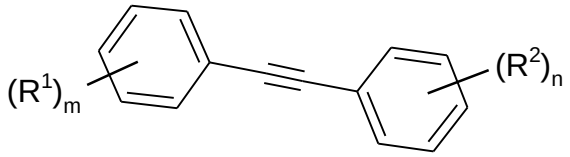
CLAIMS

What is claimed is:

1. A method for inhibiting growth of, or killing, suspected pathogenic microbes on a physical surface, comprising contacting the physical surface with an antimicrobial formulation comprising:

an anti-microbially effective amount of a substituted tolan compound having the structure (I):



(I)

wherein R^1 and R^2 are independent substituents at any available position of the phenyl rings, and m and n are independently 1, 2, or 3, representing the number of substituents on the phenyl rings, respectively; and

wherein each R^1, R^2 is independently selected from hydroxy, thiol, -(C_1-C_6)alkoxy, -(C_1-C_6)RH" where R is O or S, or (halo)$_p$(C_1-C_6)alkyl-, where p is 1, 2, or 3;

and salts thereof;

provided, however, that the substituted tolan compound is not 3,4′,5-trihydroxytolan.

2. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the tolan is a methoxy tolan.

3. The method of claim 1 or 25, or the use of claim 41 or 43, wherein at least one of R^1 and R^2 is hydroxy.

4. The method of claim 1 or 25, or the use of claim 41 or 43, wherein R^1 a is -(C_1-C_6) alkoxy and m is 1 or 2.

5. The method of claim 4, wherein R^2 is hydroxy and n is 1, 2, or 3.

6. The method of claim 1 or 25, or the use of claim 41 or 43, wherein R^2 is hydroxy and n is 1, 2, or 3.

7. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the substituted tolan is selected from 4,4'-dihydroxytolan, 4,4′-dihydroxy-3-methoxytolan, 4-hydroxy-4′-methoxytolan, 3,5,3',5' tetrahydroxytolan, 2,4,4'-trimethoxytolan, 3,5,3',5' tetramethoxytolan, and 4-hydroxy-4'-trifluoromethyltolan.

8. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the substituted tolan compound is present in an amount from 0.01% to 30% by weight, based on total weight of the antimicrobial formulation.

9. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the antimicrobial formulation has a pH of from 4.1 to 8.5, and wherein the antimicrobial formulation further includes a cleansing agent and a secondary antimicrobial agent.

10. The method of claim 9, wherein the cleansing agent is substantially free of phenol.

11. The method of claim 9, wherein the secondary antimicrobial agent is selected from phenol derivatives, dichlorophene, hexachlorophene, aldehydes, alcohols, antimicrobial carboxylic acids and derivatives thereof, organometallic compounds, iodine compounds, quaternary ammonium compounds, sulfonium and phosphonium compounds, mercapto compounds and the alkali metal, alkaline earth metal and heavy metal salts thereof, ureas, tribromosalicylanilide, 2-bromo-2-nitro-1,3-dihydroxypropane, dichlorobenzoxazolone, chlorohexidine, isothiazolone, benzisothiazolone derivatives and combinations of any two or more of these.

12. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the physical surface is selected from surgical equipment, surgical instruments, and countertop surfaces that must be sterilized and remain sterile throughout a surgical procedure.

13. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the physical surface is selected from food preparation surfaces selected from cutting boards, countertops, and cookware.

14. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the surface is a biological surface at a site where skin is not fully intact, the site selected from intravenous lines or ports, arterial lines or ports, PICC lines, catheters, drains, and incision sites.

15. The method of claim 1 or 25, comprising disrupting a bacterial biofilm in situ.

16. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the suspected pathogenic microbes are Gram-negative bacteria.

17. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the suspected pathogenic microbes are Gram-positive bacteria.

18. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the suspected pathogenic microbes are fungi.

19. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the suspected pathogenic microbes are bacterial pathogens selected from methicillin resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa, Acinetobacter baumannii*, and *E. coli* species.

20. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the suspected pathogenic microbes are fungi of the Candida genus.

21. The method of claim 20, wherein the fungi are *Candida albicans*.

22. The method of claim 1 or 25, or the use of claim 41 or 43, wherein the antimicrobial formulation further comprises an antibiotic, or wherein the physical or biological surface is further contacted with the antibiotic.

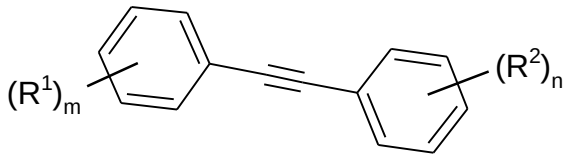
23. The method of claim 22, wherein the antibiotic comprises an aminoglycosides, ansamycin, a carbacephem, a flagyl (metronidazole), a neomycin sulfate, a carbapenem, a cephalosporin, a glycopeptide, a macrolide, a monobactam, a penicillin, a polypeptide, a polymyxin, a quinolone, a sulfonamide, or a tetracycline.

24. The method of claim 22, wherein the antibiotic is selected from the group consisting of: clindamycin, tigecycline, vancomycin, ciprofloxacin, ofloxacin, sulfamethoxazole, trimethoprim/sulfamethoxazole, amoxicillin, penicillin V, penicillin G, procaine penicillin, benzathine penicillin, carbencillin, mezlocillin, ampicillin, piperacillin, arsphenamine, chloramphenicol, clindamycin, lincomycin, ethambutol, fosfomycin, fusidic acid, furazolidone, isoniazid, linezolid,

metronidazole, mupirocin, nitrofurantoin, platensimycin, pyrazinamide, quinupristin/dalfopristin, rifampicin (rifampin in US), thiamphenicol, timidazole, dapsone, lofazimine, bacampicillin, tiearcillin, ticarcillin, piperacillin/tazobactam, aztreonam, cefotetan, loracarbef, mefoxin, merrem, levofloxacin, lomefioxacin, primaxim, cycloserine, kanamycin, dicloxacillin, demeclocycline, minocycline, doxycycline, oxytetracycline, tobramycin, gentamicin, neomycin, amikacin, craramyein, nebcin, erythromycin/sulfisoxazole, netromycin, streptomycin, tobramycin, cefotaxime, cefuroxime, cefazoline, ceffibuten, ceffizoxime, cefaclor, cefopoerazone, cefprozil, cefadroxil monohydrate, ceftazidime, trimethoprim/sulfamethoxazole, cephalexin, cefazolin, cefamandole nafate, cefepime, cefonicid, sulfadiazine, norfloxacin, enoxacin, cefdinir, seromycin, ceftriaxone, cefixime, ceftazidime, clarithromycin, dirithromycin, methenamine, ethionamide, trovafioxacin, sparfloxacin, interfon-α, indinavir, ganciclovir, foscamet, lamivudine, famciclovir, rimantadine, zalcitabine, interferon-β, saquinavir, ritonavir, ribavirin, erythromycin, troleandomycin, azithromycin, eliiidamycin, colistin, amphotericin B, flucytosine, fluconazole, griseofulvin, grepafloxacin, ultramicrosize griseofulvin, terbinafine, ketoconazole, clotrimazole, dapsone, delavirdine, ziduvudine, amantadine, palivizumab, valacyclovir, didanosine, nelfinavir, nevirapine, ribavirin, cidofovir, pyrimethamine, metronidazole, furazolidone, atovaquone, stavudine, lamiduvine, acyclovir, mionazole, nystatin, itraconazole, chloroquine, pyrimethamine, mefloquine, hydroxychloroquine, capreomycin, permethrin, crotamiton, lindane, fluoro-uracil, ethambutol, rifabutin, isoniazid, aminosalicyclic acid, rifapentine, pyrazinamide, coenzoyl peroxide, chlorhexidine gluconate, sodium oxychlorosene, benzoyl peroxide, rifampin, rifampin/isoniazid, rifampin/isoniazid/pyrazinamide, nitrofurantoin, linezolid, nitrofurantoin, fosfomycin, nalidixic acid, atropine, oxytetracycline/sulfamethizole/phenazopyridine, chloramphenical, neomycin/polymyxin, tfimetorpim/polythyxin, tobramycin/dexamethasone, vidatabine, ciprofloxacin, ofioxacin, sulfacetamide, povidoneodine, gentamicin, chloramphenicol, bacitracin, sulconazole, terbinafine, tetrachlorosalicylanilide, metronidazole, metromdazole, ciclopiroxolamine, clotrimazole, clotrimazole/betamethasone, butenafine, clotrimazole, nattifine, oxiconazole, selenium, econazole, penciclovir, or a pharmaceutically acceptable salt thereof.

25. A method of inhibiting or disrupting biofilm formation of a microbe or microbes, the method comprising contacting the microbe or microbes on a physical surface with an antimicrobial formulation comprising:

an effective amount of a substituted tolan compound having the structure (I):



(I)

wherein R^1 and R^2 are independent substituents at any available position of the phenyl rings, and m and n are independently 1, 2, or 3, representing the number of substituents on the phenyl rings, respectively; and

wherein each R^1, R^2 is independently selected from hydroxy, thiol, -(C_1-C_6)alkoxy, -(C_1-C_6)RH" where R is O or S, or $(halo)_p$(C_1-C_6)alkyl-, where p is 1, 2, or 3;

and salts thereof;

provided, however, that the substituted tolan compound is not 3,4′,5-trihydroxytolan.

26. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the tolan compound is present in the antimicrobial formulation at a concentration ranging from 0.008 mM to 1 mM.

27. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the tolan compound is present in the antimicrobial formulation at a concentration of 0.625 mM.

28. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the tolan compound is present in the antimicrobial formulation in an amount ranging from 0.0001% to 30% by weight, based on total weight of the antimicrobial formulation.

29. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the tolan compound is present in the antimicrobial formulation in an amount ranging from about 0.01% to 25% by weight, based on total weight of the antimicrobial formulation.

30. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the tolan compound is present in the antimicrobial formulation in an amount ranging from 0.1% to 30% by weight, based on total weight of the antimicrobial formulation.

31. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the antimicrobial formulation is administered from once daily up to 6 times per day.

32. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the antimicrobial formulation is administered via an administration route selected from the group consisting of topical, transdermal, oral, nasal, ophthalmic, otic, intravenous, intramuscular, subcutaneous, rectal, and vaginal.

33. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the tolan compound comprises 4-hydroxy-4′-methoxytolan.

34. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the microbe or microbes comprise Gram-positive bacteria.

35. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the microbe or microbes comprise Gram-negative bacteria.

36. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the microbe or microbes comprise a fungi.

37. The method of claim 25, or the use of claim 43, wherein the microbe or microbes comprise methicillin resistant *Staphylococcus aureus* (MRSA).

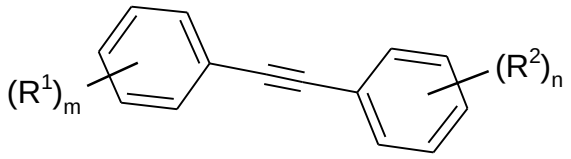
38. The method of claim 25 or 1, or the use of claim 41 or 43, wherein the antimicrobial formulation further comprises an antibiotic, or wherein the microbe or microbes are further contacted with the antibiotic.

39. The method of claim 38, wherein the antibiotic comprises an aminoglycoside, ansamycin, a carbacephem, a flagyl (metronidazole), a neomycin sulfate, a carbapenem, a cephalosporin, a glycopeptide, a macrolide, a monobactam, a penicillin, a polypeptide, a polymyxin, a quinolone, a sulfonamide, or a tetracycline.

40. The method of claim 38, wherein the antibiotic is selected from the group consisting of: clindamycin, tigecycline, vancomycin, ciprofloxacin, ofloxacin, sulfamethoxazole, trimethoprim/sulfamethoxazole, amoxicillin, penicillin V, penicillin G, procaine penicillin, benzathine penicillin, carbencillin, mezlocillin, ampicillin, piperacillin, arsphenamine, chloramphenicol, clindamycin, lincomycin, ethambutol, fosfomycin, fusidic acid, furazolidone, isoniazid, linezolid, metronidazole, mupirocin, nitrofurantoin, platensimycin, pyrazinamide, quinupristin/dalfopristin,

rifampicin (rifampin in US), thiamphenicol, timidazole, dapsone, lofazimine, bacampicillin, tiearcillin, ticarcillin, piperacillin/tazobactam, aztreonam, cefotetan, loracarbef, mefoxin, merrem, levofloxacin, lomefioxacin, primaxim, cycloserine, kanamycin, dicloxacillin, demeclocycline, minocycline, doxycycline, oxytetracycline, tobramycin, gentamicin, neomycin, amikacin, craramyein, nebcin, erythromycin/sulfisoxazole, netromycin, streptomycin, tobramycin, cefotaxime, cefuroxime, cefazoline, ceffibuten, ceffizoxime, cefaclor, cefopoerazone, cefprozil, cefadroxil monohydrate, ceftazidime, trimethoprim/sulfamethoxazole, cephalexin, cefazolin, cefamandole nafate, cefepime, cefonicid, sulfadiazine, norfloxacin, enoxacin, cefdinir, seromycin, ceftriaxone, cefixime, ceftazidime, clarithromycin, dirithromycin, methenamine, ethionamide, trovafioxacin, sparfloxacin, interfon-α, foscamet, lamivudine, famciclovir, rimantadine, zalcitabine, interferon-β, indinavir, ganciclovir, saquinavir, ritonavir, ribavirin, erythromycin, troleandomycin, azithromycin, eliiidamycin, colistin, amphotericin B, flucytosine, fluconazole, griseofulvin, grepafloxacin, ultramicrosize griseofulvin, terbinafine, ketoconazole, clotrimazole, dapsone, delavirdine, ziduvudine, amantadine, palivizumab, valacyclovir, didanosine, nelfinavir, nevirapine, ribavirin, cidofovir, pyrimethamine, metronidazole, furazolidone, atovaquone, stavudine, lamiduvine, acyclovir, mionazole, itraconazole, chloroquine, pyrimethamine, mefloquine, hydroxychloroquine, capreomycin, permethrin, crotamiton, lindane, fluoro-uracil, ethambutol, rifabutin, isoniazid, aminosalicyclic acid, rifapentine, pyrazinamide, coenzoyl peroxide, chlorhexidine gluconate, sodium oxychlorosene, benzoyl peroxide, rifampin, rifampin/isoniazid, rifampin/isoniazid/pyrazinamide, nitrofurantoin, linezolid, nitrofurantoin, fosfomycin, nalidixic acid, atropine, oxytetracycline/sulfamethizole/phenazopyridine, chloramphenical, neomycin/polymyxin, tfimetorpim/polythyxin, tobramycin/dexamethasone, vidatabine, ciprofloxacin, ofioxacin, sulfacetamide, povidoneodine, gentamicin, nystatin, chloramphenicol, bacitracin, sulconazole, terbinafine, tetrachlorosalicylanilide, metronidazole, metromdazole, ciclopiroxolamine, clotrimazole, clotrimazole/betamethasone, butenafine, clotrimazole, nattifine, oxiconazole, selenium, econazole, penciclovir, or a pharmaceutically acceptable salt thereof.

41. Use of a substituted tolan compound having the structure (I) in the manufacture of an antimicrobial formulation for treating a methicillin resistant *Staphylococcus aureus* (MRSA) infection:



(I)

wherein R^1 and R^2 are independent substituents at any available position of the phenyl rings, and m and n are independently 1, 2, or 3, representing the number of substituents on the phenyl rings, respectively; and

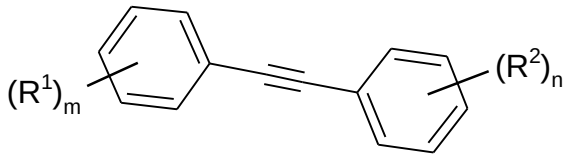
wherein each R^1, R^2 is independently selected from hydroxy, thiol, -(C_1-C_6)alkoxy, -(C_1-C_6)RH" where R is O or S, or (halo)$_p$(C_1-C_6)alkyl-, where p is 1, 2, or 3;

and salts thereof;

provided, however, that the substituted tolan compound is not 3,4′,5-trihydroxytolan.

42. The use of claim 41, wherein the substituted tolan is selected from 4,4'-dihydroxytolan, 4,4′-dihydroxy-3-methoxytolan, 4-hydroxy-4′-methoxytolan, 3,5,3',5' tetrahydroxytolan, 2,4,4'-trimethoxytolan, 3,5,3',5' tetramethoxytolan, and 4-hydroxy-4'-trifluoromethyltolan.

43. Use of a substituted tolan compound having the structure (I) in the manufacture of a biofilm-disrupting agent:



(I)

wherein R^1 and R^2 are independent substituents at any available position of the phenyl rings, and m and n are independently 1, 2, or 3, representing the number of substituents on the phenyl rings, respectively; and

wherein each R^1, R^2 is independently selected from hydroxy, thiol, -(C_1-C_6)alkoxy, -(C_1-C_6)RH" where R is O or S, or (halo)$_p$(C_1-C_6)alkyl-, where p is 1, 2, or 3; and salts thereof;

provided, however, that the substituted tolan compound is not 3,4′,5-trihydroxytolan.

44. The use of claim 43, wherein the substituted tolan is selected from 4,4'-dihydroxytolan, 4,4′-dihydroxy-3-methoxytolan, 4-hydroxy-4′-methoxytolan, 3,5,3',5' tetrahydroxytolan, 2,4,4'-trimethoxytolan, 3,5,3',5' tetramethoxytolan, and 4-hydroxy-4'-trifluoromethyltolan.