

[0010] Some embodiments described herein relate to a method for treating a bacterial infection, comprising administering to a subject in need thereof a composition comprising a cyclic boronic acid ester compound I or a pharmaceutically acceptable salt thereof and a carbapenem antibacterial agent to achieve an in vivo Compound I 24 h AUC from about 3 mg*h/L to about 800 mg*h/L.

[0011] In some embodiments, the carbapenem antibacterial agent is selected from the group consisting of Imipenem, Biapenem, Doripenem, Meropenem, and Ertapenem. In some such embodiments, the carbapenem antibacterial agent is Biapenem.

[0012] In some embodiments, Compound I is administered in a dosage range from about 0.1 mg/kg to about 1000 mg/kg of body weight. In some further embodiments, Compound I is administered in a dosage range from about 0.5 mg/kg to about 150 mg/kg of body weight.

[0013] In some embodiments, the composition is administered intravenously.

[0014] In some embodiments, the infection is caused by a bacteria selected from *Pseudomonas aeruginosa*, *Pseudomonas fluorescens*, *Stenotrophomonas maltophilia*, *Escherichia coli*, *Citrobacter freundii*, *Salmonella typhimurium*, *Salmonella typhi*, *Salmonella paratyphi*, *Salmonella enteritidis*, *Shigella dysenteriae*, *Shigella flexneri*, *Shigella sonnei*, *Enterobacter cloacae*, *Enterobacter aerogenes*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Serratia marcescens*, *Acinetobacter calcoaceticus*, *Acinetobacter haemolyticus*, *Yersinia enterocolitica*, *Yersinia pestis*, *Yersinia pseudotuberculosis*, *Yersinia intermedia*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Haemophilus haemolyticus*, *Haemophilus parahaemolyticus*, *Helicobacter pylori*, *Campylobacter fetus*, *Campylobacter jejuni*, *Campylobacter coli*, *Vibrio cholerae*, *Vibrio parahaemolyticus*, *Legionella pneumophila*, *Listeria monocytogenes*, *Neisseria gonorrhoeae*, *Neisseria meningitidis*, *Moraxella*, *Bacteroides fragilis*, *Bacteroides vulgatus*, *Bacteroides ovalis*, *Bacteroides thetaiotaomicron*, *Bacteroides uniformis*, *Bacteroides eggerthii*, or *Bacteroides splanchnicus*.

[0015] In some embodiments, the composition further comprises an additional medicament selected from an antibacterial agent, antifungal agent, an antiviral agent, an anti-inflammatory agent, or an anti-allergic agent.

[0016] In some embodiments, the subject treated by the method described above is a mammal. In some further embodiments, the subject is a human.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] FIG. 1 is a graph depicting the plasma concentration profile of 5, 15 or 50 mg/kg Compound I as a function of time after administration to Swiss Webster mice.

[0018] FIG. 2 is a graph depicting the plasma concentration profile of 25 or 100 mg/kg Biapenem as a function of time after administration to Swiss Webster mice.

[0019] FIG. 3 is a graph depicting the plasma concentration profile of 20 mg/kg Biapenem as a function of time after administration to Swiss Webster mice.

[0020] FIG. 4 is a graph depicting the plasma concentration profile of 20 mg/kg Compound I as a function of time after administration to Sprague-Dawley rats.

[0021] FIG. 5 is a graph depicting the plasma concentration profile of 20 mg/kg Biapenem in combination with 20 mg/kg Compound I as a function of time after administration to Sprague-Dawley rats.

[0022] FIG. 6 is a graph depicting the plasma concentration profile of 20 mg/kg Compound I in combination with 20 mg/kg Biapenem as a function of time after administration to Sprague-Dawley rats.

DETAILED DESCRIPTION

Definitions

[0023] The compounds provided herein may encompass various stereochemical forms. The compounds also encompasses diastereomers as well as optical isomers, e.g. mixtures of enantiomers including racemic mixtures, as well as individual enantiomers and diastereomers, which arise as a consequence of structural asymmetry in certain compounds. Separation of the individual isomers or selective synthesis of the individual isomers is accomplished by application of various methods which are well known to practitioners in the art.

[0024] The term “agent” or “test agent” includes any substance, molecule, element, compound, entity, or a combination thereof. It includes, but is not limited to, e.g., protein, polypeptide, peptide or mimetic, small organic molecule, polysaccharide, polynucleotide, and the like. It can be a natural product, a synthetic compound, or a chemical compound, or a combination of two or more substances. Unless otherwise specified, the terms “agent”, “substance”, and “compound” are used interchangeably herein.

[0025] The term “mammal” is used in its usual biological sense. Thus, it specifically includes humans, cattle, horses, dogs, cats, rats and mice but also includes many other species.

[0026] The term “microbial infection” refers to the invasion of the host organism, whether the organism is a vertebrate, invertebrate, fish, plant, bird, or mammal, by pathogenic microbes. This includes the excessive growth of microbes that are normally present in or on the body of a mammal or other organism. More generally, a microbial infection can be any situation in which the presence of a microbial population (s) is damaging to a host mammal. Thus, a mammal is “suffering” from a microbial infection when excessive numbers of a microbial population are present in or on a mammal’s body, or when the effects of the presence of a microbial population(s) is damaging the cells or other tissue of a mammal. Specifically, this description applies to a bacterial infection. Note that the compounds of preferred embodiments are also useful in treating microbial growth or contamination of cell cultures or other media, or inanimate surfaces or objects, and nothing herein should limit the preferred embodiments only to treatment of higher organisms, except when explicitly so specified in the claims.

[0027] The term “pharmaceutically acceptable carrier” or “pharmaceutically acceptable excipient” includes any and all solvents, dispersion media, coatings, antibacterial and antifungal agents, isotonic and absorption delaying agents and the like. The use of such media and agents for pharmaceutically active substances is well known in the art. Except insofar as any conventional media or agent is incompatible with the active ingredient, its use in the therapeutic compositions is contemplated. Supplementary active ingredients can also be incorporated into the compositions. In addition, various adjuvants such as are commonly used in the art may be included. These and other such compounds are described in the literature, e.g., in the Merck Index, Merck & Company, Rahway, N.J. Considerations for the inclusion of various components in pharmaceutical compositions are described, e.g., in Gil-