Daltons; or from about 350,000 Daltons to about 375,000 Daltons; or from about 375,000 Daltons to about 400,000 Daltons.

[0077] In some embodiments, the copolymer and/or the silver sulfadiazine functionalized copolymer of the present application is bioresorbable.

[0078] In some embodiments, the composition is an anti-fouling composition and an anti-bacterial composition.

[0079] In some embodiments, the coating composition of the present application is in the form of powder, granules, pellets, grains, or flakes.

[0080] In some embodiments, the coating composition of the present application kills or inhibits microorganisms selected from the group consisting of, but not limited to, *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, and combinations thereof.

[0081] According to another non-limiting embodiment, the coating composition of the present application is effective in killing or inhibiting microorganisms selected from the group consisting of *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Enterococcus faecalis*, *Haemophilus influenzae*, *Moraxella species*, *salmonella species*, *Campylobacter species*, *Pseudomonas aeruginosa*, *Clostridium botulinum*, *Clostridium perfringens*, *Corynebacteria species*, *Diplococci species*, *Mycobacteria species*, *Streptomyces species*, *Escherichia coli*, *Salmonella typhimurium*, *Salmonella enteritidis*, *Vibrio parahaemolyticus*, *Bacillus anthracis*, *Bacillus azotoformans*, *Bacillus cereus*, *Bacillus coagulans*, *Bacillus israelensis*, *Bacillus larvae*, *Bacillus mycoides*, *Bacillus polymyxa*, *Bacillus pumilis*, *Bacillus stearothermophilus*, *Bacillus subtilis*, *Bacillus thuringiensis*, *Bacillus validus*, *Bacillus weihenstephanensis*, *Bacillus pseudomycoides*, *Burkholderia cepacia*, *Burkholderia multivorans*, *Burkholderia cenocepacia*, *Burkholderia vietnamiensis*, *Burkholderia stabilis*, *Burkholderia ambifaria*, *Burkholderia dolosa*, *Burkholderia anthina*, *Burkholderia pyrrocinia*, *Candida tropicalis*, *Candida albicans*, *Hansenula anomala*, *Saccharomyces cerevisiae*, *Torulaspora delbreuckii*, *Zygosaccharomyces bailii*,

Zygosaccharomyces rouxii, *Aspergillus niger*, *Aspergillus flavus*, *Aspergillus brasiliensis*, *Penicillium islandicum*, *Penicillium citrinum*, *Penicillium chrysogenum*, *Fusarium oxysporum*, *Fusarium graminearum*, *Fusarium solani*, *Alternaria alternata*, *Mucor racemosus* and combinations thereof.

[0082] In some embodiments, the coating composition of the present application is used for coating surfaces selected from the group consisting of, but not limited to, metallic surface, polymeric surface, masonry surface, wooden surface, glass surface, fabric surface, and elastomeric surface.

[0083] In some embodiments, the non-limiting use of the coating composition of the present application include coating medical devices, hospital equipments, diagnostic equipments, laboratory instruments, surgical instruments, utensils, electronic equipments, safety equipments, furniture, and building walls and floors.

[0084] In some embodiments, the medical devices are selected from the group consisting of, but not limited to, biomedical implants, dental implants, hard tissue and soft tissue prosthetic devices, joint replacements, plates, screws, stents, sheets, scaffolds, matrixes, endoscopes, catheters, probes, electrodes, mitral clips, balloon device, guidewires, drain tubes, urinary devices, needles, sutures, surgical staples, and contact lenses.

[0085] In some embodiments, the coating composition of the present application is coated by techniques including, but not limited to, solvent casting, spin coating, dip coating, spray coating, slot die coating, brushing, doctor blade coating, roller coating, screen printing, nozzle printing, 3D-printing, extrusion coating, and curtain coating.

[0086] In another embodiment, it is contemplated to employ the spin coating technique to apply the coating composition of the present application on aforementioned substrates. While performing spin coating of inventive polymer compositions having high PEG % on to said substrates, high hydrophilicity of the PEG may cause adverse effects such as peeling off or early detachment of the coating layer from the surface, and difficult to remain physically bonded to the coated surfaces. High PEG % polymer demonstrated a good antifouling property, approximately above 20 wt.% of PEG causes chances of premature detachment from the coated surfaces.

[0087] In some embodiments, the present application provides a multi-layer coating technique to tackle the aforementioned premature detachment and peeling off issue and found to be highly effective. Multi-layer spin coating is performed using two or more layers of (A) a mixture of: (i) a

copolymer comprising (a) methyl ether polyethylene glycol (mPEG), a first component; and (b) at least one second component selected from poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); and (ii) about 0.01 wt. % to about 10 wt. % silver sulfadiazine (AgSD), an antimicrobial agent; or using (B) a silver sulfadiazine (AgSD) functionalized copolymer, wherein, the copolymer comprises (a) polyethylene glycol (PEG), a first component; and (b) at least one second component selected from poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); or using (C) a mixture of A and B.

[0088] According to another aspect of the invention, the multilayer coating includes, but not limited to about two layers, about three layers, about four layers, about five layers, or about six layers.

[0089] According to another aspect of the invention, the multilayer coating comprising the structure of first layer includes but not limited to at least one polymer selected from poly(D,L-lactide), poly(lactic-co-glycolic acid), or poly(ϵ -caprolactone); and, a second to sixth layer comprises compositions of: (A) a mixture of (i) about 0.01 wt. % to about 99.99 wt. % at least one copolymer comprising: (a) methyl ether polyethylene glycol (mPEG), a first component; and (b) at least one second component selected from poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); and (ii) about 0.01 wt. % to about 10 wt. % silver sulfadiazine (AgSD), an antimicrobial agent; or (B) about 0.01 wt. % to about 99.99 wt. % at least one silver sulfadiazine (AgSD) functionalized copolymer, wherein, the copolymer comprises (a) polyethylene glycol (PEG), a first component; and (b) at least one second component selected from poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); or, (C) about 0.01 wt. % to about 99.99 wt. % mixture of A and B

[0090] According to a typical embodiment, present invention provides an antifouling coating by applying multiple layers of coating compositions including but not limited to (i) poly(D,L-lactide), (ii) poly(D,L-lactide) - polyethylene glycol 5000 copolymer (80:20 wt. ratio) and (iii) poly(D,L-lactide) - polyethylene glycol 5000 copolymer (60:40 wt. ratio); or (i) poly(lactic-co-glycolic acid), (ii) poly(lactic-co-glycolic acid) - polyethylene glycol 5000 copolymer (80:20 wt. ratio) and (iii) poly(lactic-co-glycolic acid) - polyethylene glycol 5000 copolymer (60:40 wt. ratio); or (i) poly(ϵ -caprolactone), (ii) poly(ϵ -caprolactone) - polyethylene glycol 5000 copolymer (80:20 wt. ratio) and (iii) poly(ϵ -caprolactone) - polyethylene glycol 5000 copolymer (60:40 wt. ratio); in the

specific given order, using a bottom-up spin coating procedure where the top layer will have higher PEG % than the previous layer. The coating was performed at 3000 rpm for a period of 45 seconds for each layer and given enough time to dry to improve the adhesion. This approach also enables the detachment and degradation of the PEGylated polymer layers in faster, and therefore, each exposed layer will detach and degrade faster due to higher water surface contact, also facilitate a self-cleaning process of the surface to avoid secondary infections due to dead-live bacterial adhesion or protein-bacterial adhesion.

[0091] According to a typical embodiment, present invention provides an antifouling and antimicrobial coating by applying multiple layers of coatings wherein the layers include but not limited to (i) poly(D,L-lactide), (ii) poly(D,L-lactide) - polyethylene glycol 5000 copolymer (80:20 wt. ratio) with AgSD (mixture) and (iii) poly(D,L-lactide) - polyethylene glycol 5000 copolymer (60:40 wt. ratio) with AgSD (mixture); or (i) poly(lactic-co-glycolic acid), (ii) poly(lactic-co-glycolic acid) - polyethylene glycol 5000 copolymer (80:20 wt. ratio) with AgSD (mixture), and (iii) poly(lactic-co-glycolic acid) - polyethylene glycol 5000 copolymer (60:40 wt. ratio) with AgSD (mixture); or (i) poly(ϵ -caprolactone), (ii) poly(ϵ -caprolactone) - polyethylene glycol 5000 copolymer (80:20 wt. ratio) with AgSD (mixture), and (iii) poly(ϵ -caprolactone) - polyethylene glycol 5000 copolymer (60:40 wt. ratio) with AgSD (mixture); or (i) poly(D,L-lactide), (ii) AgSD functionalized poly(D,L-lactide) - polyethylene glycol 6000 copolymer (80:20 wt. ratio) and (iii) AgSD functionalized poly(D,L-lactide) - polyethylene glycol 6000 copolymer (60:40 wt. ratio); or (i) poly(lactic-co-glycolic acid), (ii) AgSD functionalized poly(lactic-co-glycolic acid) - polyethylene glycol 6000 copolymer (80:20 wt. ratio) and (iii) AgSD functionalized poly(lactic-co-glycolic acid) - polyethylene glycol 6000 copolymer (60:40 wt. ratio); or (i) poly(ϵ -caprolactone), (ii) AgSD functionalized poly(ϵ -caprolactone) - polyethylene glycol 6000 copolymer (80:20 wt. ratio) and (iii) AgSD functionalized poly(ϵ -caprolactone) - polyethylene glycol 6000 copolymer (60:40 wt. ratio) copolymer; in the specific given order, using a bottom-up spin coating procedure where the top layer will have higher PEG % than the previous layer. The coating was performed at 3000 rpm for a period of 45 seconds for each layer and given enough time to dry to improve the adhesion. This approach also enables the detachment and degradation of the PEGylated polymer layers in faster, and therefore, each exposed layer will detach and degrade faster due to higher water surface contact, also facilitate a self-cleaning process

of the surface to avoid secondary infections due to dead-live bacterial adhesion or protein-bacterial adhesion.

[0092] Another embodiment of the present application discloses a process for preparing the copolymer of the coating composition comprising copolymerizing: about 0.01 wt.% to about 60 wt.% methyl ether polyethylene glycol (mPEG), a first component; and (b) about 40 wt.% to about 99.99 wt.% at least one second component selected from poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); wherein, the polymerization is carried out using a Tin based catalyst, in presence of an inert gas and at a temperature ranging from about 100° C to about 200° C.

[0093] Another embodiment of the present application discloses a process for preparing the silver sulfadiazine functionalized copolymer of the coating composition comprising the steps of: (i) reacting polyethylene glycol (PEG) with succinic anhydride at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one solvent to obtain carboxylic acid-PEG-carboxylic acid; (ii) reacting carboxylic acid-PEG-carboxylic acid of step (i) and at least one polymer selected from acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ϵ -caprolactone), at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one carbodiimide to obtain a copolymer; and (iii) reacting the copolymer of step (ii) and silver sulfadiazine at a molar ratio ranging from about 1:15 to about 15:1 in presence of at least one solvent and at least one catalyst to obtain the silver sulfadiazine functionalized copolymer.

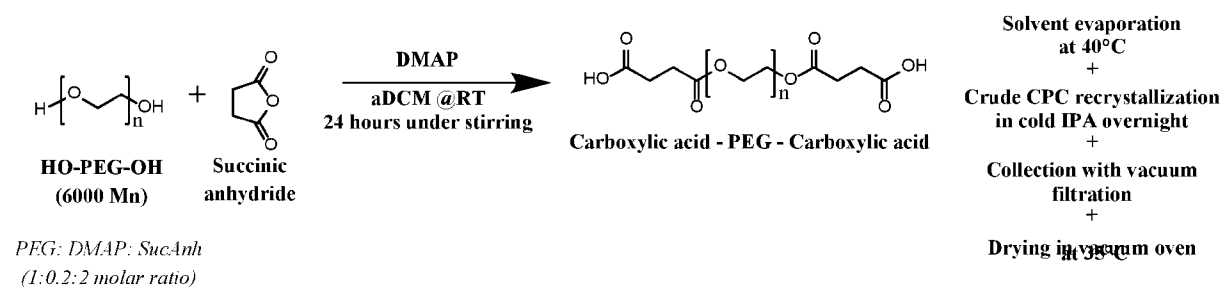
[0094] In some embodiments the amine of the present application is selected from the group consisting of, but not limited to, dimethylaminopyridine, triethylamine, triisopropylamine, methylmorpholine, triethylamine, 2-ethyl-5-methylpyridine, anhydrous pyridine, N-methylimidazole, diazabicyclooctane, and combinations thereof.

[0095] In some embodiments the solvent of the present application is selected from the group consisting of, but not limited to, anhydrous dichloromethane, dichloroethane, tetrachloroethane, chloroform, tetrachloromethane, trichloroethane, ethylene dichloride, and combinations thereof.

[0096] In some embodiments the carbodiimide of the present application is selected from the group consisting of, but not limited to, 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide, 1-cyclohexyl-3-(2-morpholinoethyl) carbodiimide, N,N'-dicyclohexylcarbodiimide, dicyclohexylcarbodiimide, diisopropyl carbodiimide, and combinations thereof.

[0097] In some embodiments the catalyst of the present application is selected from the group consisting of, but not limited to, Uronium based catalysts, amine based catalysts, Tin based catalysts, and combinations thereof.

[0098] In some embodiments, Step (i) of the process for preparing the silver sulfadiazine functionalized copolymer of the coating composition begins with the modification of OH-PEG-OH (MN 6000), succinic anhydride and 4-Dimethylaminopyridine (DMAP), are dissolved in anhydrous Dichloromethane (DCM) at room temperature (23°-25° C) and left stirring (100-1000RPM) for at least 24 hours. The reaction product contains >95% of carboxylic acid-PEG-carboxylic acid (CPC), and <5% of a combination of half reacted OH-PEG-carboxylic acid and unreacted OH-PEG-OH, succinic anhydride and DMAP. The resultant mixture is then subjected to solvent evaporation for 24 hours at 40° C and followed by recrystallization of carboxylic acid-PEG-carboxylic acid in cold (4° C) Isopropyl alcohol (IPA) for 12-24 hours. Resultant cold mixture is then filtered by vacuum filtration and dried at 35°C for 24 hours to obtain pure carboxylic acid-PEG-carboxylic acid.



[0099] In some embodiments, Step (ii) of the process for preparing the silver sulfadiazine functionalized copolymer of the coating composition comprises reacting the carboxylic acid-PEG-carboxylic acid of step (i), 4-Dimethylaminopyridine (DMAP) and 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide (EDCI) with at least one component selected from acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ε-caprolactone), dissolved in anhydrous Dichloromethane (DCM) at room temperature (23°-25° C) and left stirring (100-1000RPM) for at least 48 hours.

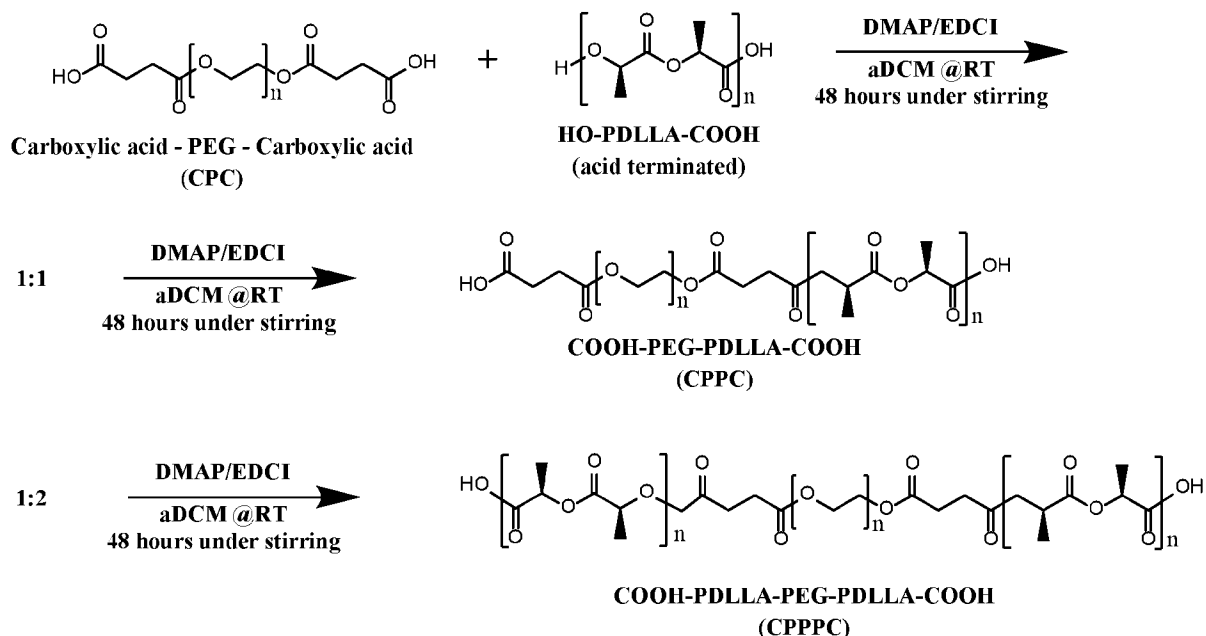
[00100] If the amount of components (i) acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ε-caprolactone), and (ii) carboxylic acid-PEG-carboxylic acid are taken in 1:1 ratio, the resultant mixture contains >95% COOH-PEG-

PDLLA-COOH, COOH-PEG-PLGA-COOH, or COOH-PEG-PCL-COOH which is a di-block copolymer, and <5% mixture of (i) unreacted carboxylic acid-PEG-carboxylic acid, (ii) acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ϵ -caprolactone), (iii) 4-Dimethylaminopyridine (DMAP), and (iv) 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide (EDCI).

[00101] If the amount of components (i) acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ϵ -caprolactone), and (ii) carboxylic acid-PEG-carboxylic acid are taken in 2:1 weight ratio, the resultant mixture contains >90% COOH-PDLLA-PEG-PDLLA-COOH, COOH-PLGA-PEG-PLGA-COOH, or COOH-PCL-PEG-PCL-COOH which is a tri-block polymer, and <10% mixture of (i) unreacted CPC, (ii) acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ϵ -caprolactone), (iii) di-block copolymer of COOH-PEG-PDLLA-COOH, COOH-PEG-PLGA-COOH, or COOH-PEG-PCL-COOH (iv) 4-Dimethylaminopyridine (DMAP), and (v) 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide (EDCI).

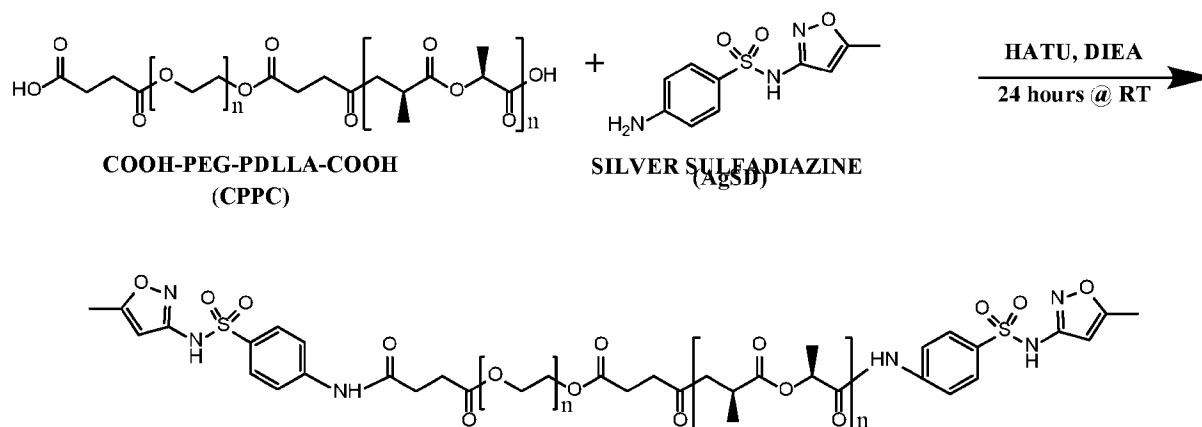
[00102] The resultant mixture is then subjected to solvent evaporation for 24 hours at 40° C, followed by recrystallization of (i) diblock copolymer of COOH-PEG-PDLLA-COOH, COOH-PEG-PLGA-COOH, or COOH-PEG-PCL-COOH and/or (ii) triblock copolymer of COOH-PDLLA-PEG-PDLLA-COOH, COOH-PLGA-PEG-PLGA-COOH, or COOH-PCL-PEG-PCL-COOH in cold (4° C) Isopropyl alcohol (IPA) for 12-24 hours. Resultant cold mixture was then filtered by vacuum filtration and dried at 35°C for 24 hours to obtain pure diblock or triblock copolymers of above configurations.

CPC: DMAP: EDCI
(1: 0.2: 5, molar ratio)

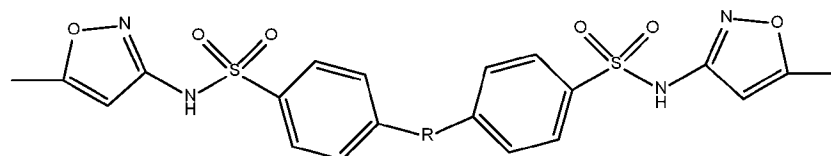


[00103] In some embodiments, Step (iii) of the process for preparing the silver sulfadiazine functionalized copolymer of the coating composition comprises dissolving the diblock or triblock copolymer of step (ii) and silver sulfadiazine in a molar ratio ranging from about 1:15 to about 15:1 in anhydrous Dichloromethane (DCM) and initiate the reaction in presence of 1-[Bis(dimethylamino)-methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium-3-oxide-hexafluorophosphate, Hexafluorophosphate Azabenzotriazole Tetramethyl Uronium (HATU) and N,N-Diisopropylethylamine (DIEA) at room temperature (23° -25° C) and left stirring at about 100 to about 1000 rpm for at least 24 hours. Resultant silver sulfadiazine functionalized copolymer is then extracted and purified for further use.

CPPC : AgSD
(1 : 5, molar ratio)



[00104] Another important embodiment of the present application discloses a silver sulfadiazine functionalized copolymer having formula:



wherein, R is a copolymer of: (a) polyethylene glycol (PEG), a first component; and (b) at least one second component selected from poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL).

[00105] According to one embodiment, the polyethylene glycol (PEG) of the present application has a molecular weight ranging from about 1,000 Daltons to about 2,000 Daltons; or about 2,000 Daltons to about 3,000 Daltons; or about 3,000 Daltons to about 4,000 Daltons; or about 4,000 Daltons to about 5,000 Daltons; or about 5,000 Daltons to about 6,000 Daltons; or about 6,000 Daltons to about 7,000 Daltons; or about 7,000 Daltons to about 8,000 Daltons; or about 8,000 Daltons to about 9,000 Daltons; or about 9,000 Daltons to about 10,000 Daltons; or about 10,000 Daltons to about 11,000 Daltons; or about 11,000 Daltons to about 12,000 Daltons; or about 12,000 Daltons to about 13,000 Daltons; or about 13,000 Daltons to about 14,000 Daltons; or about 14,000 Daltons to about 15,000 Daltons.

[00106] According to another aspect of the invention, the polyethylene glycol (PEG) of the present application is ranging from about 0.01 wt.% to about 5 wt.%; or about 5 wt.% to about 10 wt.%; or from about 10 wt.% to about 15 wt.%; or from about 15 wt.% to about 20 wt.%; or from

about 20 wt.% to about 25 wt.%; or from about 25 wt.% to about 30 wt.%; or from about 30 wt.% to about 35 wt.%; or from about 35 wt.% to about 40 wt.%; or from about 40 wt.% to about 45 wt.%; or from about 45 wt.% to about 50 wt.%; or from about 50 wt.% to about 55 wt.%; or from about 55 wt.% to about 60 wt.%; or from about 60 wt.% to about 65 wt.%; of the total weight of the copolymer.

[00107] According to another aspect of the invention, the poly(D,L-lactide) (PDLLA) has a molecular weight ranging from about 5,000 Daltons to about 10,000 Daltons; or about 10,000 Daltons to about 20,000 Daltons; or about 20,000 Daltons to about 30,000 Daltons; or about 30,000 Daltons to about 40,000 Daltons; or about 40,000 Daltons to about 50,000 Daltons; or about 50,000 Daltons to about 60,000 Daltons; or about 60,000 Daltons to about 70,000 Daltons; or about 70,000 Daltons to about 80,000 Daltons; or about 80,000 Daltons to about 90,000 Daltons; or about 90,000 Daltons to about 100,000 Daltons.

[00108] According to another aspect of the invention, the poly(lactic-co-glycolic acid) (PLGA) has a molecular weight ranging from about 5,000 Daltons to about 10,000 Daltons; or about 10,000 Daltons to about 20,000 Daltons; or about 20,000 Daltons to about 30,000 Daltons; or about 30,000 Daltons to about 40,000 Daltons; or about 40,000 Daltons to about 50,000 Daltons; or about 50,000 Daltons to about 60,000 Daltons; or about 60,000 Daltons to about 70,000 Daltons; or about 70,000 Daltons to about 80,000 Daltons; or about 80,000 Daltons to about 90,000 Daltons; or about 90,000 Daltons to about 100,000 Daltons.

[00109] According to another aspect of the invention, the poly(lactic-co-glycolic acid) (PLGA) comprises lactic acid and glycolic acid comonomers in the ratio of about 1:10 to about 10:1; or about 1:9 to about 9:1; or about 1:8 to about 8:1; or about 1:7 to about 7:1; or about 1:6 to about 6:1; or about 1:5 to about 5:1; or about 1:4 to about 4:1; or about 1:3 to about 3:1; or about 1:2 to about 2:1; or about 10:1 to about 1:10; or about 9:1 to about 1:9; or about 8:1 to about 1:8; or about 7:1 to about 1:7; or about 6:1 to about 1:6; or about 5:1 to about 1:5; or about 4:1 to about 1:4; or about 3:1 to about 1:3; or about 2:1 to about 1:2; or about 1:1.

[00110] According to another aspect of the invention, the poly(ϵ -caprolactone) (PCL) has a molecular weight ranging from about 5,000 Daltons to about 20,000 Daltons; or about 20,000 Daltons to about 40,000 Daltons; or about 40,000 Daltons to about 60,000 Daltons; or about 60,000 Daltons to about 80,000 Daltons; or about 80,000 Daltons to about 100,000 Daltons; or about 100,000 Daltons to about 120,000 Daltons; or 120,000 Daltons to about 140,000 Daltons; or

140,000 Daltons to about 160,000 Daltons; or 160,000 Daltons to about 180,000 Daltons; or 180,000 Daltons to about 200,000 Daltons; or 200,000 Daltons to about 220,000 Daltons; or 220,000 Daltons to about 240,000 Daltons or 240,000 Daltons to about 260,000 Daltons; or 260,000 Daltons to about 280,000 Daltons; or 280,000 Daltons to about 300,000 Daltons.

[00111] According to another aspect of the invention, the amount of second component is ranging from about 35 wt.% to about 40 wt.%; or from about 40 wt.% to about 45 wt.%; or from about 45 wt.% to about 50 wt.%; or from about 50 wt.% to about 55 wt.%; or from about 55 wt.% to about 60 wt.%; or from about 60 wt.% to about 65 wt.%; or from about 65 wt.% to about 70 wt.%; or from about 70 wt.% to about 75 wt.%; or from about 75 wt.% to about 80 wt.%; or from about 80 wt.% to about 85 wt.%; or from about 85 wt.% to about 90 wt.%; or from about 90 wt.% to about 95 wt.%; or from about 95 wt.% to about 99.99 wt.%; of the total weight of the copolymer.

[00112] According to another aspect of the invention, the degradation time of the silver sulfadiazine functionalized copolymer is ranging from about 5 days to about 50 days; or 50 days to about 100 days; or 100 days to about 150 days; or 150 days to about 200 days; or 200 days to about 250 days; or 250 days to about 300 days; or 300 days to about 350 days; or 350 days to about 400 days; or 400 days to about 450 days; or 450 days to about 500 days; or 500 days to about 550 days; or 550 days to about 600 days; or 600 days to about 650 days;

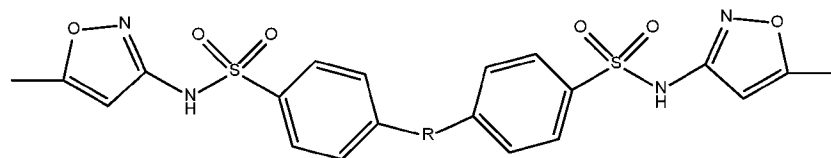
[00113] According to another aspect of the invention, the weight average molecular weight of the silver sulfadiazine functionalized copolymer is ranging from about 10,000 Daltons to about 25,000 Daltons; or from about 25,000 Daltons to about 50,000 Daltons; or from about 50,000 Daltons to about 75,000 Daltons; or from about 75,000 Daltons to about 100,000 Daltons; or from about 100,000 Daltons to about 125,000 Daltons; or from about 125,000 Daltons to about 150,000 Daltons; or from about 150,000 Daltons to about 175,000 Daltons; or from about 150,000 Daltons to about 175,000 Daltons; or from about 175,000 Daltons to about 200,000 Daltons; or from about 200,000 Daltons to about 225,000 Daltons; or from about 225,000 Daltons to about 250,000 Daltons; or from about 250,000 Daltons to about 275,000 Daltons; or from about 275,000 Daltons to about 300,000 Daltons; or from about 300,000 Daltons to about 325,000 Daltons; or from about 325,000 Daltons to about 350,000 Daltons; or from about 350,000 Daltons to about 375,000 Daltons; or from about 375,000 Daltons to about 400,000 Daltons.

[00114] In some embodiments, the silver sulfadiazine functionalized copolymer of the present application is bioresorbable.

[00115] According to another aspect of the invention, the silver sulfadiazine functionalized copolymer is used in personal care compositions, home care compositions, pharmaceutical compositions, industrial compositions, coating compositions, ink compositions, oral care compositions, health care compositions, packaging materials, food compositions, and beverage compositions.

[00116] According to another aspect of the invention, the silver sulfadiazine functionalized copolymer is used in medical devices selected from the group consisting of biomedical implants, dental implants, hard tissue and soft tissue prosthetic devices, joint replacements, plates, screws, stents, sheets, scaffolds, matrixes, endoscopes, catheters, probes, electrodes, mitral clips, balloon device, guidewires, drain tubes, urinary devices, needles, sutures, surgical staples, glue, contact lenses, and combinations thereof.

[00117] Another aspect of the present application discloses a process for preparing the silver sulfadiazine functionalized copolymer having formula:



wherein, the process comprising the steps of: (i) reacting polyethylene glycol (PEG) with succinic anhydride at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one solvent to obtain carboxylic acid-PEG-carboxylic acid; (ii) reacting carboxylic acid-PEG-carboxylic acid of step (i) and at least one polymer selected from acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ϵ -caprolactone), at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one carbodiimide to obtain a copolymer; and (iii) reacting the copolymer of step (ii) and silver sulfadiazine at a molar ratio ranging from about 1:15 to about 15:1 in presence of at least one solvent and at least one catalyst to obtain the silver sulfadiazine functionalized copolymer.

[00118] In some embodiments the amine of the present application is selected from the group consisting of, but not limited to, dimethylaminopyridine, triethylamine, triisopropylamine, methylmorpholine, triethylamine, 2-ethyl-5-methylpyridine, anhydrous pyridine, N-methylimidazole, diazabicyclooctane, and combinations thereof.

[00119] In some embodiments the solvent of the present application is selected from the group consisting of, but not limited to, anhydrous dichloromethane, dichloroethane, tetrachloroethane, chloroform, tetrachloromethane, trichloroethane, ethylene dichloride, and combinations thereof.

[00120] In some embodiments the carbodiimide of the present application is selected from the group consisting of, but not limited to, 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide, 1-cyclohexyl-3-(2-morpholinoethyl) carbodiimide, N,N'-dicyclohexylcarbodiimide, dicyclohexylcarbodiimide, diisopropyl carbodiimide, and combinations thereof.

[00121] In some embodiments the catalyst of the present application is selected from the group consisting of, but not limited to, Uronium based catalysts, amine based catalysts, Tin based catalysts, 1-[Bis(dimethylamino)-methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium-3-oxide-hexafluorophosphate, Hexafluorophosphate Azabenzotriazole Tetramethyl Uronium (HATU) N,N-Diisopropylethylamine (DIEA), and combinations thereof.

[00122] According to another embodiment of the present application, it is contemplated to employ a composition comprising (i) about 0.01 wt. % to about 99.99 wt. % of at least one copolymer comprising: (a) methyl ether polyethylene glycol (mPEG), a first component; and, (b) at least one second component selected from poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); and, (ii) about 0.01 wt. % to about 10 wt. % of an antimicrobial agent or a therapeutically active ingredient.

[00123] According to another embodiment of the present application, the antimicrobial agent or a therapeutically active ingredient is selected from the group consisting of analgesics, angiogenesis drugs, anti-angiogenesis agents, antibiotics, antibodies, anti-cancer agents, anti-fibrotic agents, anti-inflammatories, anti-migratory agents, anti-neoplastics, anti-oxidants, antiphlogistics, anti-platelet agents, anti-proliferatives, anti-thrombotics, antiviral agents, bisphosphonates, calcium channel blockers, cell permeabilizers, chemotherapeutics, copper ion source, cyclooxygenase inhibitors, cytokine activators, cytokine inhibitors, free radical scavengers, growth factor antagonists, nitrogen oxide donors, non-steroidal anti-inflammatory drugs, osteoporotic drug, parathyroid hormone (PTH), phosphodiesterase inhibitors, proapoptotics, radioactive compounds, radiopaque agents, silver ion source, steroids, strontium, thrombolytics, vasodilators, angiogenic agents, antispasmodic agents, proteins, peptides, nucleic acids, and combinations thereof.

[00124] Further, certain aspects of the present application are illustrated in detail by way of the following examples. The examples are given herein for illustration of the application and are not intended to be limiting thereof.

EXAMPLES

[00125] **EXAMPLE 1:** PDLLA-PEG (80:20) Loaded with AgSD

Ingredients	Wt.%
Poly (D,L-Lactide)	79.00
Poly (ethylene glycol) methyl ether (Mw 5000)	20.00
Silver Sulfadiazine (AgSD)	1.00
Total	100.00

[00126] A reactor vessel having up to 800 mL capacity was pre-dried for 1 hour with an inert gas mixture to obtain ultra dry conditions within the vessel. Poly (D,L-Lactide), Poly (ethylene glycol) methyl ether (Mw 5000-6000), and Silver Sulfadiazine (AgSD) were charged in the reactor vessel by maintaining a usable volume of 70-75% of the vessel capacity. Reaction was carried out in bulk using up to 200 ppm of Tin(II) 2-ethylhexanoate catalyst for about 4-8 hours in presence of an inert gas. Temperature is maintained in the range of 100° - 200° C to control the speed of reaction/polymerization.

[00127] **EXAMPLE 2:** PDLLA-PEG (60:40) Loaded with AgSD

Ingredients	Wt.%
Poly (D,L-Lactide)	59.00
Poly (ethylene glycol) methyl ether (Mw 5000)	40.00
Silver Sulfadiazine (AgSD).	1.00
Total	100.00

[00128] A reactor vessel having up to 800 mL capacity was pre-dried for 1 hour with a gas mixture to decrease humidity within the vessel. Poly (D,L-Lactide), Poly (ethylene glycol) methyl ether (Mw 5000-6000), and Silver Sulfadiazine (AgSD) were charged in the reactor vessel by maintaining a usable volume of 70-75% of the vessel capacity. Reaction was carried out in bulk using up to 200 ppm of Tin(II) 2-ethylhexanoate catalyst for about 4-8 hours in presence of an inert gas. Temperature is maintained in the range of 100° - 200° C to control the speed of reaction/polymerization.

[00129] **EXAMPLE 3:** PLGA-PEG (90:10) Loaded with AgSD

Ingredients	Wt.%
Poly (Lactide-co-Glycolide)	89.00

Poly (ethylene glycol) methyl ether (Mw 5000)	10.00
Silver Sulfadiazine (AgSD).	1.00
Total	100.00

[00130] A reactor vessel having up to 800 mL capacity was pre-dried for 1 hour with a gas mixture to decrease humidity within the vessel. Poly (Lactide-co-Glycolide), Poly (ethylene glycol) methyl ether (Mw 5000-6000), and Silver Sulfadiazine (AgSD) were charged in the reactor vessel by maintaining a usable volume of 70-75% of the vessel capacity. Reaction was carried out in bulk using up to 200 ppm of Tin(II) 2-ethylhexanoate catalyst for about 4-8 hours in presence of an inert gas. Temperature is maintained in the range of 100° - 200° C to control the speed of reaction/polymerization.

[00131] **EXAMPLE 4: PCL-PEG Loaded with AgSD**

Ingredients	Wt.%
Poly(ϵ -caprolactone)	98.00
Poly (ethylene glycol) methyl ether (Mw 5000)	1.00
Silver Sulfadiazine (AgSD).	1.00
Total	100.00

[00132] A reactor vessel having up to 800 mL capacity was pre-dried for 1 hour with a gas mixture to decrease humidity within the vessel. Poly(ϵ -caprolactone), Poly (ethylene glycol) methyl ether (Mw 5000-6000), and Silver Sulfadiazine (AgSD) were charged in the reactor vessel by maintaining a usable volume of 70-75% of the vessel capacity. Reaction was carried out in bulk using up to 200 ppm of Tin(II) 2-ethylhexanoate catalyst for about 20-30 hours in presence of an inert gas. Temperature is maintained in the range of 100° - 200° C to control the speed of reaction/polymerization.

[00133] **EXAMPLE 5: Halo assay (drug diffusion experiment).**

[00134] Halo assay was performed using as substrate Ti6Al4V discs (10mm diameter and 1 mm thickness) in Lysogeny broth (LB) agar for 24 and 48 hours. **Fig. 1** indicates the silver sulfadiazine (AgSD) diffusion behavior when mixed with synthesized polymers to generate PDLLA, PDLLA-PEG (80:20) and multilayer (PDLLA + PDLLA-PEG (80:20) + PDLLA-PEG (60:40)) coating samples containing a drug-load concentration of 0, 0.5, 1, 2, and 5% wt/vol. **Fig. 1A** shows fluorescence microscopy of Ti6Al4V discs used for Halo Assay at 24 hours and 48 hours to corroborate presence of *Staphylococcus Aureus* (132) labelled with Green Fluorescent Protein (GFP). This shows a clear decrease of viable bacteria with the increase of drug concentration. A

drug concentration of 1-2% wt/vol. is selected as best balance dosage for PEGylated polymers as antimicrobial to avoid damaging host cells.

[00135] A significant enhancement was observed on the diffusion of the drug on the PEGylated polymer formulations with drug release on the first 24 hours in comparison to the unmodified polymer which is not releasing the drug in time.

[00136] **EXAMPLE 6:** Crystal Violet assay (0.5%).

[00137] Bacterial staining: measurement of biofilm formation through Ultraviolet–visible spectroscopy at 595nm: coated and uncoated glass discs (13mm diameter and 0.25mm thickness) with PDLLA, PDLLA-PEG (80:20), PLGA and PLGA-PEG (90:10) and drug loaded versions with 1% Silver Sulfadiazine were submerged for 24 hours in a liquid Lysogeny broth (LB) with bacteria *Staphylococcus Aureus* (SH1000) at 0.1 optical density (O.D.) as initial inoculum concentration.

[00138] The obtained biofilm (24 hours incubation) was washed with phosphate buffer saline (PBS) to remove planktonic bacteria, stained with crystal violet (0.5%) for 10 min, further PBS washes were performed to finalize with elution of crystal violet through ethanol: acetic acid (90:10). The biofilm formation was then measured in UV-vis spectrometer.

[00139] **Fig. 2** provides a clear indication of the antifouling and antimicrobial effect in these PEGylated formulations when compared to the unmodified polymers. 20 wt.% PEG with 1% silver sulfadiazine in the formulation, proved to be highly efficient against *Staphylococcus Aureus* reducing the biofilm formation by 80%.

[00140] **EXAMPLE 7:** Crystal Violet assay (0.5%).

[00141] Bacterial staining: measurement of biofilm formation through Ultraviolet–visible spectroscopy at 595nm: coated and uncoated glass discs (13mm diameter and 0.25mm thickness) with PDLLA, PDLLA-PEG (80:20), PLGA and PLGA-PEG (90:10) and drug loaded versions with 1% Silver Sulfadiazine were submerged for 24 hours in a liquid Lysogeny broth (LB) with bacteria *Pseudomonas Aeruginosa* (PA01) at 0.1 optical density (O.D.) as initial inoculum concentration.

[00142] The obtained biofilm (24 hours incubation) was washed with phosphate buffer saline (PBS) to remove planktonic bacteria, stained with crystal violet (0.5%) for 10 min, further PBS washes were performed to finalize with elution of crystal violet through ethanol: acetic acid (90:10). The biofilm formation was then measured in UV-vis spectrometer.

[00143] **Fig. 3** illustrates a clear indication of the antifouling effect in the PEGylated formulations when compared to the unmodified polymers. 20 wt.% PEG with 1% silver sulfadiazine in the formulation, proved to be highly efficient against *Pseudomonas Aeruginosa* reducing the biofilm formation by 80%.

[00144] **EXAMPLE 8:** Atomic Force Microscopy (AFM) topographical analysis.

[00145] Atomic Force Microscopy (AFM) topographical analysis was performed using 90x90 microns of Titanium+ Aluminium+ Vanadium (Ti6Al4V) substrate of medical grade level 5 and having a medium level of roughness (average of 648.7nm) which is useful for implant integration to hard tissues (bone). When the substrate is incubated for 1-2 hours at 37°C in liquid Lysogeny broth (LB) media with *Staphylococcus Aureus* (0.1 OD), the change on the surface and the roughness gives a clear indication of the bacterial adherence and attachment on the surface, localizing the anchoring points to initiate the biofilm formation.

[00146] **Fig. 4** indicates topography and roughness analysis of Ti6Al4V samples before incubation, meanwhile **Fig. 5** shows topography and roughness analysis of Ti6Al4V samples after incubation with *Staphylococcus Aureus*, decrease in roughness indicates possible bacterial biomass coating the surface. **Fig. 6** zoom-in section of the AFM topographical analysis after incubation with bacteria in 10x10 microns area, it is clearly visible the round shape of the bacteria confirming the presence of *Staphylococcus Aureus*, and how it is taking advantage of the irregular topography to adhere, agglomerate and proliferate, especially on the lower parts of the topography.

[00147] **EXAMPLE 9:** Biological adherence analysis.

[00148] Biological adherence analysis was performed on Ti6Al4V samples with and without polymeric coatings, after 1-2 hours of incubation at 37°C in liquid Lysogeny broth (LB) media with *Staphylococcus Aureus* using Atomic Force Microscopy (AFM) in 90x90 microns.

[00149] As indicated in **Fig. 7**, samples of bare titanium, and titanium coated with PDLLA-PEG5000 (80:20) at 10, 20 and 30 wt.% solutions of polymer in Dichloromethane (DCM), spin coated at 6000 RPM. Red color indicates the presence of a bacteria cell. In the bare substrate (Ti6Al4V) the bacteria are widely colonized on all the surface, with minimum area left untouched, meanwhile for the coated titanium samples had a clear reduction in the bacterial attachment, not seeing a significative difference in antifouling effect between concentrations.

[00150] **EXAMPLE 10:** Contact angle measurement.

[00151] Contact angle measurement (wettability behavior) was performed with 10 microliters of pure water on top of bare titanium and coated samples with the polymers at 10% concentration during spin coating for a measurement time of 60 seconds. Titanium is more hydrophobic than the polymer formulations. When the amount of PEG is increased in the formulation, the contact angle was found to be decreased due to the increased water intake due to the hydrophilicity of PEG in the polymer chain.

[00152] **Fig. 8-9** provides contact angle behavior of above test samples. Contact angle images of **Fig. 9** illustrates bare titanium and titanium coated with polymer samples of PDLLA (100:0), PDLLA-PEG (80:20), PDLLA-PEG (60:40), measured at 60 sec. Significant impact in the enhancement of wettability with polymer coated samples was observed, and a progressive difference in wettability was seen with increased PEG %. Higher PEG% resulted in a lower contact angle therefore indicates an increased wettability behavior (more hydrophilic material), which reduces surface energy creating the antifouling barrier preventing bacterial adhesion and biofilm formation on the surface.

[00153] **EXAMPLE 11:** Fluorescent microscopy (*S. Aureus*)

[00154] Fluorescent microscopy was performed with samples of PDLLA, PDLLA-PEG (80:20), and PDLLA-PEG (60:40) using bacteria *Staphylococcus Aureus* (0.1 OD). Sytox Green (Death or compromised bacteria) and TAMRA Red (live bacteria) staining were used for this study. Incubation with bacteria in liquid Lysogeny broth (LB) broth for 24 hours were done and then proceeded to stain for 30 min each stain, with 3xPBS washes in between to remove unreacted staining. **Fig. 10** indicates a decrease of the bacterial presence and adherence into the substrate after 24 hours in comparison to the control (Glass), the decrease was more noticeable when the PEG% was increased in the polymer formulation.

[00155] **EXAMPLE 12:** Fluorescent microscopy (*P. Aeruginosa*)

[00156] Fluorescent microscopy was performed with samples of PDLLA, PDLLA-PEG (80:20), and PDLLA-PEG (60:40) using bacteria *Pseudomonas Aeruginosa* (0.1 OD). Sytox Green (Death or compromised bacteria) and TAMRA Red (live bacteria) staining were used for this study. Incubation with bacteria in liquid Lysogeny broth (LB) broth for 24 hours were done and then proceeded to stain for 30 min each stain, with 3xPBS washes in between to remove unreacted staining. **Fig. 11** indicates a decrease of the bacterial presence and adherence into the substrate

after 24 hours in comparison to the control (Glass), the decrease was more noticeable when the PEG% was increased in the polymer formulation.

[00157] **EXAMPLE 13:** Confocal microscopy

[00158] Confocal microscopy was performed to analyze 3D structure of biofilm adhered to the coatings of samples made from PDLA, PDLA-PEG (20%), and multilayer coating of (PDLA + PDLA-PEG (80:20) + PDLA-PEG (60:40)), as well on drug loaded version with 1% AgSD .

[00159] In **Fig. 12**, the green dots indicate Green Fluorescent Protein (GFP) representing live cells and red dots indicates Propidium Iodide (PI) depicts dead cells. Titanium is fully covered and PDLA reduce slightly the coverage. PDLA-PEG (80:20) and Multilayer show hydration layer and peeling effect that decrease the presence and viability of *Staphylococcus Aureus*. **Fig. 13** illustrates the Confocal microscopy on monocyte (THP-1) cell line, to simulate immune system response to foreign elements, these cells were in contact with the polymer coatings for 24 hours in Roswell Park Memorial Institute (RPMI) 1640 Medium, the differentiation of THP-1 monocytes into macrophages is mainly conducted at a phorbol 12-myristate 13-acetate (PMA) concentration of 10-400 ng/ml. Polymers are designed to degrade over time in contact with water, this process will begin after implantation and leave the titanium surface exposed, increasing attachment overtime. **Fig. 13** shows THP-1 cells without morphological negative effects nor complete antifouling effects, even though there is a reduction on cells adhered they are still able to adhere over time, this shows that the polymer coatings are not having a cytotoxic effect nor damaging the membrane or nucleus.

[00160] **Example 14:** Cytotoxicity analysis.

[00161] Lactate dehydrogenase (LDH) test was performed to measure cytotoxicity of THP-1 cells, where LDH is an important enzyme of the anaerobic metabolic pathway. The human tissue generates low levels of LDH activity as cells go through the process of senescence, higher concentrations of LDH might indicate cell lysis and/or compromised cell organelles. The cell cytoskeleton and nucleus were stained with ActinRed™ 555 ReadyProbes™ Reagent (Rhodamine phalloidin) and NucBlue™ Fixed Cell ReadyProbes™ Reagent (DAPI) (ThermoFisher Scientific) respectively.

[00162] **Fig. 14** shows the total number of cells adhered and LDH activity measurement to quantify cytotoxicity. Even though there is a decreased number of cell adhered in contact with the

polymer coatings, there is not increase LDH activity, demonstrating no cytotoxic effect, as all the polymers shown equal or lower LDH activity compared to Titanium. Silver sulfadiazine (1%) loaded samples shows an agglomeration effect but not cytotoxicity in comparison to titanium, multilayer with 1 % AgSD, showed promising results similar to the control of THP-1 cells growth in polystyrene.

[00163] **Example 15: SEM surface analysis**

[00164] Scanning electron microscopy was performed under high vacuum at 15kV analyzing secondary electron (SE) mode to characterize qualitatively the coatings applied on the surface of Ti6Al4V samples. Half coated discs were used for Energy-dispersive X-ray spectroscopy (EDS) analysis to generate an elemental mapping for visual differences and inspection of impurities with better contrast and resolution.

[00165] **Fig. 15** shows SEM analyses on half coated discs, top view, and side view to observe coating application quality and homogeneity. Energy-dispersive X-ray spectroscopy (EDS) was performed to confirm polymer presence yellow (Titanium), blue (Carbon) and red (Oxygen), polymer coating is homogeneously applied over the surface. **Fig. 15A** shows cross section of coated Ti6Al4V disc, wherein it is possible to observe (highlighted with white arrows) the polymer filling the pores in the topography of the bare Ti6Al4V sample working as physical anchoring points for the coating. **Fig. 16** shows SEM analysis of polymer coating functionalized with silver sulfadiazine (1%), EDS was performed to confirm drug presence over the polymer coatings with good homogeneity where the elemental mapping shows red (Sulfur and Silver) and purple (Titanium).

[00166] **EXAMPLE 16: Modification of OH-PEG-OH**

[00167] A 250mL round bottom flask is charged with 30g of PEG (MN 6000), 1.15g of succinic anhydride and 0.123g of 4-Dimethylaminopyridine (DMAP) in a molar ratio of (1:2:0.2), were dissolved in 50mL of anhydrous Dichloromethane (DCM) at room temperature (23°-25° C), the system was purged with Nitrogen for 1 hours and was left filled with Nitrogen and stirring at 100-1000 rpm for at least 24 hours. The reaction product had >95% of carboxylic acid-PEG-carboxylic acid, and <5% of a combination of half reacted OH-PEG-carboxylic acid and unreacted PEG, succinic anhydride and 4-Dimethylaminopyridine (DMAP). The resultant mixture was then subjected to solvent evaporation for 24 hours at 40° C and followed by recrystallization of

carboxylic acid-PEG-carboxylic acid in cold (4° C) Isopropyl alcohol (IPA) for 12-24 hours. Resultant cold mixture was then filtered by vacuum filtration to obtain pure carboxylic acid-PEG-carboxylic acid.

[00168] **EXAMPLE 17:** Silver Sulfadiazine functionalization of PEG-PDLLA copolymer.

[00169] 10g of the carboxylic acid-PEG-carboxylic acid of Example 16, 0.0814g of 4-Dimethylaminopyridine (DMAP) and 2.5874g of 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide (EDCI) were taken at a molar ratio (1:0.2:5) and reacted with 10.5g of HO-PDLLA-COOH (acid terminated PDLLA), dissolved 30mL in anhydrous Dichloromethane (DCM) at room temperature (23° -25° C) and left stirring (100-1000RPM) for at least 48 hours. HO-PDLLA-COOH (acid terminated PDLLA) and carboxylic acid-PEG-carboxylic acid were taken in 1:1 weight ratio with a slight excess of PDLLA to promote a full functionalization of PEG. The resultant mixture had >95% COOH-PEG-PDLLA-COOH, which is a di-block polymer, and <5% mixture of (i) unreacted carboxylic acid-PEG-carboxylic acid, (ii) acid terminated PDLLA, (iii) 4-Dimethylaminopyridine (DMAP), and (iv) 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide (EDCI). The resultant mixture was then subjected to solvent evaporation for 24 hours at 40° C, followed by recrystallization of diblock copolymer of COOH-PEG-PDLLA-COOH in cold (4° C) Isopropyl alcohol (IPA) for 12-24 hours. Resultant cold mixture was then filtered by vacuum filtration to obtain pure diblock copolymer of COOH-PEG-PDLLA-COOH.

[00170] The resultant COOH-PEG-PDLLA-COOH (2g) copolymer and silver sulfadiazine (0.40g) were taken at a molar ratio (1:10) and dissolved in 15mL anhydrous Dichloromethane (DCM), and initiated the reaction in presence of 0.055g 1-[Bis(dimethylamino)-methylene]-1H-1,2,3-triazolo[4,5-b] pyridinium-3-oxide-hexafluorophosphate, Hexafluorophosphate Azabenzotriazole Tetramethyl Uronium (HATU) and 0.150g of N,N-Diisopropylethylamine (DIEA) at a molar ratio (1:0.1:0.1) at room temperature (23° -25° C) and left stirring at about 100 to about 1000 rpm for at least 24 hours. Resultant silver sulfadiazine functionalized PEG-PDLLA copolymer was then extracted and purified.

[00171] **EXAMPLE 18:** Silver Sulfadiazine functionalization of PEG-PLGA copolymer.

[00172] 10g of the carboxylic acid-PEG-carboxylic acid of Example 16, 0.0814g of 4-Dimethylaminopyridine (DMAP) and 2.5874g of 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide (EDCI) were taken at a molar ratio (1:0.2:5) and reacted with 10.5g HO- PLGA-COOH (acid terminated PLGA), dissolved in anhydrous Dichloromethane (DCM) at room

temperature (23° -25° C) and left stirring (100-1000RPM) for at least 48 hours. HO- PLGA-COOH (acid terminated PLGA) and carboxylic acid-PEG-carboxylic acid were taken in 1:1 weight ratio. The resultant mixture had >95% COOH-PEG- PLGA-COOH, which is a di-block polymer, and <5% mixture of (i) unreacted carboxylic acid-PEG-carboxylic acid, (ii) acid terminated PLGA, (iii) 4-Dimethylaminopyridine (DMAP), and (iv) 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide (EDCI). The resultant mixture was then subjected to solvent evaporation for 24 hours at 40° C, followed by recrystallization of diblock copolymer of COOH-PEG- PLGA-COOH in cold (4° C) Isopropyl alcohol (IPA) for 12-24 hours. Resultant cold mixture was then filtered by vacuum filtration and dried in vacuum oven to obtain pure diblock copolymer of COOH-PEG- PLGA-COOH.

[00173] The resultant COOH-PEG- PLGA-COOH (2g) copolymer and silver sulfadiazine (0.40g) were taken at a molar ratio (1:10) and dissolved in 15mL anhydrous Dichloromethane (DCM), and initiated the reaction in presence of 0.055g 1-[Bis(dimethylamino)-methylene]-1H-1,2,3-triazolo[4,5-b] pyridinium-3-oxide-hexafluorophosphate, Hexafluorophosphate Azabenzotriazole Tetramethyl Uronium (HATU) and 0.150g of N,N-Diisopropylethylamine (DIEA) at a molar ratio (1:0.1:0.1) at room temperature (23° -25° C) and left stirring at about 100 to about 1000 rpm for at least 24 hours. Resultant silver sulfadiazine functionalized PEG- PLGA copolymer was then extracted and purified.

[00174] **EXAMPLE 19:** Silver Sulfadiazine functionalization of PEG-PCLcopolymer.

[00175] 10g of the carboxylic acid-PEG-carboxylic acid of Example 16, 0.0814g of 4-Dimethylaminopyridine (DMAP) and 2.5874g of 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide (EDCI) were taken at a molar ratio (1:0.2:5) and reacted with 10.5g HO-PCL-COOH (acid terminated PCL), dissolved in anhydrous Dichloromethane (DCM) at room temperature (23° -25° C) and left stirring (100-1000RPM) for at least 48 hours. HO-PCL-COOH (acid terminated PCL) and carboxylic acid-PEG-carboxylic acid were taken in 1:1 weight ratio. The resultant mixture had >95% COOH-PEG-PCL-COOH, which is a di-block polymer, and <5% mixture of (i) unreacted carboxylic acid-PEG-carboxylic acid, (ii) acid terminated PCL, (iii) 4-Dimethylaminopyridine (DMAP), and (iv) 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide (EDCI). The resultant mixture was then subjected to solvent evaporation for 24 hours at 40° C, followed by recrystallization of diblock copolymer of COOH-PEG-PCL-COOH in cold (4° C)

Isopropyl alcohol (IPA) for 12-24 hours. Resultant cold mixture was then filtered by vacuum filtration and dried under vacuum to obtain pure diblock copolymer of COOH-PEG-PCL-COOH.

[00176] The resultant COOH-PEG- PCL-COOH (2g) copolymer and silver sulfadiazine (0.40g) were taken at a molar ratio (1:10) and dissolved in 15mL anhydrous Dichloromethane (DCM), and initiated the reaction in presence of 0.055g 1-[Bis(dimethylamino)-methylene]-1H-1,2,3-triazolo[4,5-b] pyridinium-3-oxide-hexafluorophosphate, Hexafluorophosphate Azabenzotriazole Tetramethyl Uronium (HATU) and 0.150g of N,N-Diisopropylethylamine (DIEA) at a molar ratio (1:0.1:0.1) at room temperature (23° -25° C) and left stirring at about 100 to about 1000 rpm for at least 24 hours. Resultant silver sulfadiazine functionalized PEG- PCL copolymer was then extracted and purified.

[00177] **EXAMPLE 20:** Multi-layer spin coating.

Table -1: multilayer coating configuration of coating compositions.

Samples	Layer 1	Layer 2	Layer 3
1	PDLLA	PDLLA - PEG 5000 (80:20 wt. ratio)	PDLLA - PEG 5000 (60:40 wt. ratio)
2	PLGA	PLGA - PEG 5000 (80:20 wt. ratio)	PLGA - PEG 5000 (60:40 wt. ratio)
3	PCL	PCL - PEG 5000(80:20 wt. ratio)	PCL - PEG 5000 (60:40 wt. ratio)
4	PDLLA	PDLLA - PEG 5000 (80:20 wt. ratio) with AgSD (mixture)	PDLLA - PEG 5000 (60:40 wt. ratio) with AgSD (mixture)
5	PLGA	PLGA - PEG 5000 (80:20 wt. ratio) with AgSD (mixture)	PLGA - PEG 5000 (60:40 wt. ratio) with AgSD (mixture)
6	PCL	PCL - PEG 5000 (80:20 wt. ratio) with AgSD (mixture)	PCL - PEG 5000 (60:40 wt. ratio) with AgSD (mixture)
7	PDLLA	AgSD functionalized PDLLA - PEG 6000 copolymer (80:20 wt. ratio)	AgSD functionalized PDLLA - PEG 6000 copolymer (60:40 wt. ratio)
8	PLGA	AgSD functionalized PLGA - PEG 6000 copolymer (80:20 wt. ratio)	AgSD functionalized PLGA - PEG 6000 copolymer (60:40 wt. ratio)
9	PCL	AgSD functionalized PCL - PEG 6000 copolymer (80:20 wt. ratio)	AgSD functionalized PCL - PEG 6000 copolymer (60:40 wt. ratio)

[00178] A Titanium substrate was coated with multiple layers of polymer compositions according to Table-1 in a bottom-up spin coating procedure in the specific order wherein, the top layer will have higher PEG % than the previous layer. The coating was performed at 3000-6000 rpm for a period of 30 seconds for each layer with the exception of 60 seconds for the last layer of PDLLA-PEG (60:40) to give enough time to dry.

[00179] While the compositions and methods of the disclosed and/or claimed inventive concept(s) have been described in terms of particular aspects, it will be apparent to those of ordinary skill in the art that variations may be applied to the compositions and/or methods and in

the steps or in the sequence of steps of the method described herein without departing from the concept, spirit, and scope of the disclosed and/or claimed inventive concept(s). All such similar substitutes and modifications apparent to those skilled in the art are deemed to be within the spirit, scope, and concept of the disclosed and/or claimed inventive concept(s).

What is claimed is:

1. A coating composition comprising:
 - A. a mixture of:
 - (i) about 0.01 wt. % to about 99.99 wt. % at least one copolymer comprising:
 - (a) methyl ether polyethylene glycol (mPEG), a first component; and (b) at least one second component comprises poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); and,
 - (ii) about 0.01 wt. % to about 10 wt. % silver sulfadiazine (AgSD), an antimicrobial agent;
 - B. about 0.01 wt. % to about 99.99 wt. % at least one silver sulfadiazine (AgSD) functionalized copolymer, wherein, the copolymer comprises (a) polyethylene glycol (PEG), a first component; and (b) at least one second component comprises poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL);
 - or,
 - C. about 0.01 wt. % to about 99.99 wt. % mixture of A and B.
2. The coating composition according to claim 1(A), wherein the methyl ether polyethylene glycol (mPEG) has a molecular weight ranging from about 2000 Daltons to about 15000 Daltons.
3. The coating composition according to claim 1(B), wherein the polyethylene glycol (PEG) has a molecular weight ranging from about 2000 Daltons to about 15000 Daltons.
4. The coating composition according to claim 1, wherein
 - the amount of methyl ether polyethylene glycol (mPEG) of claim 1(A) is ranging from about 0.01 wt.% to about 60 wt.% of the total weight of the copolymer; and,
 - the amount of polyethylene glycol (PEG) of claim 1(B) is ranging from about 0.01 wt.% to about 60 wt.% of the total weight of the silver sulfadiazine functionalized copolymer.
5. The coating composition according to claim 1, wherein the poly(D,L-lactide) (PDLLA) has a molecular weight ranging from about 10,000 Daltons to about 100,000 Daltons.

6. The coating composition according to claim 1, wherein the poly(lactic-co-glycolic acid) (PLGA) has a molecular weight ranging from about 10,000 Daltons to about 100,000 Daltons.

7. The coating composition according to claim 1, wherein the poly(lactic-co-glycolic acid) (PLGA) comprises lactic acid and glycolic acid comonomers in the ratio of 1:10 to 10:1.

8. The coating composition according to claim 1, wherein the poly(ϵ -caprolactone) (PCL) has a molecular weight ranging from about 10,000 Daltons to about 300,000 Daltons.

9. The coating composition according to claim 1(A) and claim 1(B), wherein the amount of second component of the copolymer is ranging from about 40 wt.% to about 99.99 wt.% of the total weight of the copolymer.

10. The coating composition according to claim 1(A), wherein the antimicrobial agent further comprises silver iodide, silver benzoate, silver oxide, silver nitrite, silver laurate, silver acetate, silver palmitate, silver lactate, silver iodate, silver carbonate, and combinations thereof.

11. The coating composition according to claim 1, wherein the copolymer has a degradation time ranging from about 10 days to about 600 days.

12. The coating composition according to claim 1(A), wherein the weight average molecular weight of the copolymer is ranging from about 10,000 Daltons to about 400,000 Daltons.

13. The coating composition according to claim 1(B), wherein the weight average molecular weight of the silver sulfadiazine functionalized copolymer is ranging from about 10,000 Daltons to about 400,000 Daltons.

14. The coating composition according to claim 1(A), wherein the copolymer is bioresorbable.

15. The coating composition according to claim 1(B), wherein the silver sulfadiazine functionalized copolymer is bioresorbable.

16. The coating composition according to claim 1, wherein the composition is an anti-fouling composition and an anti-bacterial composition.

17. The coating composition according to claim 1, wherein the composition kills or inhibits microorganisms selected from the group consisting of *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, and combinations thereof.

18. The coating composition according to claim 1, wherein the composition is in the form of powder, granules, pellets, grains, or flakes.

19. The coating composition according to claim 1, wherein the composition is used for coating surfaces selected from the group consisting of metallic surface, polymeric surface, masonry surface, wooden surface, glass surface, fabric surface, and elastomeric surface.

20. The coating composition according to claim 1, wherein the composition is used for coating medical devices, hospital equipments, diagnostic equipments, laboratory instruments, surgical instruments, utensils, electronic equipments, safety equipments, furniture, and building walls and floors.

21. The coating composition according to claim 20, wherein the medical devices selected from the group consisting of biomedical implants, dental implants, hard tissue and soft tissue prosthetic devices, joint replacements, plates, screws, stents, sheets, scaffolds, matrixes, endoscopes, catheters, probes, electrodes, mitral clips, balloon device, guidewires, drain tubes, urinary devices, needles, sutures, surgical staples, and contact lenses.

22. The coating composition according to claim 1, wherein the composition is coated using solvent casting, spin coating, dip coating, spray coating, slot die coating, brushing, doctor blade coating, roller coating, screen printing, nozzle printing, 3D-printing, extrusion coating, and curtain coating.

23. The coating composition according to claim 1, wherein the composition is applied as a multilayer coating.

24. The coating composition according to claim 23, wherein the multilayer coating comprises up to five layers or up to three layers.

25. The coating composition according to claim 23, wherein the multilayer coating comprising the structure of:

first layer comprises at least one polymer selected from poly(D,L-lactide), poly(lactic-co-glycolic acid), or poly(ϵ -caprolactone); and,
second to fifth layer comprises composition of claim 1(A) or claim 1(B).

26. The coating composition according to claim 1(A), wherein the mixture is prepared by copolymerizing:

(a) about 0.01 wt.% to about 60 wt.% methyl ether polyethylene glycol (mPEG),
a first component; and,

- (b) about 40 wt.% to about 99.99 wt.% at least one second component comprises poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL);

wherein, the polymerization is carried out using a Tin based catalyst, in presence of an inert gas and at a temperature ranging from about 100° C to about 200° C.

27. The coating composition according to claim 1(B), wherein the silver sulfadiazine functionalized copolymer is prepared by:

- (i) reacting polyethylene glycol (PEG) with succinic anhydride at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one solvent to obtain carboxylic acid-PEG-carboxylic acid;
- (ii) reacting carboxylic acid-PEG-carboxylic acid of step (i) and at least one polymer selected from acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ϵ -caprolactone), at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one carbodiimide to obtain a copolymer; and,
- (iii) reacting the copolymer of step (ii) and silver sulfadiazine at a molar ratio ranging from about 1:15 to about 15:1 in presence of at least one solvent and at least one catalyst to obtain the silver sulfadiazine functionalized copolymer.

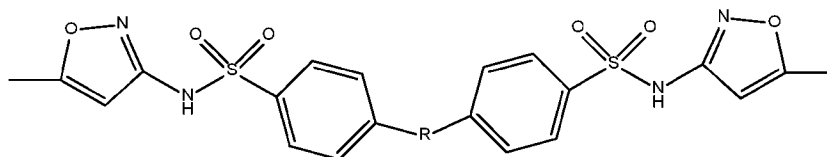
28. The coating composition according to claim 27, wherein the amine is selected from the group consisting of dimethylaminopyridine, triethylamine, triisopropylamine, methylmorpholine, triethylamine, 2-ethyl-5-methylpyridine, anhydrous pyridine, N-methylimidazole, diazabicyclooctane, and combinations thereof.

29. The coating composition according to claim 27, wherein the solvent is selected from the group consisting of anhydrous dichloromethane, dichloroethane, tetrachloroethane, chloroform, tetrachloromethane, trichloroethane, ethylene dichloride, and combinations thereof.

30. The coating composition according to claim 27, wherein the carbodiimide is selected from the group consisting of 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide, 1-cyclohexyl-3-(2-morpholinoethyl) carbodiimide, N,N'-dicyclohexylcarbodiimide, dicyclohexylcarbodiimide, diisopropyl carbodiimide, and combinations thereof.

31. The coating composition according to claim 27, wherein the catalyst is selected from the group consisting of Uronium based catalysts, amine based catalysts, Tin based catalysts, and combinations thereof.

32. A silver sulfadiazine functionalized copolymer having formula:



wherein, R is a copolymer of:

- (a) polyethylene glycol (PEG), a first component; and,
- (b) at least one second component selected from poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL).

33. The copolymer according to claim 32, wherein the first component polyethylene glycol (PEG) has a molecular weight ranging from about 2000 Daltons to about 15,000 Daltons.

34. The copolymer according to claim 32, wherein the amount of first component polyethylene glycol (PEG) of the copolymer is ranging from about 0.01 wt.% to about 60 wt.% of the total weight of the copolymer.

35. The copolymer according to claim 32, wherein the poly(D,L-lactide) (PDLLA) has a molecular weight ranging from about 10,000 Daltons to about 100,000 Daltons.

36. The copolymer according to claim 32, wherein the poly(lactic-co-glycolic acid) (PLGA) has a molecular weight ranging from about 10,000 Daltons to about 100,000 Daltons.

37. The copolymer according to claim 32, wherein the poly(lactic-co-glycolic acid) (PLGA) comprises lactic acid and glycolic acid comonomers in the ratio of 1:10 to 10:1.

38. The copolymer according to claim 32, wherein the poly(ϵ -caprolactone) (PCL) has a molecular weight ranging from about 10,000 Daltons to about 300,000 Daltons.

39. The copolymer according to claim 32, wherein the amount of second component of the copolymer is ranging from about 40 wt.% to about 99.99 wt.% of the total weight of the copolymer.

40. The copolymer according to claim 32, wherein the copolymer has a degradation time ranging from about 10 days to about 600 days.

41. The copolymer according to claim 32, wherein the weight average molecular weight of the copolymer is ranging from about 10,000 Daltons to about 400,000 Daltons.

42. The copolymer according to claim 32, wherein the copolymer is bioresorbable.

43. The copolymer according to claim 32 is used in personal care compositions, home care compositions, pharmaceutical compositions, industrial compositions, coating compositions, ink compositions, oral care compositions, health care compositions, packaging materials, food compositions, and beverage compositions.

44. The copolymer according to claim 32 is used in medical devices selected from the group consisting of biomedical implants, dental implants, hard tissue and soft tissue prosthetic devices, joint replacements, plates, screws, stents, sheets, scaffolds, matrixes, endoscopes, catheters, probes, electrodes, mitral clips, balloon device, guidewires, drain tubes, urinary devices, needles, sutures, surgical staples, glue, and contact lenses.

45. A process for preparing the copolymer of claim 32, wherein the process comprising the steps of:

(i) reacting polyethylene glycol (PEG) with succinic anhydride at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one solvent to obtain carboxylic acid-PEG-carboxylic acid;

(ii) reacting carboxylic acid-PEG-carboxylic acid of step (i) and at least one polymer selected from acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ϵ -caprolactone), at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one carbodiimide to obtain a copolymer; and,

(iii) reacting the copolymer of step (ii) and silver sulfadiazine at a molar ratio ranging from about 1:15 to about 15:1 in presence of at least one solvent and at least one catalyst to obtain the silver sulfadiazine functionalized copolymer.

46. The process according to claim 45, wherein the amine is selected from the group consisting of dimethylaminopyridine, triethylamine, triisopropylamine, methylmorpholine, triethylamine, 2-ethyl-5-methylpyridine, anhydrous pyridine, N-methylimidazole, diazabicyclooctane, and combinations thereof.

47. The process according to claim 45, wherein the solvent is selected from the group consisting of anhydrous dichloromethane, dichloroethane, tetrachloroethane, chloroform, tetrachloromethane, trichloroethane, ethylene dichloride, and combinations thereof.

48. The process according to claim 45, wherein the carbodiimide is selected from the group consisting of 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide, 1-cyclohexyl-3-(2-morpholinoethyl) carbodiimide, N,N'-dicyclohexylcarbodiimide, dicyclohexylcarbodiimide, diisopropyl carbodiimide, and combinations thereof.

49. The process according to claim 45, wherein the catalyst is selected from the group consisting of Uronium based catalysts, amine based catalysts, Tin based catalysts, and combinations thereof.

ABSTRACT

Present application relates to a coating composition comprising (A) a copolymer of (a) methyl ether polyethylene glycol, and (b) at least one component selected from poly(D,L-lactide), poly(lactic-co-glycolic acid), or poly(ϵ -caprolactone); or (ii) silver sulfadiazine; or (B) a silver sulfadiazine functionalized copolymer of (a) polyethylene glycol, and (b) at least one component selected from poly(D,L-lactide), poly(lactic-co-glycolic acid), or poly(ϵ -caprolactone); or (C) a mixture of A and B. Also discloses the process for preparing the claimed copolymers and its use thereof.

What is claimed is:

1. A coating composition comprising:
 - A. a mixture of:
 - (i) about 0.01 wt. % to about 99.99 wt. % at least one copolymer comprising:
 - (a) methyl ether polyethylene glycol (mPEG), a first component; and (b) at least one second component comprises poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL); and,
 - (ii) about 0.01 wt. % to about 10 wt. % silver sulfadiazine (AgSD), an antimicrobial agent;
 - B. about 0.01 wt. % to about 99.99 wt. % at least one silver sulfadiazine (AgSD) functionalized copolymer, wherein, the copolymer comprises (a) polyethylene glycol (PEG), a first component; and (b) at least one second component comprises poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL);
 - or,
 - C. about 0.01 wt. % to about 99.99 wt. % mixture of A and B.
2. The coating composition according to claim 1(A), wherein the methyl ether polyethylene glycol (mPEG) has a molecular weight ranging from about 2000 Daltons to about 15000 Daltons.
3. The coating composition according to claim 1(B), wherein the polyethylene glycol (PEG) has a molecular weight ranging from about 2000 Daltons to about 15000 Daltons.
4. The coating composition according to claim 1, wherein
 - the amount of methyl ether polyethylene glycol (mPEG) of claim 1(A) is ranging from about 0.01 wt.% to about 60 wt.% of the total weight of the copolymer; and,
 - the amount of polyethylene glycol (PEG) of claim 1(B) is ranging from about 0.01 wt.% to about 60 wt.% of the total weight of the silver sulfadiazine functionalized copolymer.
5. The coating composition according to claim 1, wherein the poly(D,L-lactide) (PDLLA) has a molecular weight ranging from about 10,000 Daltons to about 100,000 Daltons.

6. The coating composition according to claim 1, wherein the poly(lactic-co-glycolic acid) (PLGA) has a molecular weight ranging from about 10,000 Daltons to about 100,000 Daltons.

7. The coating composition according to claim 1, wherein the poly(lactic-co-glycolic acid) (PLGA) comprises lactic acid and glycolic acid comonomers in the ratio of 1:10 to 10:1.

8. The coating composition according to claim 1, wherein the poly(ϵ -caprolactone) (PCL) has a molecular weight ranging from about 10,000 Daltons to about 300,000 Daltons.

9. The coating composition according to claim 1(A) and claim 1(B), wherein the amount of second component of the copolymer is ranging from about 40 wt.% to about 99.99 wt.% of the total weight of the copolymer.

10. The coating composition according to claim 1(A), wherein the antimicrobial agent further comprises silver iodide, silver benzoate, silver oxide, silver nitrite, silver laurate, silver acetate, silver palmitate, silver lactate, silver iodate, silver carbonate, and combinations thereof.

11. The coating composition according to claim 1, wherein the copolymer has a degradation time ranging from about 10 days to about 600 days.

12. The coating composition according to claim 1(A), wherein the weight average molecular weight of the copolymer is ranging from about 10,000 Daltons to about 400,000 Daltons.

13. The coating composition according to claim 1(B), wherein the weight average molecular weight of the silver sulfadiazine functionalized copolymer is ranging from about 10,000 Daltons to about 400,000 Daltons.

14. The coating composition according to claim 1(A), wherein the copolymer is bioresorbable.

15. The coating composition according to claim 1(B), wherein the silver sulfadiazine functionalized copolymer is bioresorbable.

16. The coating composition according to claim 1, wherein the composition is an anti-fouling composition and an anti-bacterial composition.

17. The coating composition according to claim 1, wherein the composition kills or inhibits microorganisms selected from the group consisting of *Pseudomonas aeruginosa*, *Staphylococcus epidermidis*, *Staphylococcus aureus*, and combinations thereof.

18. The coating composition according to claim 1, wherein the composition is in the form of powder, granules, pellets, grains, or flakes.

19. The coating composition according to claim 1, wherein the composition is used for coating surfaces selected from the group consisting of metallic surface, polymeric surface, masonry surface, wooden surface, glass surface, fabric surface, and elastomeric surface.

20. The coating composition according to claim 1, wherein the composition is used for coating medical devices, hospital equipments, diagnostic equipments, laboratory instruments, surgical instruments, utensils, electronic equipments, safety equipments, furniture, and building walls and floors.

21. The coating composition according to claim 20, wherein the medical devices selected from the group consisting of biomedical implants, dental implants, hard tissue and soft tissue prosthetic devices, joint replacements, plates, screws, stents, sheets, scaffolds, matrixes, endoscopes, catheters, probes, electrodes, mitral clips, balloon device, guidewires, drain tubes, urinary devices, needles, sutures, surgical staples, and contact lenses.

22. The coating composition according to claim 1, wherein the composition is coated using solvent casting, spin coating, dip coating, spray coating, slot die coating, brushing, doctor blade coating, roller coating, screen printing, nozzle printing, 3D-printing, extrusion coating, and curtain coating.

23. The coating composition according to claim 1, wherein the composition is applied as a multilayer coating.

24. The coating composition according to claim 23, wherein the multilayer coating comprises up to five layers or up to three layers.

25. The coating composition according to claim 23, wherein the multilayer coating comprising the structure of:

first layer comprises at least one polymer selected from poly(D,L-lactide), poly(lactic-co-glycolic acid), or poly(ϵ -caprolactone); and,
second to fifth layer comprises composition of claim 1(A) or claim 1(B).

26. The coating composition according to claim 1(A), wherein the mixture is prepared by copolymerizing:

(a) about 0.01 wt.% to about 60 wt.% methyl ether polyethylene glycol (mPEG),
a first component; and,

- (b) about 40 wt.% to about 99.99 wt.% at least one second component comprises poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL);

wherein, the polymerization is carried out using a Tin based catalyst, in presence of an inert gas and at a temperature ranging from about 100° C to about 200° C.

27. The coating composition according to claim 1(B), wherein the silver sulfadiazine functionalized copolymer is prepared by:

- (i) reacting polyethylene glycol (PEG) with succinic anhydride at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one solvent to obtain carboxylic acid-PEG-carboxylic acid;
- (ii) reacting carboxylic acid-PEG-carboxylic acid of step (i) and at least one polymer selected from acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ϵ -caprolactone), at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one carbodiimide to obtain a copolymer; and,
- (iii) reacting the copolymer of step (ii) and silver sulfadiazine at a molar ratio ranging from about 1:15 to about 15:1 in presence of at least one solvent and at least one catalyst to obtain the silver sulfadiazine functionalized copolymer.

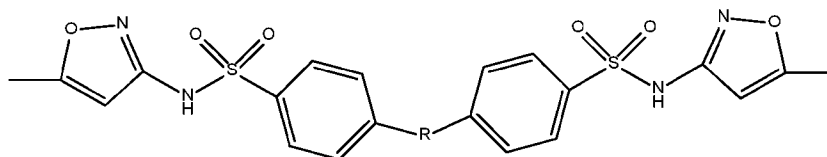
28. The coating composition according to claim 27, wherein the amine is selected from the group consisting of dimethylaminopyridine, triethylamine, triisopropylamine, methylmorpholine, triethylamine, 2-ethyl-5-methylpyridine, anhydrous pyridine, N-methylimidazole, diazabicyclooctane, and combinations thereof.

29. The coating composition according to claim 27, wherein the solvent is selected from the group consisting of anhydrous dichloromethane, dichloroethane, tetrachloroethane, chloroform, tetrachloromethane, trichloroethane, ethylene dichloride, and combinations thereof.

30. The coating composition according to claim 27, wherein the carbodiimide is selected from the group consisting of 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide, 1-cyclohexyl-3-(2-morpholinoethyl) carbodiimide, N,N'-dicyclohexylcarbodiimide, dicyclohexylcarbodiimide, diisopropyl carbodiimide, and combinations thereof.

31. The coating composition according to claim 27, wherein the catalyst is selected from the group consisting of Uronium based catalysts, amine based catalysts, Tin based catalysts, and combinations thereof.

32. A silver sulfadiazine functionalized copolymer having formula:



wherein, R is a copolymer of:

- (a) polyethylene glycol (PEG), a first component; and,
- (b) at least one second component selected from poly(D,L-lactide) (PDLLA), poly(lactic-co-glycolic acid) (PLGA), or poly(ϵ -caprolactone) (PCL).

33. The copolymer according to claim 32, wherein the first component polyethylene glycol (PEG) has a molecular weight ranging from about 2000 Daltons to about 15,000 Daltons.

34. The copolymer according to claim 32, wherein the amount of first component polyethylene glycol (PEG) of the copolymer is ranging from about 0.01 wt.% to about 60 wt.% of the total weight of the copolymer.

35. The copolymer according to claim 32, wherein the poly(D,L-lactide) (PDLLA) has a molecular weight ranging from about 10,000 Daltons to about 100,000 Daltons.

36. The copolymer according to claim 32, wherein the poly(lactic-co-glycolic acid) (PLGA) has a molecular weight ranging from about 10,000 Daltons to about 100,000 Daltons.

37. The copolymer according to claim 32, wherein the poly(lactic-co-glycolic acid) (PLGA) comprises lactic acid and glycolic acid comonomers in the ratio of 1:10 to 10:1.

38. The copolymer according to claim 32, wherein the poly(ϵ -caprolactone) (PCL) has a molecular weight ranging from about 10,000 Daltons to about 300,000 Daltons.

39. The copolymer according to claim 32, wherein the amount of second component of the copolymer is ranging from about 40 wt.% to about 99.99 wt.% of the total weight of the copolymer.

40. The copolymer according to claim 32, wherein the copolymer has a degradation time ranging from about 10 days to about 600 days.

41. The copolymer according to claim 32, wherein the weight average molecular weight of the copolymer is ranging from about 10,000 Daltons to about 400,000 Daltons.

42. The copolymer according to claim 32, wherein the copolymer is bioresorbable.

43. The copolymer according to claim 32 is used in personal care compositions, home care compositions, pharmaceutical compositions, industrial compositions, coating compositions, ink compositions, oral care compositions, health care compositions, packaging materials, food compositions, and beverage compositions.

44. The copolymer according to claim 32 is used in medical devices selected from the group consisting of biomedical implants, dental implants, hard tissue and soft tissue prosthetic devices, joint replacements, plates, screws, stents, sheets, scaffolds, matrixes, endoscopes, catheters, probes, electrodes, mitral clips, balloon device, guidewires, drain tubes, urinary devices, needles, sutures, surgical staples, glue, and contact lenses.

45. A process for preparing the copolymer of claim 32, wherein the process comprising the steps of:

(i) reacting polyethylene glycol (PEG) with succinic anhydride at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one solvent to obtain carboxylic acid-PEG-carboxylic acid;

(ii) reacting carboxylic acid-PEG-carboxylic acid of step (i) and at least one polymer selected from acid terminated poly(D,L-lactide), acid terminated poly(lactic-co-glycolic acid), or acid terminated poly(ϵ -caprolactone), at a molar ratio ranging from about 1:5 to about 5:1 in presence of at least one amine and at least one carbodiimide to obtain a copolymer; and,

(iii) reacting the copolymer of step (ii) and silver sulfadiazine at a molar ratio ranging from about 1:15 to about 15:1 in presence of at least one solvent and at least one catalyst to obtain the silver sulfadiazine functionalized copolymer.

46. The process according to claim 45, wherein the amine is selected from the group consisting of dimethylaminopyridine, triethylamine, triisopropylamine, methylmorpholine, triethylamine, 2-ethyl-5-methylpyridine, anhydrous pyridine, N-methylimidazole, diazabicyclooctane, and combinations thereof.

47. The process according to claim 45, wherein the solvent is selected from the group consisting of anhydrous dichloromethane, dichloroethane, tetrachloroethane, chloroform, tetrachloromethane, trichloroethane, ethylene dichloride, and combinations thereof.

48. The process according to claim 45, wherein the carbodiimide is selected from the group consisting of 1-Ethyl-3-(3dimethylaminopropyl) carbodiimide, 1-cyclohexyl-3-(2-morpholinoethyl) carbodiimide, N,N'-dicyclohexylcarbodiimide, dicyclohexylcarbodiimide, diisopropyl carbodiimide, and combinations thereof.

49. The process according to claim 45, wherein the catalyst is selected from the group consisting of Uronium based catalysts, amine based catalysts, Tin based catalysts, and combinations thereof.

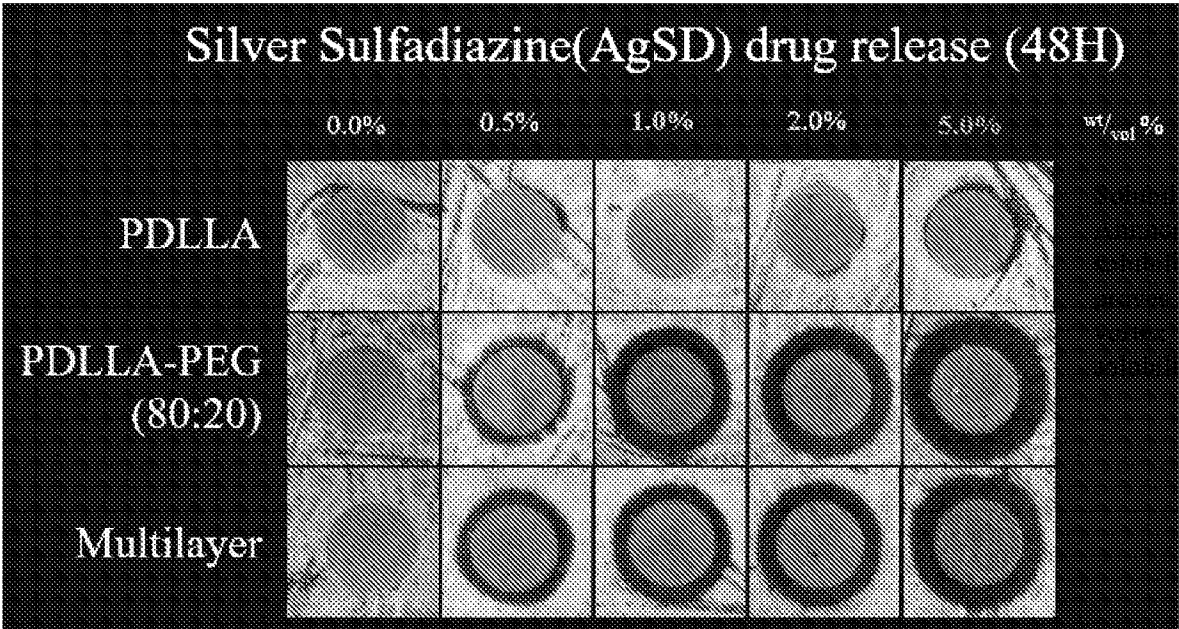


FIG. 1

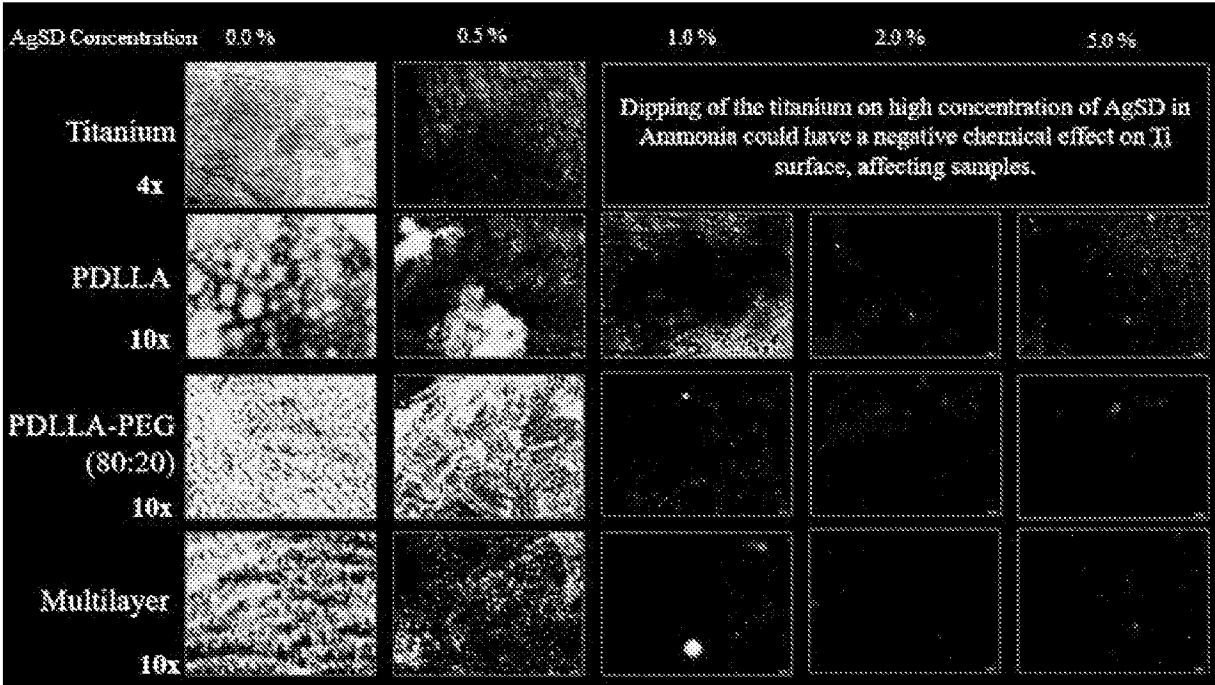


FIG. 1A

2/9

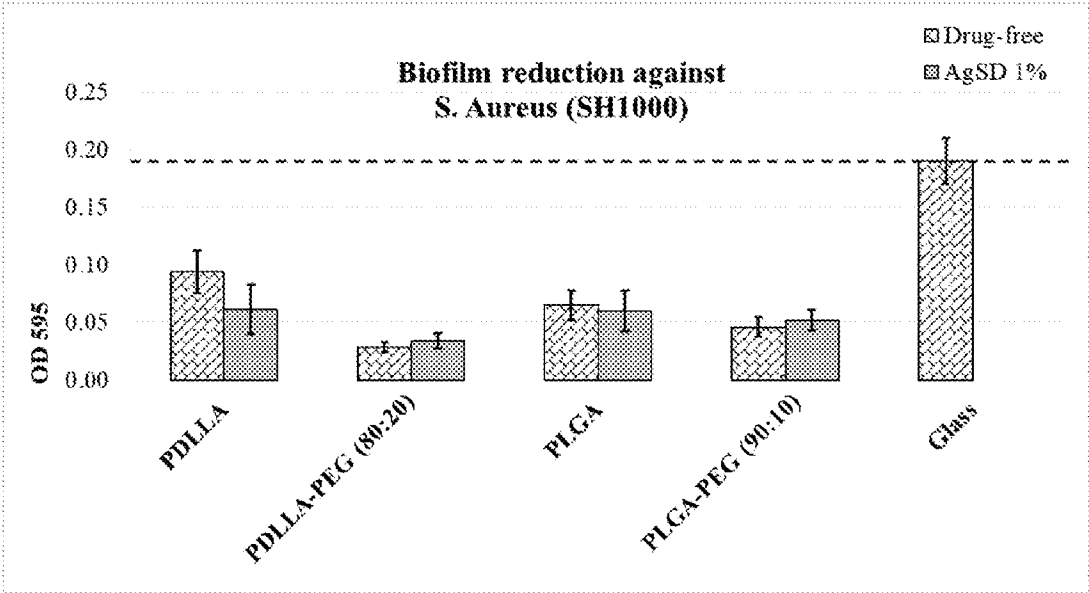


FIG. 2

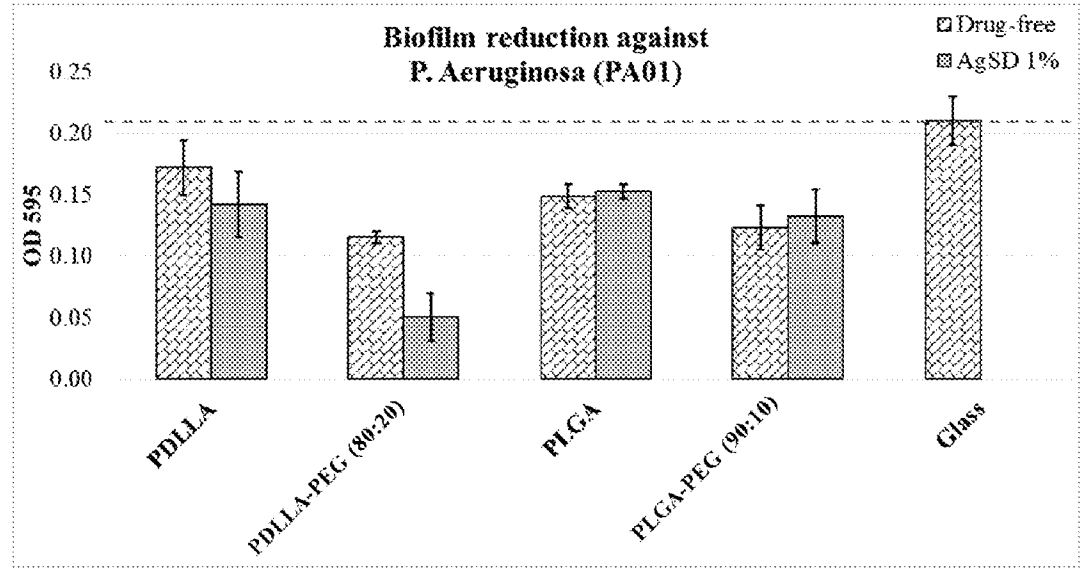


FIG. 3

3/9

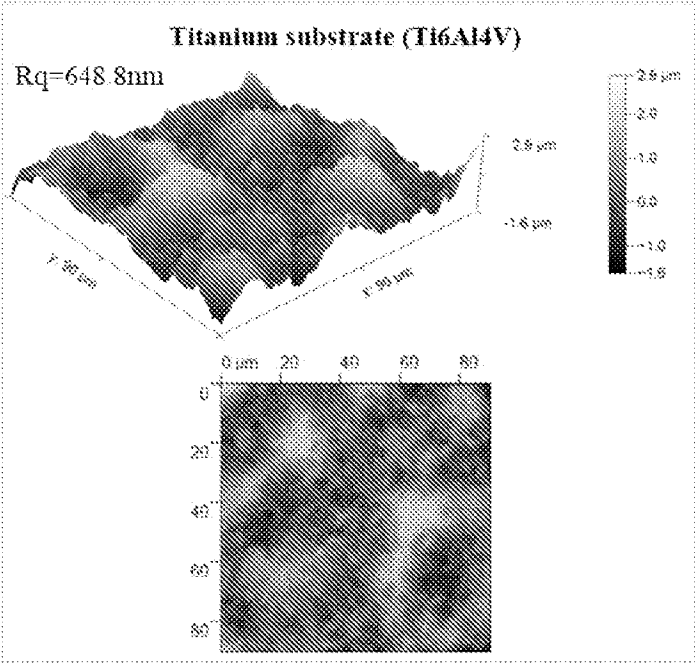


FIG. 4

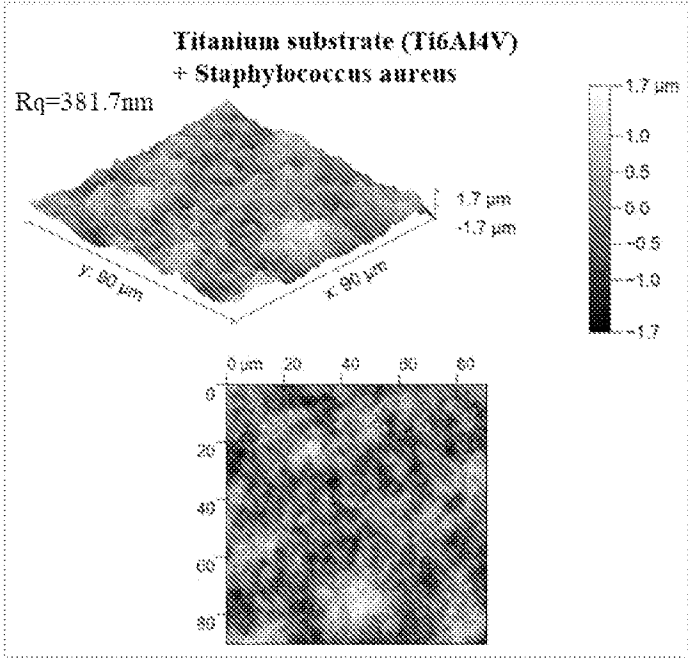


FIG. 5

4/9

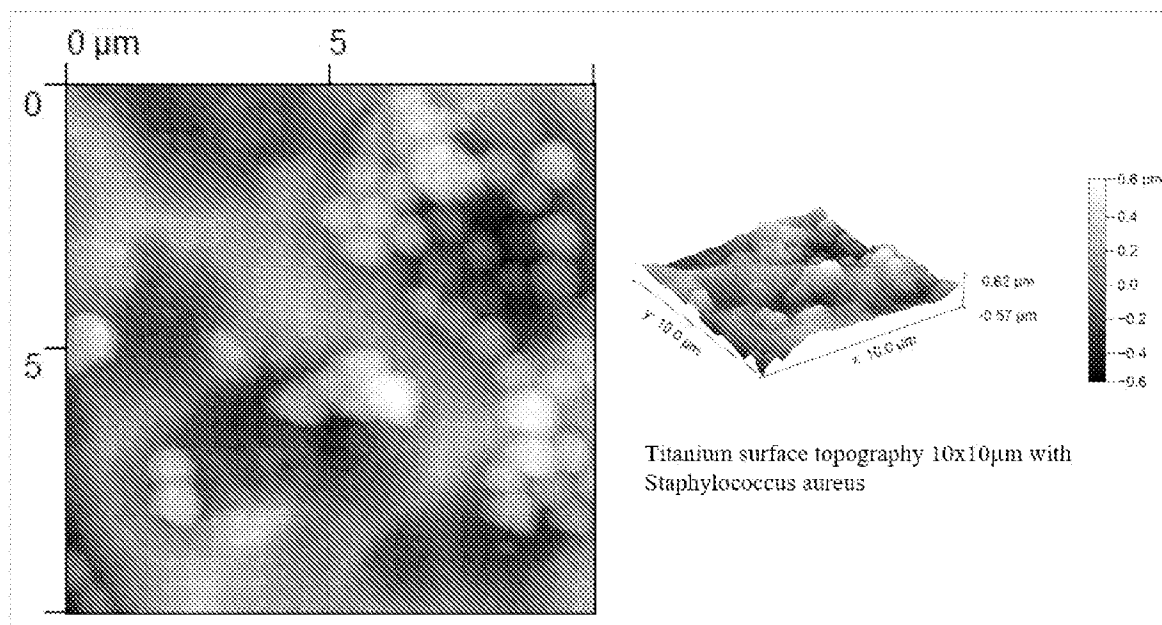


FIG. 6

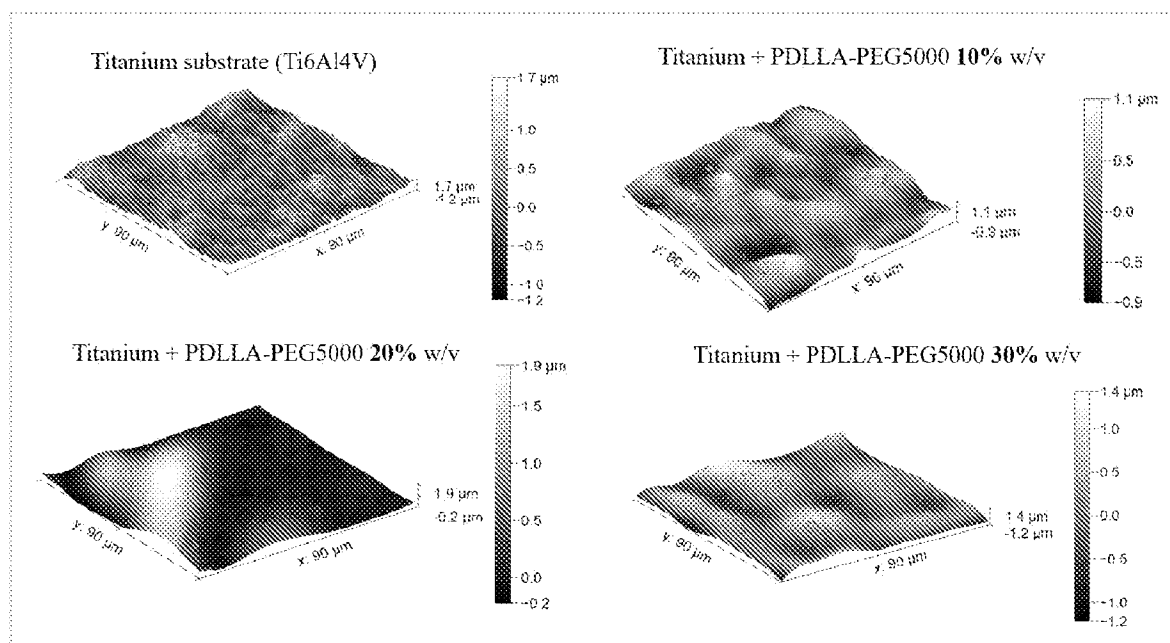


FIG. 7

5/9

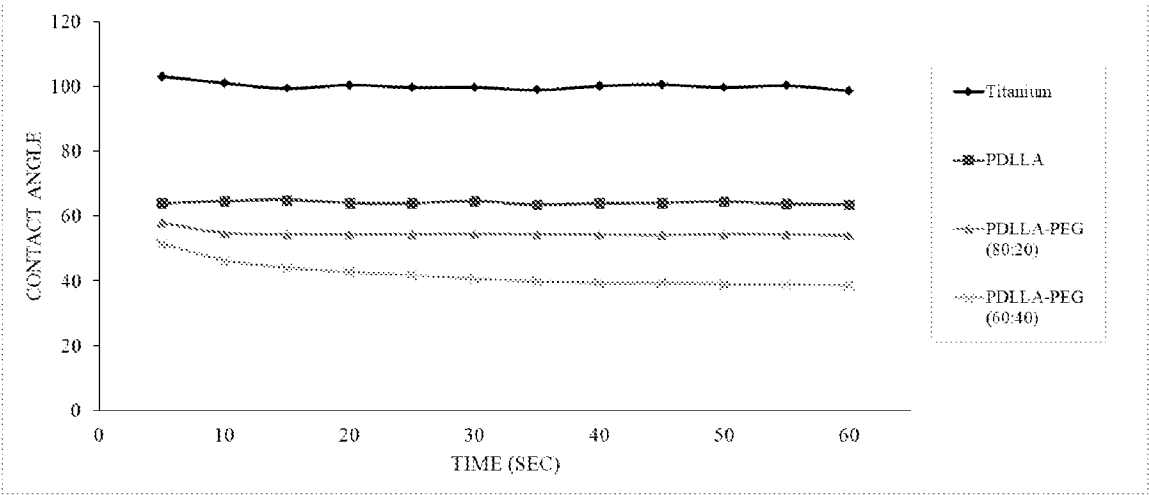


FIG. 8

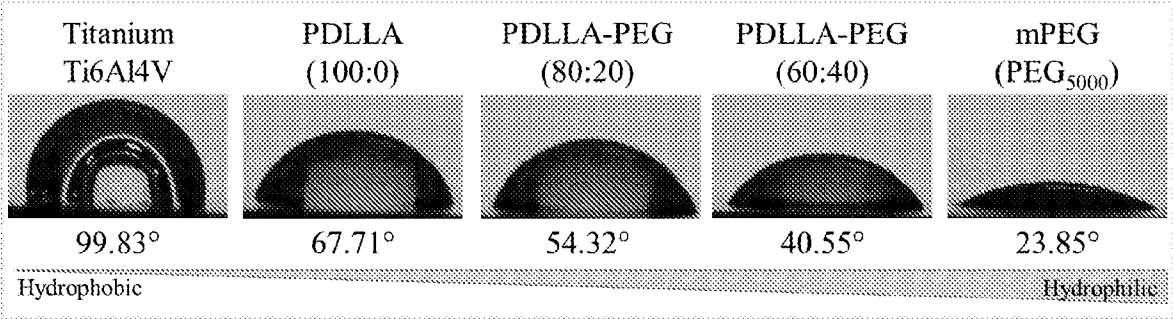


FIG. 9

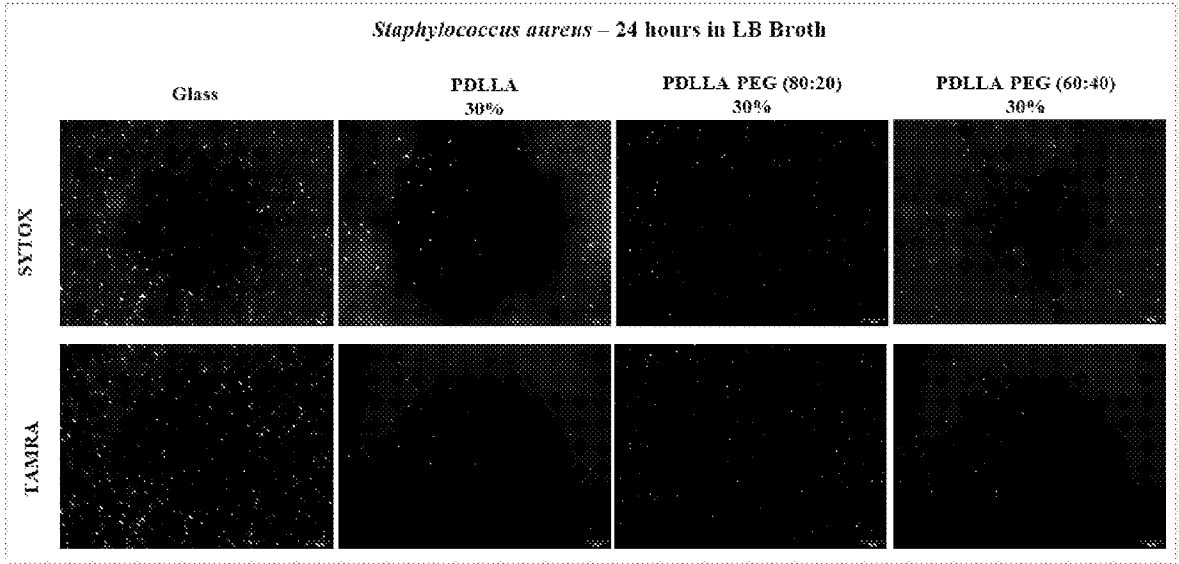


FIG. 10

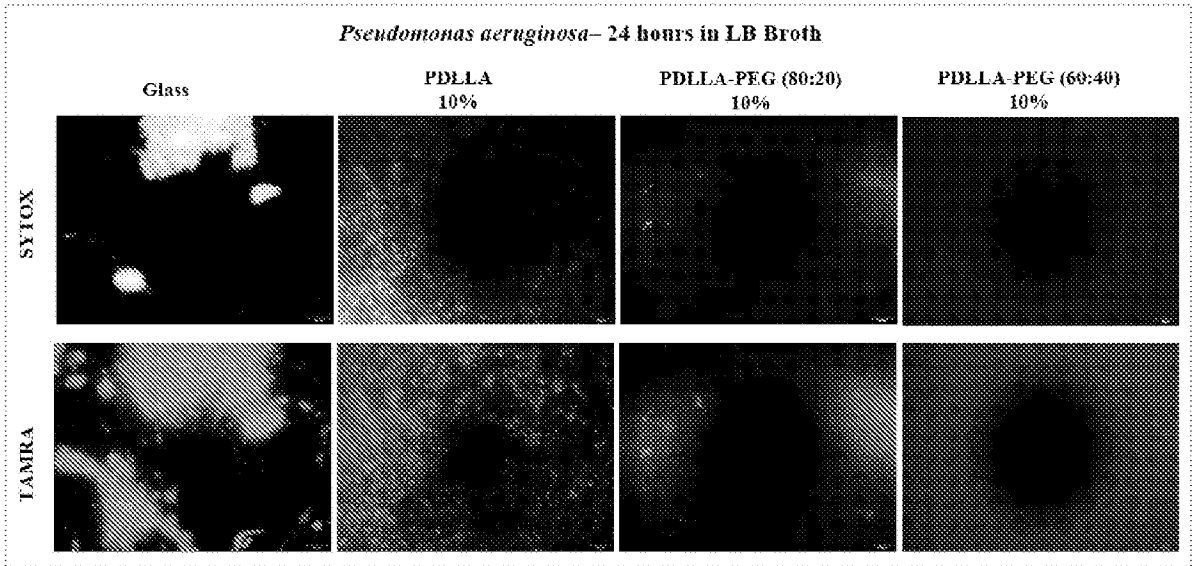


FIG. 11

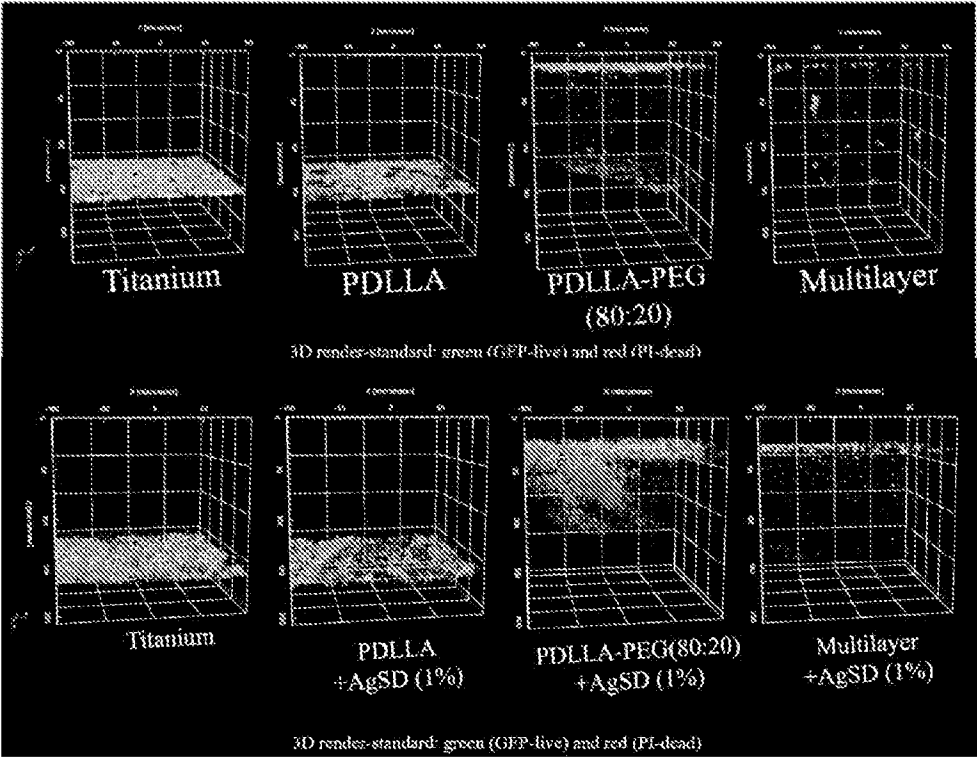


FIG. 12

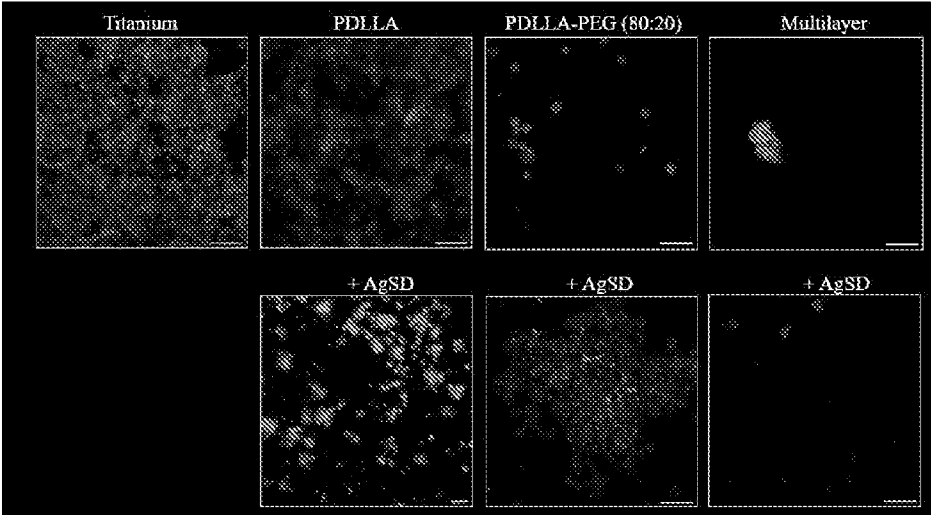


FIG. 13

8/9

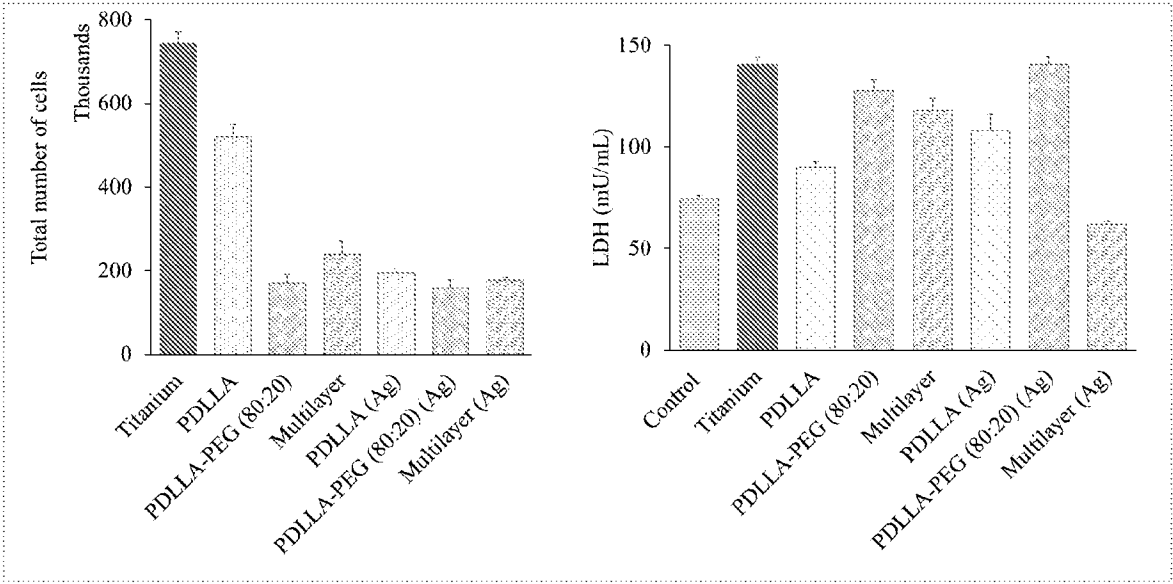


FIG. 14

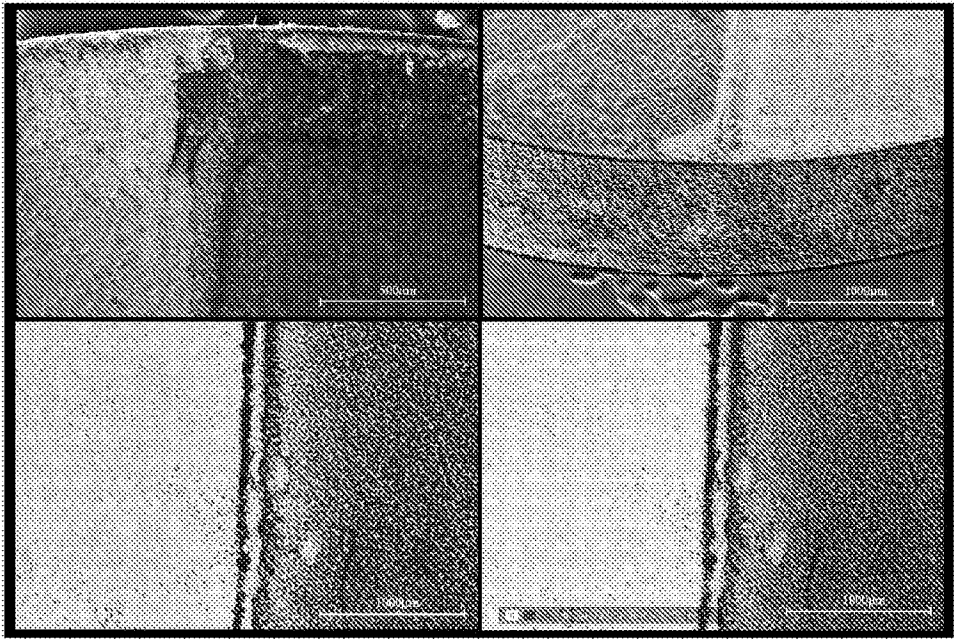


FIG. 15

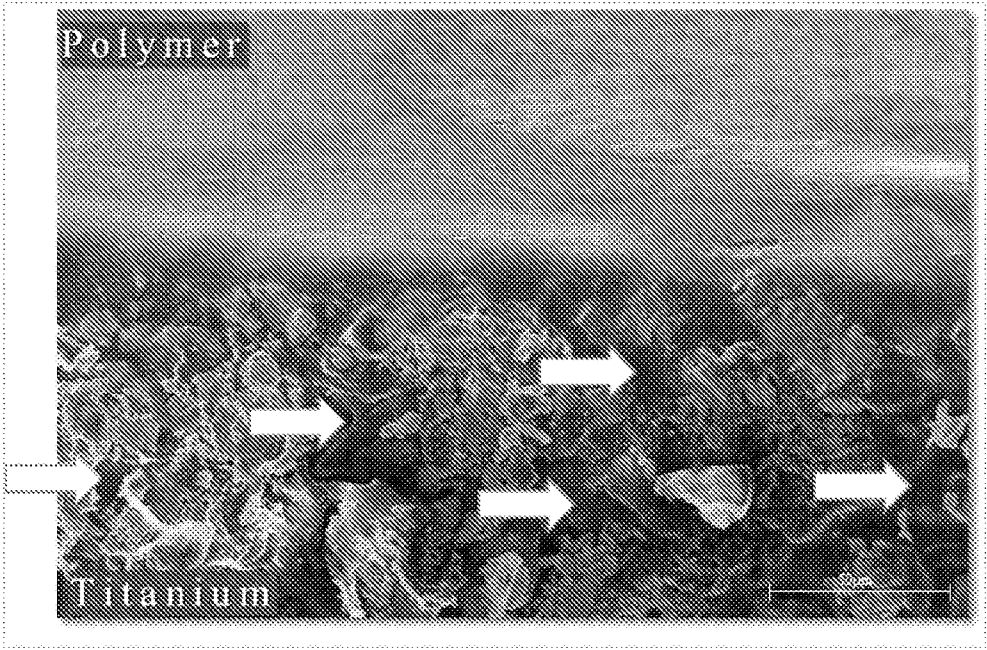


Fig. 15A

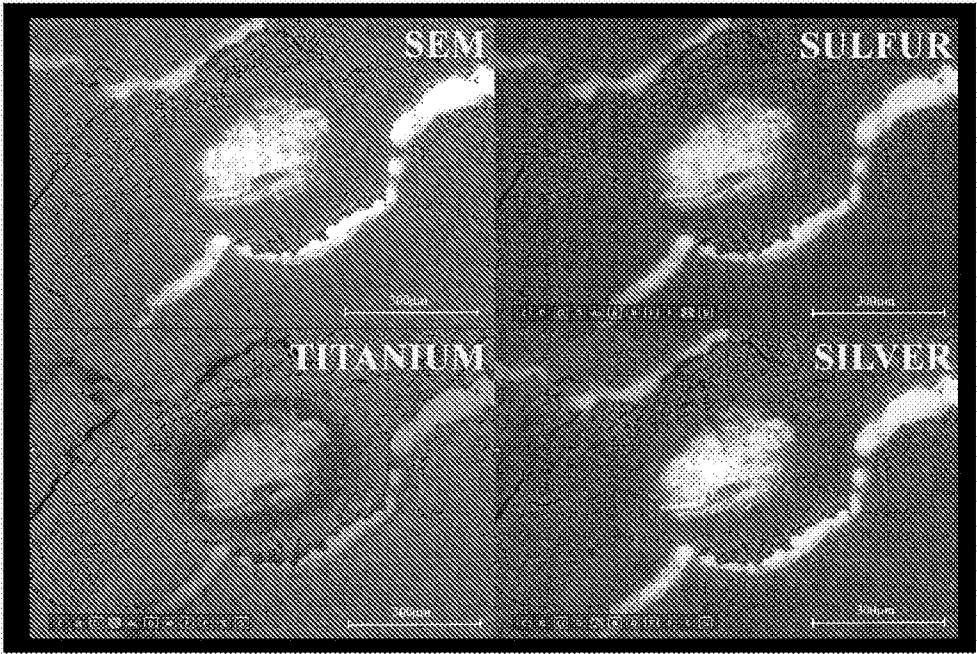


FIG. 16