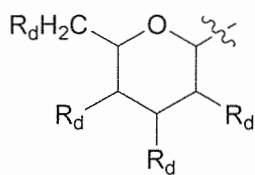


[0055] The term “alkyl heterocycle”, as used herein, generally refers to a chemical substituent containing an alkyl group coupled to a heterocycle or a substituted heterocycle.

[0056] In present context, the term “heteroaryl” refers to an aromatic heterocycle. Heteroaryl rings may be formed by five, six, seven, eight, nine, or more than nine atoms. Heteroaryls may be optionally substituted. Examples of heteroaryl groups include, but are not limited to, aromatic C<sub>5</sub>-C<sub>15</sub> heterocyclic groups comprising one oxygen or sulfur atom or up to four nitrogen atoms, or a combination of one oxygen or sulfur atom and up to two nitrogen atoms, and their substituted as well as benzo- and pyrido-fused derivatives, for example, connected via one of the ring-forming carbon atoms.

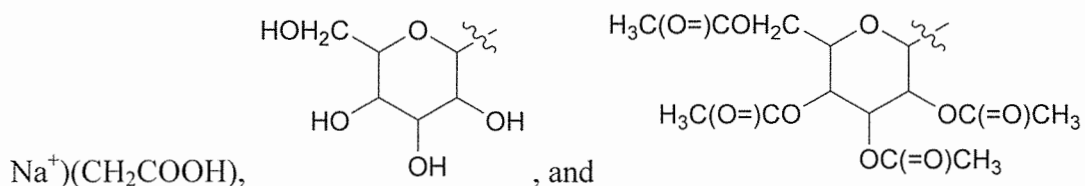
[0057] In various embodiments, G is a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl, a substituted or unsubstituted C<sub>3</sub>-C<sub>20</sub> heterocycle, or a substituted or unsubstituted C<sub>4</sub>-C<sub>30</sub> alkyl-heterocycle.

[0058] In some embodiments, G is  $-C(R^a)(R^b)(R^c)$ , wherein R<sup>a</sup>, R<sup>b</sup>, and R<sup>c</sup> are independently selected from the group consisting of H, a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl, and salts



thereof; or , wherein each R<sup>d</sup> is independently  $-OC(=O)R'$  or  $-OH$ , wherein R' is a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl.

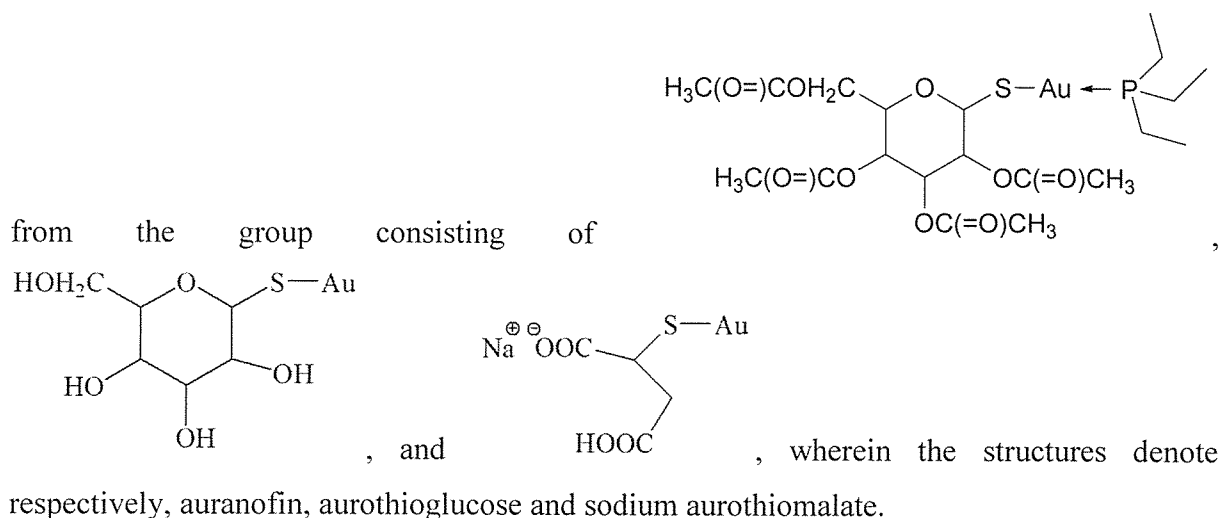
[0059] In specific embodiments, G is selected from the group consisting of  $-CH(COO^-$



[0060] In various embodiments, Q is nothing,  $-Cl$ , or  $-P(R^e)_3$ , wherein each R<sup>e</sup> is independently a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl.

[0061] In specific embodiments, Q is nothing or  $-P(CH_2CH_3)_3$ .

[0062] Accordingly, in various embodiments, the gold(I) thiolate complex may be selected



[0063] In some embodiments, the gold(I) thiolate complex is auranofin. Auranofin is an FDA-approved drug and comprises a gold(I) ion coordinated by one thiolate and one phosphine ligand in a linear fashion. Due to its anti-inflammatory activities, it may be used for the treatment of rheumatoid arthritis, and has also been investigated for treatment of cancer and parasitic infections such as malaria and amoebiasis, where it is postulated to work via inhibiting thioredoxin reductases and thioredoxin glutathione reductases, which are enzymes important for maintaining redox balance.

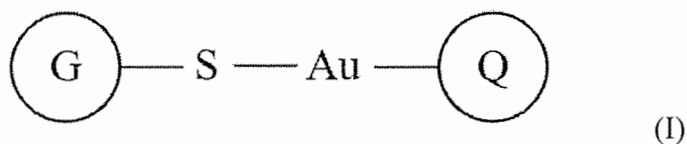
[0064] Apart from the above-mentioned, gold(I) thiolate complexes such as aurothiomalate, and/or disodium aurothiomalate having formula  $\text{AuSCH}(\text{CO}_2\text{Na})\text{CH}_2\text{CO}_2\text{Na}$  may also be used.

[0065] As mentioned above, gold(I) thiolate complexes, such as auranofin, sodium aurothiomalate, and aurothioglucose have been shown to inhibit quorum sensing in *Pseudomonas aeruginosa*, which is a Gram-negative bacteria. Inhibiting the quorum sensing in *Pseudomonas aeruginosa* may comprise inhibiting a cyclic-AMP-dependent transcription regulator Vfr, which also controls Type III secretion and Type IV pilus assembly. Type IV pilus is also essential for biofilm formation and maturation, thus auranofin targets multiple processes that are important for *P. aeruginosa* virulence and biofilm formation.

[0066] The terms “microorganism” and “microbe” are used interchangeably herein, and refer to an organism that is unicellular or lives in a colony of cellular organisms such as bacteria, fungi, protest, or archea. The method of inhibiting quorum sensing disclosed herein is used in *Pseudomonas aeruginosa*, which is a type of Gram-negative quorum sensing

## CLAIMS

1. A method of inhibiting quorum sensing in *Pseudomonas aeruginosa*, the method comprising contacting *Pseudomonas aeruginosa* with a gold(I) thiolate complex *ex vivo* in an amount effective to inhibit quorum sensing in the *Pseudomonas aeruginosa*.
2. The method according to claim 1, wherein the gold(I) thiolate complex has Formula (I)



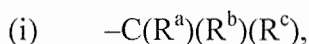
wherein

G is selected from the group consisting of a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl, a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkoxy, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkenyl, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkynyl, a substituted or unsubstituted C<sub>3</sub>-C<sub>20</sub> alicyclic group, a substituted or unsubstituted C<sub>5</sub>-C<sub>15</sub> aryl, a substituted or unsubstituted C<sub>6</sub>-C<sub>30</sub> alkyl-aryl, a substituted or unsubstituted C<sub>3</sub>-C<sub>20</sub> heterocycle, a substituted or unsubstituted C<sub>4</sub>-C<sub>30</sub> alkyl-heterocycle, a substituted or unsubstituted C<sub>5</sub>-C<sub>15</sub> heteroaryl, and

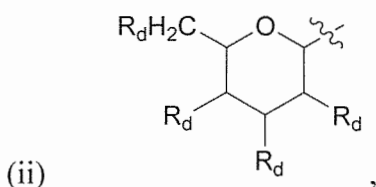
Q is nothing, halogen, or -PR<sub>3</sub>, wherein each R is independently selected from the group consisting of H, halogen, a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl, a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkoxy, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkenyl, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkynyl, and a substituted or unsubstituted C<sub>5</sub>-C<sub>15</sub> aryl; or a salt thereof.

3. The method according to claim 2, wherein G is a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl, a substituted or unsubstituted C<sub>3</sub>-C<sub>20</sub> heterocycle, or a substituted or unsubstituted C<sub>4</sub>-C<sub>30</sub> alkyl-heterocycle.

4. The method according to claim 2 or 3, wherein G is

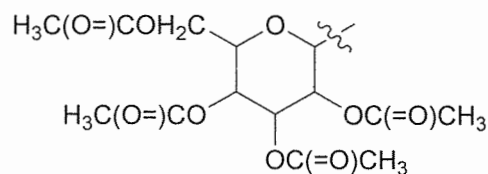


wherein R<sup>a</sup>, R<sup>b</sup>, and R<sup>c</sup> are independently selected from the group consisting of H, a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl, and salts thereof; or



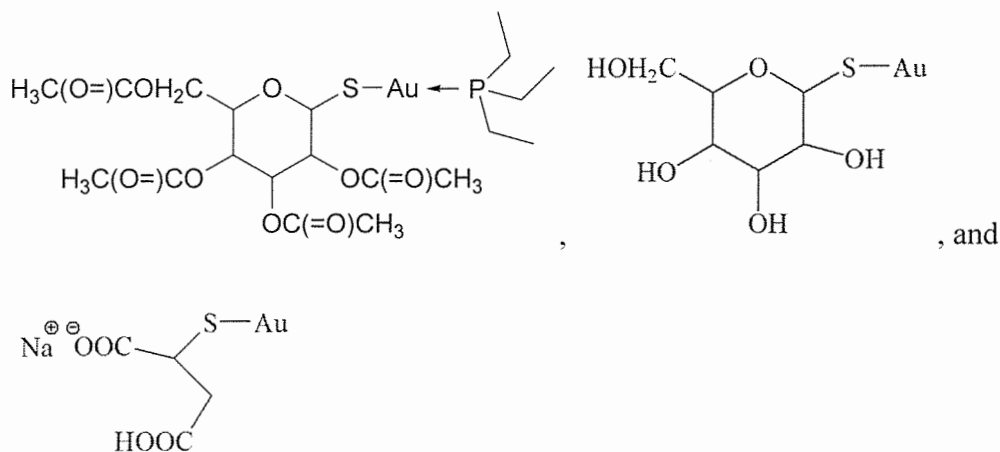
wherein each R<sup>d</sup> is independently  $-OC(=O)R'$  or  $-OH$ , wherein R' is a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl.

5. The method according to any one of claims 2 to 4, wherein G is selected from the

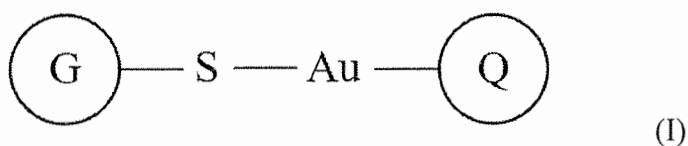


6. The method according to any one of claims 2 to 5, wherein Q is nothing,  $-Cl$ , or  $-P(R^e)_3$ , wherein each R<sup>e</sup> is independently a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl.

7. The method according to any one of claims 2 to 6, wherein Q is nothing or – P(CH<sub>2</sub>CH<sub>3</sub>)<sub>3</sub>.
8. The method according to any one of claims 1 to 7, wherein the gold(I) thiolate complex is selected from the group consisting of



9. The method according to any one of claims 1 to 8, wherein inhibiting the quorum sensing in the *Pseudomonas aeruginosa* comprises inhibiting a cyclic-AMP-dependent transcription regulator Vfr.
10. The method according to any one of claims 1 to 9, wherein the gold(I) thiolate complex is administered to a surface in an amount effective to inhibit biofilm formation associated with quorum sensing of the *Pseudomonas aeruginosa* on a medical device.
11. A gold(I) thiolate complex for use in therapy.
12. The gold(I) thiolate complex for use according to claim 11, wherein the gold(I) thiolate complex has Formula (I)

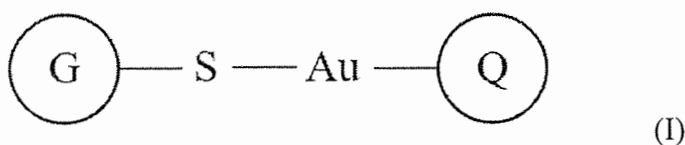


wherein

G is selected from the group consisting of a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl, a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkoxy, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkenyl, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkynyl, a substituted or unsubstituted C<sub>3</sub>-C<sub>20</sub> alicyclic group, a substituted or unsubstituted C<sub>5</sub>-C<sub>15</sub> aryl, a substituted or unsubstituted C<sub>6</sub>-C<sub>30</sub> alkyl-aryl, a substituted or unsubstituted C<sub>3</sub>-C<sub>20</sub> heterocycle, a substituted or unsubstituted C<sub>4</sub>-C<sub>30</sub> alkyl-heterocycle, a substituted or unsubstituted C<sub>5</sub>-C<sub>15</sub> heteroaryl, and

Q is nothing, halogen, or -PR<sub>3</sub>, wherein each R is independently selected from the group consisting of H, halogen, a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl, a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkoxy, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkenyl, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkynyl, and a substituted or unsubstituted C<sub>5</sub>-C<sub>15</sub> aryl; or a salt thereof.

13. Use of a gold(I) thiolate complex in the manufacture of a medicament for the inhibition of quorum sensing in *Pseudomonas aeruginosa*, the inhibition comprising contacting the gold(I) thiolate complex with the *Pseudomonas aeruginosa*.
14. Use of the gold(I) thiolate complex according to claim 13, wherein the gold(I) thiolate complex has Formula (I)



wherein

G is selected from the group consisting of a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl, a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkoxy, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkenyl, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkynyl, a substituted or unsubstituted C<sub>3</sub>-C<sub>20</sub> alicyclic group, a substituted or unsubstituted C<sub>5</sub>-C<sub>15</sub> aryl, a substituted or unsubstituted C<sub>6</sub>-C<sub>30</sub> alkyl-aryl, a substituted or unsubstituted C<sub>3</sub>-C<sub>20</sub> heterocycle, a substituted or unsubstituted C<sub>4</sub>-C<sub>30</sub> alkyl-heterocycle, a substituted or unsubstituted C<sub>5</sub>-C<sub>15</sub> heteroaryl, and

Q is nothing, halogen, or -PR<sub>3</sub>, wherein each R is independently selected from the group consisting of H, halogen, a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkyl, a substituted or unsubstituted C<sub>1</sub>-C<sub>20</sub> alkoxy, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkenyl, a substituted or unsubstituted C<sub>2</sub>-C<sub>20</sub> alkynyl, and a substituted or unsubstituted C<sub>5</sub>-C<sub>15</sub> aryl; or a salt thereof.

15. The use according to claim 13 or 14, wherein the contacting comprises administering the gold(I) thiolate complex to a subject.
16. The use according to claim 15, wherein the subject is afflicted with a disorder associated with quorum sensing and/or biofilm formation and the gold(I) thiolate complex is administered in an amount effective to treat the disorder.
17. The use according to any one of claims 13 to 16, wherein the gold(I) thiolate complex is present in a composition comprising a pharmaceutically-acceptable additive, adjuvant, and/or excipient.
18. The use according to any one of claims 13 to 17, wherein the gold(I) thiolate complex is present in a composition comprising an antibiotic, preferably  
  
wherein the antibiotic is at least one of colistin or tobramycin.

19. The use according to any one of claims 13 to 18, for the treatment or prevention of damage or disease associated with quorum sensing and/or biofilm formation in a subject.
20. Use of a method according to any one of claims 1 to 10, for the treatment of biofilm and/or for inhibiting biofilm formation of a medical device, personal hygiene article, toiletries, cosmetics, disinfectant, cleaning solution, or in a water treatment or distribution system.