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(54) Title: DELIVERY OF ERECTILE DYSFUNCTION DRUGS THROUGH AN INHALATION ROUTE

(57) Abrégé/Abstract:
The present invention relates to the delivery of erectile dysfunction drugs through an inhalation route. Specifically, it relates to aerosols containing erectile dysfunction drugs that are used in inhalation therapy. In a composition aspect of the present invention, the aerosol comprises particles comprising at least 5 percent by weight of an erectile dysfunction drug. In a method aspect of the present invention, an erectile dysfunction drug is delivered to a mammal through an inhalation route. The method comprises: a) heating a composition, wherein the composition comprises at least 5 percent by weight of an erectile dysfunction drug, to form a vapor; and, b) allowing the vapor to cool, thereby forming a condensation aerosol comprising particles, which is inhaled by the mammal. In a kit aspect of the present invention, a kit for delivering an erectile dysfunction drug through an inhalation route to a mammal is provided which comprises: a) a composition comprising at least 5 percent by weight of an erectile dysfunction drug; and, b) a device that forms an erectile dysfunction drug aerosol from the composition, for inhalation by the mammal.

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(54) Title: DELIVERY OF ERECTILE DYSFUNCTION DRUGS THROUGH AN INHALATION ROUTE

(57) Abstract: The present invention relates to the delivery of erectile dysfunction drugs through an inhalation route. Specifically, it relates to aerosols containing erectile dysfunction drugs that are used in inhalation therapy. In a composition aspect of the present invention, the aerosol comprises particles comprising at least 5 percent by weight of an erectile dysfunction drug. In a method aspect of the present invention, an erectile dysfunction drug is delivered to a mammal through an inhalation route. The method comprises: a) heating a composition, wherein the composition comprises at least 5 percent by weight of an erectile dysfunction drug, to form a vapor; and, b) allowing the vapor to cool, thereby forming a condensation aerosol comprising particles, which is inhaled by the mammal. In a kit aspect of the present invention, a kit for delivering an erectile dysfunction drug through an inhalation route to a mammal is provided which comprises: a) a composition comprising at least 5 percent by weight of an erectile dysfunction drug; and, b) a device that forms an erectile dysfunction drug aerosol from the composition, for inhalation by the mammal.

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DELIVERY OF ERECTILE DYSFUNCTION DRUGS THROUGH AN INHALATION ROUTE

Field of the Invention

[0002] The present invention relates to the delivery of erectile dysfunction drugs through an inhalation route. Specifically, it relates to aerosols containing erectile dysfunction drugs that are used in inhalation therapy.

Background of the Invention

[0003] There are a number of compositions currently marketed for the treatment of erectile dysfunction. The compositions contain at least one active ingredient that provides for observed therapeutic effects. Among the active ingredients given in such erectile dysfunction compositions are sildenafil, tadalafil and vardenafil.

[0004] It is desirable to provide a new route of administration for erectile dysfunction drugs that rapidly produces peak plasma concentrations of the compounds.

Summary of the Invention

[0005] The present invention relates to the delivery of erectile dysfunction drugs through an inhalation route. Specifically, it relates to aerosols containing erectile dysfunction drugs that are used in inhalation therapy.

[0005.1] In one aspect, the invention provides a composition for delivery of an erectile dysfunction drug, comprising a condensation aerosol a) formed by volatilizing an erectile dysfunction drug under conditions effective to produce a heated vapor of the erectile dysfunction drug, and condensing the heated vapor of the erectile dysfunction

drug to form condensation aerosol particles, and b) wherein said condensation aerosol particles are characterized by less than 5% erectile dysfunction drug degradation products, and c) the aerosol has a MMAD less than 3 microns.

[0005.2] In a further aspect, the invention provides a composition for delivery of sildenafil, tadalafil or vardenafil comprising a condensation aerosol a) formed by volatilizing sildenafil, tadalafil or vardenafil under conditions effective to produce a heated vapor of sildenafil, tadalafil or vardenafil, and condensing the heated vapor of sildenafil, tadalafil or vardenafil to form condensation aerosol particles, and b) wherein said condensation aerosol particles are characterized by less than 5% sildenafil, tadalafil or vardenafil drug degradation products, and c) the aerosol has a MMAD less than 3 microns.

[0005.3] In a still further aspect, the invention provides a method of producing sildenafil, tadalafil or vardenafil in an aerosol form comprising a) volatilizing sildenafil, tadalafil or vardenafil under conditions effective to produce a heated vapor of the sildenafil, tadalafil or vardenafil, and b) during said volatilizing, passing air through the heated vapor to produce aerosol particles of sildenafil, tadalafil or vardenafil comprising less than 5% sildenafil, tadalafil or vardenafil degradation products and an aerosol having a MMAD less than 3 μm.

[0005.4] In a yet further aspect, the invention provides a kit for delivering a sildenafil, tadalafil or vardenafil aerosol, wherein the kit comprises: a) a composition comprising sildenafil, tadalafil or vardenafil; and, b) a device that forms a sildenafil, tadalafil or vardenafil aerosol from the composition, and wherein the device

comprises: a) an element for heating the sildenafil, tadalafil or vardenafil composition to form a vapor; b) an element allowing the vapor to cool to form an aerosol; and, c) an element permitting inhalation of the aerosol.

[0006] In a composition aspect of the present invention, the aerosol comprises particles comprising at least 5 percent by weight of an erectile dysfunction drug. Preferably, the particles comprise at least 10 percent by weight of an erectile dysfunction drug. More preferably, the particles comprise at least 20 percent, 30 percent, 40 percent, 50 percent, 60 percent, 70 percent, 80 percent, 90 percent, 95 percent, 97 percent, 99 percent, 99.5 percent or 99.97 percent by weight of an erectile dysfunction drug.

[0007] Typically, the erectile dysfunction drug is not sildenafil citrate.

[0008] Typically, the aerosol has a mass of at least 10 μg. Preferably, the aerosol has a mass of at least 100 μg. More preferably, the aerosol has a mass of at least 200 μg.

[0009] Typically, the particles comprise less than 10 percent by weight of erectile dysfunction drug degradation products. Preferably, the particles comprise less than 5 percent by weight of erectile dysfunction drug degradation products. More preferably, the particles comprise less than 2.5, 1, 0.5, 0.1 or 0.03 percent by weight of erectile dysfunction drug degradation products.

[0010] Typically, the particles comprise less than 90 percent by weight of water. Preferably, the particles comprise less than 80 percent by weight of water. More preferably, the particles comprise less than 70 percent, 60 percent, 50 percent, 40 percent, 30 percent, 20 percent, 10 percent, or 5 percent by weight of water.

[0011] Typically, at least 50 percent by weight of the aerosol is amorphous in form, wherein crystalline forms make up less than 50 percent by weight of the total aerosol weight, regardless of the nature of individual particles. Preferably, at least 75 percent by weight of the aerosol is amorphous in form. More preferably, at least 90 percent by weight of the aerosol is amorphous in form.

[0012] Typically, the aerosol has an inhalable aerosol particle density greater than 10^6 particles/mL. Preferably, the aerosol has an inhalable aerosol particle density greater than 10^7 particles/mL or 10^8 particles/mL.

[0013] Typically, the aerosol particles have a mass median aerodynamic diameter of less than 5 microns. Preferably, the particles have a mass median

aerodynamic diameter of less than 3 microns. More preferably, the particles have a mass median aerodynamic diameter of less than 2 or 1 micron(s).

[0014] Typically, the geometric standard deviation around the mass median aerodynamic diameter of the aerosol particles is less than 3.5. Preferably, the geometric standard deviation is less than 3.0. More preferably, the geometric standard deviation is less than 2.5 or 2.2.

[0015] Typically, the aerosol is formed by heating a composition containing an erectile dysfunction drug to form a vapor and subsequently allowing the vapor to condense into an aerosol.

[0016] In another composition aspect of the present invention, the aerosol comprises particles comprising at least 5 percent by weight of sildenafil, tadalafil or vardenafil. Preferably, the particles comprise at least 10 percent by weight of sildenafil, tadalafil or vardenafil. More preferably, the particles comprise at least 20 percent, 30 percent, 40 percent, 50 percent, 60 percent, 70 percent, 80 percent, 90 percent, 95 percent, 97 percent, 99 percent, 99.5 percent or 99.97 percent by weight of sildenafil, tadalafil or vardenafil.

[0017] Typically, the aerosol has a mass of at least 10 μg. Preferably, the aerosol has a mass of at least 100 μg. More preferably, the aerosol has a mass of at least 200 μg.

[0018] Typically, the particles comprise less than 10 percent by weight of sildenafil, tadalafil or vardenafil degradation products. Preferably, the particles comprise less than 5 percent by weight of sildenafil, tadalafil or vardenafil degradation products. More preferably, the particles comprise less than 2.5, 1, 0.5, 0.1 or 0.03 percent by weight of sildenafil, tadalafil or vardenafil degradation products.

[0019] Typically, the particles comprise less than 90 percent by weight of water. Preferably, the particles comprise less than 80 percent by weight of water. More preferably, the particles comprise less than 70 percent, 60 percent, 50 percent, 40 percent, 30 percent, 20 percent, 10 percent, or 5 percent by weight of water.

[0020] Typically, at least 50 percent by weight of the aerosol is amorphous in form, wherein crystalline forms make up less than 50 percent by weight of the total aerosol weight, regardless of the nature of individual particles. Preferably, at least 75 percent by weight of the aerosol is amorphous in form. More preferably, at least 90 percent by weight of the aerosol is amorphous in form.

[0021] Typically, where the aerosol comprises sildenafil, the aerosol has an inhalable aerosol drug mass density of between 5 mg/L and 40 mg/L. Preferably, the aerosol has an inhalable aerosol drug mass density of between 10 mg/L and 35 mg/L. More preferably, the aerosol has an inhalable aerosol drug mass density of between 15 mg/L and 30 mg/L.

[0022] Typically, where the aerosol comprises tadalafil, the aerosol has an inhalable aerosol drug mass density of between 2.5 mg/L and 20 mg/L. Preferably, the aerosol has an inhalable aerosol drug mass density of between 3.5 mg/L and 17.5 mg/L. More preferably, the aerosol has an inhalable aerosol drug mass density of between 5 mg/L and 15 mg/L.

[0023] Typically, where the aerosol comprises vardenafil, the aerosol has an inhalable aerosol drug mass density of between 1 mg/L and 20 mg/L. Preferably, the aerosol has an inhalable aerosol drug mass density of between 1.5 mg/L and 17.5 mg/L. More preferably, the aerosol has an inhalable aerosol drug mass density of between 2 mg/L and 15 mg/L.

[0024] Typically, the aerosol has an inhalable aerosol particle density greater than 10^6 particles/mL. Preferably, the aerosol has an inhalable aerosol particle density greater than 10^7 particles/mL or 10^8 particles/mL.

[0025] Typically, the aerosol particles have a mass median aerodynamic diameter of less than 5 microns. Preferably, the particles have a mass median aerodynamic diameter of less than 3 microns. More preferably, the particles have a mass median aerodynamic diameter of less than 2 or 1 micron(s).

[0026] Typically, the geometric standard deviation around the mass median aerodynamic diameter of the aerosol particles is less than 3.5. Preferably, the geometric standard deviation is less than 3.0. More preferably, the geometric standard deviation is less than 2.5 or 2.2.

[0027] Typically, the aerosol is formed by heating a composition containing sildenafil, tadalafil or vardenafil to form a vapor and subsequently allowing the vapor to condense into an aerosol.

[0028] In a method aspect of the present invention, an erectile dysfunction drug is delivered to a mammal through an inhalation route. The method comprises: a) heating a composition, wherein the composition comprises at least 5 percent by weight of an erectile dysfunction drug, to form a vapor; and, b) allowing the vapor to cool, thereby forming a condensation aerosol comprising particles, which is inhaled by the mammal. Preferably, the composition that is heated comprises at least 10 percent by weight of an erectile dysfunction drug. More preferably, the composition comprises at least 20 percent, 30 percent, 40 percent, 50 percent, 60 percent, 70 percent, 80 percent, 90 percent, 95 percent, 97 percent, 99 percent, 99.5 percent, 99.9 percent or 99.97 percent by weight of an erectile dysfunction drug.

[0029] Typically, the particles comprise at least 5 percent by weight of an erectile dysfunction drug. Preferably, the particles comprise at least 10 percent by weight of an erectile dysfunction drug. More preferably, the particles comprise at least 20 percent, 30 percent, 40 percent, 50 percent, 60 percent, 70 percent, 80 percent, 90 percent, 95 percent, 97 percent, 99 percent, 99.5 percent, 99.9 percent or 99.97 percent by weight of an erectile dysfunction drug.

[0030] Typically, the aerosol has a mass of at least 10 μg. Preferably, the aerosol has a mass of at least 100 μg. More preferably, the aerosol has a mass of at least 200 μg.

[0031] Typically, the particles comprise less than 10 percent by weight of erectile dysfunction drug degradation products. Preferably, the particles comprise less than 5 percent by weight of erectile dysfunction drug degradation products. More preferably, the particles comprise 2.5, 1, 0.5, 0.1 or 0.03 percent by weight of erectile dysfunction drug degradation products.

[0032] Typically, the particles comprise less than 90 percent by weight of water. Preferably, the particles comprise less than 80 percent by weight of water. More preferably, the particles comprise less than 70 percent, 60 percent, 50

percent, 40 percent, 30 percent, 20 percent, 10 percent, or 5 percent by weight of water.

[0033] Typically, at least 50 percent by weight of the aerosol is amorphous in form, wherein crystalline forms make up less than 50 percent by weight of the total aerosol weight, regardless of the nature of individual particles. Preferably, at least 75 percent by weight of the aerosol is amorphous in form. More preferably, at least 90 percent by weight of the aerosol is amorphous in form.

[0034] Typically, the particles of the delivered condensation aerosol have a mass median aerodynamic diameter of less than 5 microns. Preferably, the particles have a mass median aerodynamic diameter of less than 3 microns. More preferably, the particles have a mass median aerodynamic diameter of less than 2 or 1 micron(s).

[0035] Typically, the geometric standard deviation around the mass median aerodynamic diameter of the aerosol particles is less than 3.5. Preferably, the geometric standard deviation is less than 3.0. More preferably, the geometric standard deviation is less than 2.5 or 2.2.

[0036] Typically, the delivered aerosol has an inhalable aerosol particle density greater than 10^6 particles/mL. Preferably, the aerosol has an inhalable aerosol particle density greater than 10^7 particles/mL or 10^8 particles/mL.

[0037] Typically, the rate of inhalable aerosol particle formation of the delivered condensation aerosol is greater than 10^8 particles per second. Preferably, the aerosol is formed at a rate greater than 10^9 inhalable particles per second. More preferably, the aerosol is formed at a rate greater than 10^{10} inhalable particles per second.

[0038] Typically, the delivered condensation aerosol is formed at a rate greater than 0.5 mg/second. Preferably, the aerosol is formed at a rate greater than 0.75 mg/second. More preferably, the aerosol is formed at a rate greater than 1 mg/second, 1.5 mg/second or 2 mg/second.

[0039] Typically, the delivered condensation aerosol results in a peak plasma concentration of an erectile dysfunction drug in the mammal in less than 1 h. Preferably, the peak plasma concentration is reached in less than 0.5 h. More

preferably, the peak plasma concentration is reached in less than 0.2, 0.1, 0.05, 0.02, 0.01, or 0.005 h (arterial measurement).

[0040] In another method aspect of the present invention, either sildenafil, tadalafil or vardenafil is delivered to a mammal through an inhalation route. The method comprises: a) heating a composition, wherein the composition comprises at least 5 percent by weight of sildenafil, tadalafil or vardenafil, to form a vapor; and, b) allowing the vapor to cool, thereby forming a condensation aerosol comprising particles, which is inhaled by the mammal. Preferably, the composition that is heated comprises at least 10 percent by weight of sildenafil, tadalafil or vardenafil. More preferably, the composition comprises at least 20 percent, 30 percent, 40 percent, 50 percent, 60 percent, 70 percent, 80 percent, 90 percent, 95 percent, 97 percent, 99 percent, 99.5 percent, 99.9 percent or 99.97 percent by weight of sildenafil, tadalafil or vardenafil.

[0041] Typically, the particles comprise at least 5 percent by weight of sildenafil, tadalafil or vardenafil. Preferably, the particles comprise at least 10 percent by weight of sildenafil, tadalafil or vardenafil. More preferably, the particles comprise at least 20 percent, 30 percent, 40 percent, 50 percent, 60 percent, 70 percent, 80 percent, 90 percent, 95 percent, 97 percent, 99 percent, 99.5 percent, 99.9 percent or 99.97 percent by weight of sildenafil, tadalafil or vardenafil.

[0042] Typically, the aerosol has a mass of at least 10 μg. Preferably, the aerosol has a mass of at least 100 μg. More preferably, the aerosol has a mass of at least 200 μg.

[0043] Typically, the particles comprise less than 10 percent by weight of sildenafil, tadalafil or vardenafil degradation products. Preferably, the particles comprise less than 5 percent by weight of sildenafil, tadalafil or vardenafil degradation products. More preferably, the particles comprise 2.5, 1, 0.5, 0.1 or 0.03 percent by weight of sildenafil, tadalafil or vardenafil degradation products.

[0044] Typically, the particles comprise less than 90 percent by weight of water. Preferably, the particles comprise less than 80 percent by weight of water. More preferably, the particles comprise less than 70 percent, 60 percent, 50

percent, 40 percent, 30 percent, 20 percent, 10 percent, or 5 percent by weight of water.

[0045] Typically, at least 50 percent by weight of the aerosol is amorphous in form, wherein crystalline forms make up less than 50 percent by weight of the total aerosol weight, regardless of the nature of individual particles. Preferably, at least 75 percent by weight of the aerosol is amorphous in form. More preferably, at least 90 percent by weight of the aerosol is amorphous in form.

[0046] Typically, the particles of the delivered condensation aerosol have a mass median aerodynamic diameter of less than 5 microns. Preferably, the particles have a mass median aerodynamic diameter of less than 3 microns. More preferably, the particles have a mass median aerodynamic diameter of less than 2 or 1 micron(s).

[0047] Typically, the geometric standard deviation around the mass median aerodynamic diameter of the aerosol particles is less than 3.5. Preferably, the geometric standard deviation is less than 3.0. More preferably, the geometric standard deviation is less than 2.5 or 2.2.

[0048] Typically, where the aerosol comprises sildenafil, the delivered aerosol has an inhalable aerosol drug mass density of between 5 mg/L and 40 mg/L. Preferably, the aerosol has an inhalable aerosol drug mass density of between 10 mg/L and 35 mg/L. More preferably, the aerosol has an inhalable aerosol drug mass density of between 15 mg/L and 30 mg/L.

[0049] Typically, where the aerosol comprises tadalafil, the delivered aerosol has an inhalable aerosol drug mass density of between 2.5 mg/L and 20 mg/L. Preferably, the aerosol has an inhalable aerosol drug mass density of between 3.5 mg/L and 17.5 mg/L. More preferably, the aerosol has an inhalable aerosol drug mass density of between 5 mg/L and 15 mg/L.

[0050] Typically, where the aerosol comprises vardenafil, the delivered aerosol has an inhalable aerosol drug mass density of between 1 mg/L and 20 mg/L. Preferably, the aerosol has an inhalable aerosol drug mass density of between 1.5 mg/L and 17.5 mg/L. More preferably, the aerosol has an inhalable aerosol drug mass density of between 2 mg/L and 15 mg/L.

[0051] Typically, the delivered aerosol has an inhalable aerosol particle density greater than 10^6 particles/mL. Preferably, the aerosol has an inhalable aerosol particle density greater than 10^7 particles/mL or 10^8 particles/mL.

[0052] Typically, the rate of inhalable aerosol particle formation of the delivered condensation aerosol is greater than 10^8 particles per second. Preferably, the aerosol is formed at a rate greater than 10^9 inhalable particles per second. More preferably, the aerosol is formed at a rate greater than 10^{10} inhalable particles per second.

[0053] Typically, the delivered condensation aerosol is formed at a rate greater than 0.5 mg/second. Preferably, the aerosol is formed at a rate greater than 0.75 mg/second. More preferably, the aerosol is formed at a rate greater than 1 mg/second, 1.5 mg/second or 2 mg/second.

[0054] Typically, where the condensation aerosol comprises sildenafil, between 5 mg and 40 mg of sildenafil are delivered to the mammal in a single inspiration. Preferably, between 10 mg and 35 mg of sildenafil are delivered to the mammal in a single inspiration. More preferably, between 15 mg and 30 mg of sildenafil are delivered in a single inspiration.

[0055] Typically, where the condensation aerosol comprises tadalafil, between 2.5 mg and 20 mg of tadalafil are delivered to the mammal in a single inspiration. Preferably, between 3.5 mg and 17.5 mg of tadalafil are delivered to the mammal in a single inspiration. More preferably, between 5 mg and 15 mg of tadalafil are delivered in a single inspiration.

[0056] Typically, where the condensation aerosol comprises vardenafil, between 1 mg and 20 mg of vardenafil are delivered to the mammal in a single inspiration. Preferably, between 1.5 mg and 17.5 mg of vardenafil are delivered to the mammal in a single inspiration. More preferably, between 2 mg and 15 mg of vardenafil are delivered in a single inspiration.

[0057] Typically, the delivered condensation aerosol results in a peak plasma concentration of sildenafil, tadalafil or vardenafil in the mammal in less than 1 h. Preferably, the peak plasma concentration is reached in less than 0.5 h. More

preferably, the peak plasma concentration is reached in less than 0.2, 0.1, 0.05, 0.02, 0.01, or 0.005 h (arterial measurement).

[0058] In a kit aspect of the present invention, a kit for delivering an erectile dysfunction drug through an inhalation route to a mammal is provided which comprises: a) a composition comprising at least 5 percent by weight of an erectile dysfunction drug; and, b) a device that forms an erectile dysfunction drug aerosol from the composition, for inhalation by the mammal. Preferably, the composition comprises at least 20 percent, 30 percent, 40 percent, 50 percent, 60 percent, 70 percent, 80 percent, 90 percent, 95 percent, 97 percent, 99 percent, 99.5 percent, 99.9 percent or 99.97 percent by weight of an erectile dysfunction drug.

[0059] Typically, the device contained in the kit comprises: a) an element for heating the erectile dysfunction drug composition to form a vapor; b) an element allowing the vapor to cool to form an aerosol; and, c) an element permitting the mammal to inhale the aerosol.

[0060] In a kit aspect of the present invention, a kit for delivering sildenafil, tadalafil or vardenafil through an inhalation route to a mammal is provided which comprises: a) a composition comprising at least 5 percent by weight of sildenafil, tadalafil or vardenafil; and, b) a device that forms a sildenafil, tadalafil or vardenafil aerosol from the composition, for inhalation by the mammal. Preferably, the composition comprises at least 20 percent, 30 percent, 40 percent, 50 percent, 60 percent, 70 percent, 80 percent, 90 percent, 95 percent, 97 percent, 99 percent, 99.5 percent, 99.9 percent or 99.97 percent by weight of sildenafil, tadalafil or vardenafil.

[0061] Typically, the device contained in the kit comprises: a) an element for heating the sildenafil, tadalafil or vardenafil composition to form a vapor; b) an element allowing the vapor to cool to form an aerosol; and, c) an element permitting the mammal to inhale the aerosol.

Brief Description of the Figure

[0062] Fig. 1 shows a cross-sectional view of a device used to deliver erectile dysfunction drug aerosols to a mammal through an inhalation route.

Detailed Description of the Invention

Definitions

[0063] "Aerodynamic diameter" of a given particle refers to the diameter of a spherical droplet with a density of 1 g/mL (the density of water) that has the same settling velocity as the given particle.

[0064] "Aerosol" refers to a suspension of solid or liquid particles in a gas.

[0065] "Aerosol drug mass density" refers to the mass of sildenafil or tadalafil per unit volume of aerosol.

[0066] "Aerosol mass density" refers to the mass of particulate matter per unit volume of aerosol.

[0067] "Aerosol particle density" refers to the number of particles per unit volume of aerosol.

[0068] "Amorphous particle" refers to a particle that does not contain more than 50 percent by weight of a crystalline form. Preferably, the particle does not contain more than 25 percent by weight of a crystalline form. More preferably, the particle does not contain more than 10 percent by weight of a crystalline form.

[0069] "Condensation aerosol" refers to an aerosol formed by vaporization of a substance followed by condensation of the substance into an aerosol.

[0070] "Erectile dysfunction drug" degradation product refers to a compound resulting from a chemical modification of an erectile dysfunction drug. The modification, for example, can be the result of a thermally or photochemically induced reaction. Such reactions include, without limitation, oxidation and hydrolysis.

[0071] "Inhalable aerosol drug mass density" refers to the aerosol drug mass density produced by an inhalation device and delivered into a typical patient tidal volume.

[0072] "Inhalable aerosol mass density" refers to the aerosol mass density produced by an inhalation device and delivered into a typical patient tidal volume.

[0073] "Inhalable aerosol particle density" refers to the aerosol particle density of particles of size between 100 nm and 5 microns produced by an inhalation device and delivered into a typical patient tidal volume.

[0074] "Mass median aerodynamic diameter" or "MMAD" of an aerosol refers to the aerodynamic diameter for which half the particulate mass of the aerosol is contributed by particles with an aerodynamic diameter larger than the MMAD and half by particles with an aerodynamic diameter smaller than the MMAD.

[0075] "Rate of aerosol formation" refers to the mass of aerosolized particulate matter produced by an inhalation device per unit time.

[0076] "Rate of inhalable aerosol particle formation" refers to the number of particles of size between 100 nm and 5 microns produced by an inhalation device per unit time.

[0077] "Rate of drug aerosol formation" refers to the mass of aerosolized sildenafil or tadalafil produced by an inhalation device per unit time.

[0078] "Settling velocity" refers to the terminal velocity of an aerosol particle undergoing gravitational settling in air.

[0079] "Sildenafil" refers to 5-[2-ethoxy-5-(4-methylpiperazin-1-ylsulfonyl)phenyl]-1- methyl-3-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one.

[0080] "Sildenafil degradation product" refers to a compound resulting from a chemical modification of sildenafil. The modification, for example, can be the result of a thermally or photochemically induced reaction. Such reactions include, without limitation, oxidation and hydrolysis.

[0081] "Tadalafil" refers to (6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-[3,4-(methylenedioxy)phenyl]pyrazino[1',2':1,6]pyrido[3,4-b]indole-1,4-dione.

[0082] "Tadalafil degradation product" refers to a compound resulting from a chemical modification of tadalafil. The modification, for example, can be the

result of a thermally or photochemically induced reaction. Such reactions include, without limitation, oxidation and hydrolysis.

[0083] "Typical patient tidal volume" refers to 1 L for an adult patient and 15 mL/kg for a pediatric patient.

[0084] "Vapor" refers to a gas, and "vapor phase" refers to a gas phase. The term "thermal vapor" refers to a vapor phase, aerosol, or mixture of aerosol-vapor phases, formed preferably by heating.

[0085] "Vardenafil" refers to 1-[[3-(1,4-dihydro-5-methyl-4-oxo-7-propylimidazo[5,1-f][1,2,4]triazin-2-yl)-4-ethoxyphenyl]sulfonyl]-4-ethyl-piperazine ($C_{23}H_{32}N_6O_4S$).

[0086] "Vardenafil degradation product" refers to a compound resulting from a chemical modification of vardenafil. The modification, for example, can be the result of a thermally or photochemically induced reaction. Such reactions include, without limitation, oxidation and hydrolysis.

Formation of Erectile Dysfunction Drug Containing Aerosols

[0087] Any suitable method is used to form the aerosols of the present invention. A preferred method, however, involves heating a composition comprising an erectile dysfunction drug to form a vapor, followed by cooling of the vapor such that it condenses to provide an erectile dysfunction drug comprising aerosol (condensation aerosol). The composition is heated in one of four forms: as pure active compound (*e.g.*, pure sildenafil, tadalafil or vardenafil); as a mixture of active compound and a pharmaceutically acceptable excipient; as a salt form of the pure active compound; and, as a mixture of active compound salt form and a pharmaceutically acceptable excipient.

[0088] Salt forms of erectile dysfunction drugs (*e.g.*, sildenafil, tadalafil or vardenafil) are either commercially available or are obtained from the corresponding free base using well known methods in the art. A variety of pharmaceutically acceptable salts are suitable for aerosolization. Such salts include, without limitation, the following: hydrochloric acid, hydrobromic acid, acetic acid, maleic acid, formic acid, and fumaric acid salts.

[0089] Pharmaceutically acceptable excipients may be volatile or nonvolatile. Volatile excipients, when heated, are concurrently volatilized, aerosolized and inhaled with the erectile dysfunction drug. Classes of such excipients are known in the art and include, without limitation, gaseous, supercritical fluid, liquid and solid solvents. The following is a list of exemplary carriers within the classes: water; terpenes, such as menthol; alcohols, such as ethanol, propylene glycol, glycerol and other similar alcohols; dimethylformamide; dimethylacetamide; wax; supercritical carbon dioxide; dry ice; and mixtures thereof.

[0090] Solid supports on which the composition is heated are of a variety of shapes. Examples of such shapes include, without limitation, cylinders of less than 1.0 mm in diameter, boxes of less than 1.0 mm thickness and virtually any shape permeated by small (*e.g.*, less than 1.0 mm-sized) pores. Preferably, solid supports provide a large surface to volume ratio (*e.g.*, greater than 100 per meter) and a large surface to mass ratio (*e.g.*, greater than 1 cm^2 per gram).

[0091] A solid support of one shape can also be transformed into another shape with different properties. For example, a flat sheet of 0.25 mm thickness has a surface to volume ratio of approximately 8,000 per meter. Rolling the sheet into a hollow cylinder of 1 cm diameter produces a support that retains the high surface to mass ratio of the original sheet but has a lower surface to volume ratio (about 400 per meter).

[0092] A number of different materials are used to construct the solid supports. Classes of such materials include, without limitation, metals, inorganic materials, carbonaceous materials and polymers. The following are examples of the material classes: aluminum, silver, gold, stainless steel, copper and tungsten; silica, glass, silicon and alumina; graphite, porous carbons, carbon yarns and carbon felts; polytetrafluoroethylene and polyethylene glycol. Combinations of materials and coated variants of materials are used as well.

[0093] Where aluminum is used as a solid support, aluminum foil is a suitable material. Examples of silica, alumina and silicon based materials include amphorous silica S-5631 (Sigma, St. Louis, MO), BCR171 (an alumina of defined surface area greater than 2 m^2/g from Aldrich, St. Louis, MO) and a silicon wafer

as used in the semiconductor industry. Carbon yarns and felts are available from American Kynol, Inc., New York, NY. Chromatography resins such as octadecycl silane chemically bonded to porous silica are exemplary coated variants of silica.

[0094] The heating of the erectile drug compositions is performed using any suitable method. Examples of methods by which heat can be generated include the following: passage of current through an electrical resistance element; absorption of electromagnetic radiation, such as microwave or laser light; and, exothermic chemical reactions, such as exothermic solvation, hydration of pyrophoric materials and oxidation of combustible materials.

Delivery of Erectile Dysfunction Drug Containing Aerosols

[0095] Erectile dysfunction drug containing aerosols of the present invention are delivered to a mammal using an inhalation device. Where the aerosol is a condensation aerosol, the device has at least three elements: an element for heating an erectile dysfunction drug containing composition to form a vapor; an element allowing the vapor to cool, thereby providing a condensation aerosol; and, an element permitting the mammal to inhale the aerosol. Various suitable heating methods are described above. The element that allows cooling is, in it simplest form, an inert passageway linking the heating means to the inhalation means. The element permitting inhalation is an aerosol exit portal that forms a connection between the cooling element and the mammal's respiratory system.

[0096] One device used to deliver the erectile dysfunction drug containing aerosol is described in reference to Fig. 1. Delivery device 100 has a proximal end 102 and a distal end 104, a heating module 106, a power source 108, and a mouthpiece 110. An erectile dysfunction drug composition is deposited on a surface 112 of heating module 106. Upon activation of a user activated switch 114, power source 108 initiates heating of heating module 106 (*e.g*, through ignition of combustible fuel or passage of current through a resistive heating element). The erectile dysfunction drug composition volatilizes due to the heating of heating module 106 and condenses to form a condensation aerosol prior to

reaching the mouthpiece 110 at the proximal end of the device 102. Air flow traveling from the device distal end 104 to the mouthpiece 110 carries the condensation aerosol to the mouthpiece 110, where it is inhaled by the mammal.

[0097] Devices, if desired, contain a variety of components to facilitate the delivery of erectile dysfunction drug containing aerosols. For instance, the device may include any component known in the art to control the timing of drug aerosolization relative to inhalation (*e.g.*, breath-actuation), to provide feedback to patients on the rate and/or volume of inhalation, to prevent excessive use (*i.e.*, "lock-out" feature), to prevent use by unauthorized individuals, and/or to record dosing histories.

Dosage of Sildenafil or Tadalafil Containing Aerosols

[0098] The dosage amount of an erectile dysfunction drug in aerosol form is generally no greater than twice the standard dose of the drug given orally. For instance, sildenafil, tadalafil and vardenafil are given at strengths of 25 mg, 10 mg, and 5 mg respectively for the treatment of erectile dysfunction. As aerosols, 5 mg to 40 mg of sildenafil, 2.5 mg to 20 mg of tadalafil, and 1 to 20 mg of vardenafil are generally provided for the same indication. A typical dosage of an erectile dysfunction drug aerosol is either administered as a single inhalation or as a series of inhalations taken within an hour or less (dosage equals sum of inhaled amounts). Where the drug is administered as a series of inhalations, a different amount may be delivered in each inhalation.

[0099] One can determine the appropriate dose of erectile dysfunction drug containing aerosols to treat a particular condition using methods such as animal experiments and a dose-finding (Phase I/II) clinical trial. One animal experiment involves measuring plasma concentrations of drug in an animal after its exposure to the aerosol. Mammals such as dogs or primates are typically used in such studies, since their respiratory systems are similar to that of a human. Initial dose levels for testing in humans is generally less than or equal to the dose in the mammal model that resulted in plasma drug levels associated with a therapeutic effect in humans. Dose escalation in humans is then performed, until either an

optimal therapeutic response is obtained or a dose-limiting toxicity is encountered.

Analysis of Erectile Dysfunction Drug Containing Aerosols

[0100] Purity of an erectile dysfunction drug containing aerosol is determined using a number of methods, examples of which are described in Sekine *et al.*, *Journal of Forensic Science* 32:1271-1280 (1987) and *Martin et al.*, *Journal of Analytic Toxicology* 13:158-162 (1989). One method involves forming the aerosol in a device through which a gas flow (*e.g.*, air flow) is maintained, generally at a rate between 0.4 and 60 L/min. The gas flow carries the aerosol into one or more traps. After isolation from the trap, the aerosol is subjected to an analytical technique, such as gas or liquid chromatography, that permits a determination of composition purity.

[0101] A variety of different traps are used for aerosol collection. The following list contains examples of such traps: filters; glass wool; impingers; solvent traps, such as dry ice-cooled ethanol, methanol, acetone and dichloromethane traps at various pH values; syringes that sample the aerosol; empty, low-pressure (*e.g.*, vacuum) containers into which the aerosol is drawn; and, empty containers that fully surround and enclose the aerosol generating device. Where a solid such as glass wool is used, it is typically extracted with a solvent such as ethanol. The solvent extract is subjected to analysis rather than the solid (*i.e.*, glass wool) itself. Where a syringe or container is used, the container is similarly extracted with a solvent.

[0102] The gas or liquid chromatograph discussed above contains a detection system (*i.e.*, detector). Such detection systems are well known in the art and include, for example, flame ionization, photon absorption and mass spectrometry detectors. An advantage of a mass spectrometry detector is that it can be used to determine the structure of erectile dysfunction drug degradation products.

[0103] Particle size distribution of an erectile dysfunction drug containing aerosol is determined using any suitable method in the art (*e.g.*, cascade impaction). An Andersen Eight Stage Non-viable Cascade Impactor (Andersen

Instruments, Smyrna, GA) linked to a furnace tube by a mock throat (USP throat, Andersen Instruments, Smyrna, GA) is one system used for cascade impaction studies.

[0104] Inhalable aerosol mass density is determined, for example, by delivering a drug-containing aerosol into a confined chamber via an inhalation device and measuring the mass collected in the chamber. Typically, the aerosol is drawn into the chamber by having a pressure gradient between the device and the chamber, wherein the chamber is at lower pressure than the device. The volume of the chamber should approximate the tidal volume of an inhaling patient.

[0105] Inhalable aerosol drug mass density is determined, for example, by delivering a drug-containing aerosol into a confined chamber via an inhalation device and measuring the amount of active drug compound collected in the chamber. Typically, the aerosol is drawn into the chamber by having a pressure gradient between the device and the chamber, wherein the chamber is at lower pressure than the device. The volume of the chamber should approximate the tidal volume of an inhaling patient. The amount of active drug compound collected in the chamber is determined by extracting the chamber, conducting chromatographic analysis of the extract and comparing the results of the chromatographic analysis to those of a standard containing known amounts of drug.

[0106] Inhalable aerosol particle density is determined, for example, by delivering aerosol phase drug into a confined chamber via an inhalation device and measuring the number of particles of given size collected in the chamber. The number of particles of a given size may be directly measured based on the light-scattering properties of the particles. Alternatively, the number of particles of a given size is determined by measuring the mass of particles within the given size range and calculating the number of particles based on the mass as follows: Total number of particles = Sum (from size range 1 to size range N) of number of particles in each size range. Number of particles in a given size range = Mass in the size range/Mass of a typical particle in the size range. Mass of a typical particle in a given size range = $\pi * D^3 * \varphi/6$, where D is a typical particle diameter in

the size range (generally, the mean boundary MMADs defining the size range) in microns, φ is the particle density (in g/mL) and mass is given in units of picograms (g^{-12}).

[0107] Rate of inhalable aerosol particle formation is determined, for example, by delivering aerosol phase drug into a confined chamber via an inhalation device. The delivery is for a set period of time (*e.g.*, 3 s), and the number of particles of a given size collected in the chamber is determined as outlined above. The rate of particle formation is equal to the number of 100 nm to 5 micron particles collected divided by the duration of the collection time.

[0108] Rate of aerosol formation is determined, for example, by delivering aerosol phase drug into a confined chamber via an inhalation device. The delivery is for a set period of time (*e.g.*, 3 s), and the mass of particulate matter collected is determined by weighing the confined chamber before and after the delivery of the particulate matter. The rate of aerosol formation is equal to the increase in mass in the chamber divided by the duration of the collection time. Alternatively, where a change in mass of the delivery device or component thereof can only occur through release of the aerosol phase particulate matter, the mass of particulate matter may be equated with the mass lost from the device or component during the delivery of the aerosol. In this case, the rate of aerosol formation is equal to the decrease in mass of the device or component during the delivery event divided by the duration of the delivery event.

[0109] Rate of drug aerosol formation is determined, for example, by delivering an erectile dysfunction drug containing aerosol into a confined chamber via an inhalation device over a set period of time (*e.g.*, 3 s). Where the aerosol is pure erectile dysfunction drug, the amount of drug collected in the chamber is measured as described above. The rate of drug aerosol formation is equal to the amount of erectile dysfunction drug collected in the chamber divided by the duration of the collection time. Where the erectile dysfunction drug containing aerosol comprises a pharmaceutically acceptable excipient, multiplying the rate of aerosol formation by the percentage of erectile dysfunction drug in the aerosol provides the rate of drug aerosol formation.

Utility of Erectile Dysfunction Drug Containing Aerosols

[0110] The erectile dysfunction drug containing aerosols of the present invention are typically used for the treatment of erectile dysfunction.

[0111] The following examples are meant to illustrate, rather than limit, the present invention.

[0112] Sildenafil citrate is commercially available as the active ingredient in VIAGRA® and can be isolated using standard methods in the art. Tadalafil can be synthesized using the methods described in U.S. Pat. No. 6,143,746 (issued November 7, 2000). Vardenafil can be synthesized using the methods described in WO/99/24433 published (May 20, 1999). Other erectile dysfunction drugs can be similarly obtained.

EXAMPLE 1

General Procedure for Obtaining Free Base of a Compound Salt

[0113] Approximately 1 g of salt (*e.g.*, mono hydrochloride) is dissolved in deionized water (~30 mL). Three equivalents of sodium hydroxide (1 N $NaOH_{aq}$) is added dropwise to the solution, and the pH is checked to ensure it is basic. The aqueous solution is extracted four times with dichloromethane (~50 mL), and the extracts are combined, dried (Na_2SO_4) and filtered. The filtered organic solution is concentrated using a rotary evaporator to provide the desired free base. If necessary, purification of the free base is performed using standard methods such as chromatography or recrystallization.

EXAMPLE 2

General Procedure for Volatilizing Compounds from Halogen Bulb

[0114] A solution of drug in approximately 120 µL dichloromethane is coated on a 3.5 cm x 7.5 cm piece of aluminum foil (precleaned with acetone). The

dichloromethane is allowed to evaporate. The coated foil is wrapped around a 300 watt halogen tube (Feit Electric Company, Pico Rivera, CA), which is inserted into a glass tube sealed at one end with a rubber stopper. Running 90 V of alternating current (driven by line power controlled by a variac) through the bulb for 2.5 s affords thermal vapor (including aerosol), which is collected on the glass tube walls. Reverse-phase HPLC analysis with detection by absorption of 225 nm light is used to determine the purity of the aerosol. (When desired, the system is flushed through with argon prior to volatilization.)

[0115] Tadalafil aerosol (0.29 mg) was obtained in 98.5% purity using this procedure. To obtain higher purity aerosols, one can coat a lesser amount of drug, yielding a thinner film to heat. A linear decrease in film thickness is associated with a linear decrease in impurities.

EXAMPLE 3

Second General Procedure for Volatilizing Compounds

[0116] A flash assembly consisting of a stainless steel outer cylinder and an inner brass electrode was dipped into an organic solution containing a drug and quickly removed. Evaporation of residual solvent from the assembly was performed by air drying. This left a film of drug coated on the exterior surface of the stainless steel cylinder. The assembly was electrically connected to a capacitor network (*e.g.*, 1.5 F) and a mechanical relay using brass connectors and then placed into a glass sleeve. A filter assembly was placed between the glass sleeve and a vacuum system. Flow (~15 L/min) was instigated through the glass sleeve using the vacuum system. Heating of the flash assembly was performed for about 0.25 s by momentarily turning on the relay between the flash assembly and the capacitors (connected to DC power supply and charged to 20.5 V) to volatilize (form an aerosol of) the coated drug. The assembly was allowed to cool. Analysis of the formed aerosol involved rinsing the filter with 5 mL of acetonitrile and injecting a sample of the organic solution into an HPLC.

Sildenafil aerosol was obtained in 98.9% purity (0.075 mg) using this procedure.

Vardenafil aerosol was obtained in 81.4% purity (0.7 mg) using this procedure.

THE EMBODIMENTS OF THE INVENTION FOR WHICH AN EXCLUSIVE PROPERTY OR PRIVILEGE IS CLAIMED ARE DEFINED AS FOLLOWS:

1. A composition for delivery of an erectile dysfunction drug, comprising a condensation aerosol

a) formed by volatilizing an erectile dysfunction drug under conditions effective to produce a vapor of the drug, and condensing the vapor to form a condensation aerosol,

b) wherein the condensation aerosol comprises particles characterized by at least 5 percent by weight of the drug and less than 5 percent by weight drug degradation products, and

c) wherein the condensation aerosol has an MMAD of less than 5 μm.

2. A composition for delivery of an erectile dysfunction drug comprising a condensation aerosol

a) formed by volatilizing an erectile dysfunction drug selected from sildenafil, tadalafil or vardenafil under conditions effective to produce a vapor of the drug, and condensing the vapor to form a condensation aerosol,

b) wherein the condensation aerosol comprises particles characterized by at least 5 percent by weight of the drug and less than 5 percent by weight drug degradation products, and

c) wherein the condensation aerosol has an MMAD of less than 5 μm.

3. The composition according to claim 2, wherein the drug is in a form of a free base.

4. The composition according to claim 2 or 3, wherein the condensation aerosol particles comprise at least 95 percent by weight of the drug.

5. A method of producing an erectile dysfunction drug in an aerosol form comprising

a) heating a composition comprising an erectile dysfunction drug selected from sildenafil, tadalafil or vardenafil under conditions effective to produce a vapor of the drug,

b) passing air through the vapor,

c) allowing the vapor to cool, thereby forming condensation aerosol particles of the drug, wherein the condensation aerosol particles comprise at least 5 percent by weight of the drug and less than 5 percent by weight drug degradation products and the condensation aerosol has an MMAD of less than 5 μm.

6. The method according to claim 5, wherein the composition comprising the erectile dysfunction drug is coated on a solid support.

7. The method according to claim 5 or 6, wherein the condensation aerosol is formed at a rate of greater than 0.5 mg/sec.

8. The method according to any one of claims 5, 6 or 7, wherein the condensation aerosol particles comprise at least 70 percent by weight of the drug.

9. The method according to claim 8, wherein the condensation aerosol particles comprise at least 95 percent by weight of the drug.

10. A kit for delivering an erectile dysfunction drug condensation aerosol, wherein the kit comprises:

a) a composition comprising an erectile dysfunction drug selected from sildenafil, tadalafil or vardenafil; and

b) a device that forms a drug condensation aerosol from the composition, wherein the condensation aerosol has an MMAD of less than 5 μm and wherein the device comprises:

i) an element for heating the composition to form a vapor;

ii) an element allowing the vapor to cool to form condensation aerosol particles characterized by at least 5 percent by weight of the drug and less than 5 percent by weight drug degradation products; and

iii) an element permitting inhalation of the aerosol.

11. The composition according to claim 4, wherein the condensation aerosol particles comprise at least 97 percent by weight of the drug.

12. The composition according to any one of claims 2, 3, 4 or 11, wherein the condensation aerosol has an MMAD between 1 μm and 5 μm.

13. The composition according to claim 12, wherein the condensation aerosol has an MMAD between 1 μm and 3 μm.

14. The composition according to any one of claims 2, 3, 4, 11, 12 or 13, wherein the volatilizing includes heating a composition comprising the drug coated on a solid support to a temperature sufficient to volatilize the drug from the coating.

15. The method according to claim 8 or 9, wherein the condensation aerosol particles comprise at least 97 percent by weight of the drug.

16. The method according to any one of claims 5, 6, 7, 8, 9 or 15, wherein the condensation aerosol has an MMAD between 1 μm and 5 μm.

17. The method according to claim 16, wherein the condensation aerosol has an MMAD between 1 μm and 3 μm.

18. The method according to claim 6, wherein the drug is in the form of a free base.

19. A condensation aerosol containing an erectile dysfunction compound selected from the group consisting of sildenafil, tadalafil, and vardenafil, wherein:

a) said condensation aerosol comprises particles comprising at least 5 percent by weight of the erectile dysfunction compound and less than 10 percent by weight erectile dysfunction compound degradation products; and

b) said condensation aerosol has an MMAD of less than 5 μm.

20. A condensation aerosol according to claim 19, formed by volatilizing the erectile dysfunction compound under conditions effective to produce a vapor of the erectile dysfunction compound and condensing the vapor to form said particles.

21. A condensation aerosol according to claim 20, wherein said volatilizing includes heating a solid support coated with a composition comprising the erectile dysfunction compound to volatilize the erectile dysfunction compound from the coated composition.

22. A condensation aerosol according to claim 20 or 21, wherein said condensing includes allowing the vapor to cool.

23. A condensation aerosol according to any one of claims 19 to 22, wherein said particles comprise less than 5 percent by weight erectile dysfunction compound degradation products.

24. A condensation aerosol according to any one of claims 19 to 22, wherein said particles comprise less than 2.5 percent by weight erectile dysfunction compound degradation products.

25. A condensation aerosol according to any one of claims 19 to 24, wherein said condensation aerosol comprises at least 90 percent by weight of the erectile dysfunction compound.

26. A condensation aerosol according to any one of claims 19 to 25, wherein said condensation aerosol has an MMAD of less than 3 μm

27. A condensation aerosol according to any one of claims 19 to 26, for use in inhalation therapy.

28. A composition for delivery of an erectile dysfunction compound, the composition comprising a condensation aerosol according to any one of claims 19 to 26.

29. A method of producing an erectile dysfunction compound in an aerosol form comprising:

a) volatilizing an erectile dysfunction compound selected from the group consisting of sildenafil, tadalafil, and vardenafil under conditions effective to produce a vapor of the erectile dysfunction compound, wherein said volatilizing comprises heating a composition comprising at least 5 percent by weight of the erectile dysfunction compound; and

b) condensing the vapor thereby providing a condensation aerosol comprising particles comprising at least 5 percent by weight of the erectile dysfunction compound and less than 10 percent by weight erectile dysfunction compound degradation products and having an MMAD of less than 5 μm.

30. A method according to claim 29, wherein step a) comprises heating a solid support coated with a composition comprising the erectile dysfunction compound to volatilize the erectile dysfunction compound from the coated composition.

31. A method according to claim 29, wherein step a) comprises heating a solid support on which a composition comprising the erectile dysfunction compound is deposited to volatilize the erectile dysfunction compound from the deposited composition.

32. A method according to any one of claims 29 to 31, wherein step b) comprises allowing the vapor to cool thereby providing the condensation aerosol.

33. A method according to any one of claims 29 to 32, wherein said particles comprise less than 5 percent by weight erectile dysfunction compound degradation products.

34. A method according to any one of claims 29 to 32, wherein said particles comprise less than 2.5 percent by weight erectile dysfunction compound degradation products.

35. A method according to any one of claims 29 to 34, wherein said condensation aerosol comprises at least 90 percent by weight of the erectile dysfunction compound.

36. A method according to any one of claims 29 to 35, wherein said particles are formed at a rate of greater than 0.5 mg/sec.

37. A method according to any one of claims 29 to 35, wherein said particles are formed at a rate of greater than 1 mg/sec.

38. A method according to any one of claims 29 to 37, wherein said condensation aerosol has an MMAD of less than 3 μm.

39. A method according to any one of claims 29 to 38, wherein the condensation aerosol is for use in inhalation therapy.

40. A kit for delivering an erectile dysfunction compound, wherein the kit comprises:

a) a composition comprising the erectile dysfunction compound selected from the group consisting of sildenafil, tadalafil, and vardenafil, wherein the composition comprises at least 5 percent by weight of the erectile dysfunction compound; and

b) a device that forms condensation aerosol containing the erectile dysfunction compound from the composition, wherein the condensation aerosol has an MMAD of less than 5 μm; wherein the device comprises:

1) an element for heating the composition to form a vapour;

2) an element allowing the vapour to cool to form a condensation aerosol comprising at least 5 percent by weight of the erectile dysfunction compound and less than 10 percent by weight erectile dysfunction compound degradation products; and

3) an element permitting inhalation of the aerosol.

41. A kit according to claim 40, wherein the condensation aerosol is for use in inhalation therapy.

42. A kit according to claim 40 or 41, wherein the condensation aerosol is as defined in any one of claims 19 to 26.

43. Use of the condensation aerosol as defined in any one of claims 19 to 26, for inhalation therapy.

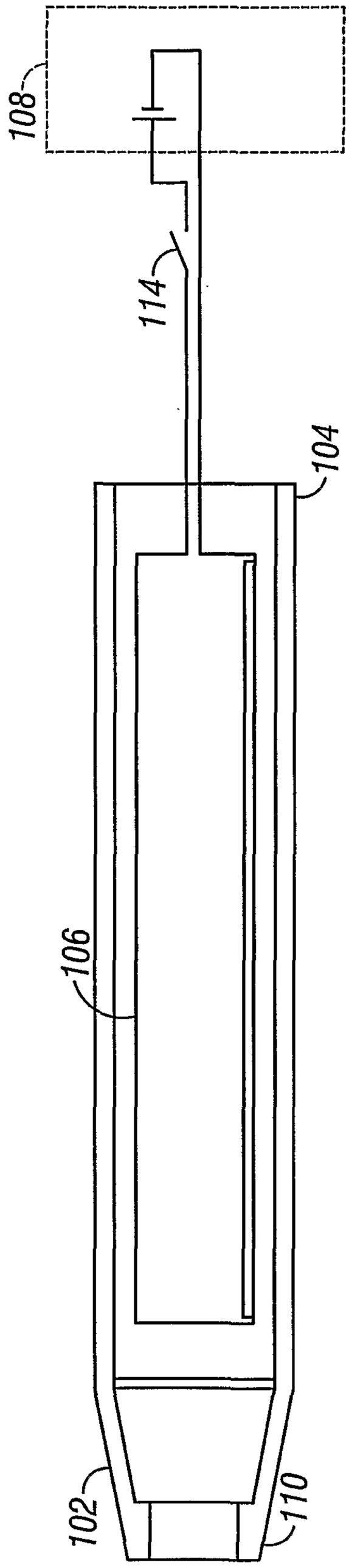

FIG. 1