Claims

1. A drug delivery device configured to be removably inserted in a patient's mouth and for continuous or semi-continuous intraoral administration of a pharmaceutical composition comprising a drug, said device comprising:

(i) a fastener to removably secure said drug delivery device to a surface of said patient's mouth;

(ii) a mechanical pump selected from a spring, an elastomer, compressed gas, and a propellant-driven pump;

(iii) an oral liquid impermeable drug reservoir comprising a pharmaceutical composition, the volume of said drug reservoir being from 0.1 mL to 5 mL; and

(iv) a flow restrictor for controlling the flow of said pharmaceutical composition from said drug reservoir.

2. The drug delivery device of claim 1, wherein said pharmaceutical composition has a viscosity of greater than 100 cP at 37ºC; or wherein said flow restrictor is of less than 4 cm length.

3. The drug delivery device of claim 1 or 2, wherein said pharmaceutical composition comprises levodopa and/or carbidopa, or a pharmaceutically acceptable salt thereof.

4. The device of any one of claims 1-3, wherein said device is configured such that 4 hours after placing a drug delivery device including a fresh reservoir in a patient's mouth and initiating the administration, less than 5% by weight of the drug-including solid or drug-including fluid in the reservoir includes an oral liquid.

5. The drug delivery device of any one of claims 1-4, wherein said mechanical pump comprises a propellant-driven pump; preferably wherein said propellant driven pump comprises 1,1,1,2 tetrafluoroethane or 1,1,1,2,3,3,3 heptafluoropropane; or wherein said device further comprises one or more of the following: (i) an automatic stop/start, (ii) a suction-induced flow limiter, (iii) a temperature-induced flow limiter, (iv) bite-resistant structural supports, or (v) a pressure-invariant pump; or wherein said device comprises a propellant-driven pump configured such that the average rate of drug delivery increases or decreases by less than 10% at 14.7 psia and at 11.3 psia, as compared to said average rate of delivery at 13.0 psia; or wherein said device is configured to withstand a patient's bite with a force of at least 200 Newtons, without rupturing and without infusing a bolus of greater than 5% of the contents of the drug reservoir, when a fresh drug reservoir is newly inserted into the mouth; or wherein said device is configured to deliver an average rate of volume of from 0.015 mL/hour to 1.25 mL/hour over a period of

from 4 hours to 168 hours at 37 °C and a constant atmospheric pressure of 13 psia, wherein said average rate varies by less than ± 20% per hour over a period of 4 or more hours; or wherein said device comprises one or more drug reservoirs and one or more pumps, wherein said drug reservoirs or said pumps are configured to be worn in the buccal vestibule, and comprising a fluidic channel from the buccal side to the lingual side of said patient's teeth for dispensing said pharmaceutical composition on the lingual side of the teeth.

6. The drug delivery device of any one of claims 1-5, wherein:

(a) said drug reservoir contains a pharmaceutical composition comprising a suspension of particles;

(b) said drug delivery device comprises a fluidic channel or orifice for dispensing of said pharmaceutical composition; and

(c) the particle diameters at all maxima of the particle size distribution are smaller than 1/5th of the narrowest internal diameter of said fluidic channel or orifice.

7. The drug delivery device of claim 6, wherein the particle diameters at all maxima of the particle size distribution are smaller than 1/10th of the narrowest internal diameter of said fluidic channel or orifice; or wherein said particles comprise solid drug particles; or wherein said pharmaceutical composition comprises baclofen, or a pharmaceutically acceptable salt thereof; or wherein said drug reservoir comprises a paste.

8. The drug delivery device of claim 7, wherein said device is a propellant-driven drug delivery device configured and arranged for continuous or semi-continuous extrusion of said paste into said patient's mouth at a rate between 0.015 mL/hour and 0.25 mL/hour through a flow rate controlling orifice, tube or flow restrictor; or wherein the vapor pressure of said propellant is greater than 4 bars at 37ºC; or wherein said particles comprise solid drug particles; or wherein said orifice, tube or flow restrictor minimum inner diameter is at least 5 times greater than the maximum effective particle size of the solid drug; or wherein said orifice, tube or flow restrictor minimum inner diameter is at least 10 times greater than the maximum effective particle size of the solid drug; or wherein said drug reservoir comprises a suspension comprising a drug suitable for continuous or frequent intermittent intra-oral delivery, said suspension comprising at 37 °C solid particles of said drug, a concentration of said drug greater than 2 M, and a viscosity of greater than 100 Poise wherein said suspension remains free of sedimented solid drug for 6 months or more.

9. A fluid pharmaceutical composition comprising a suspension comprising a drug suitable for continuous or frequent intermittent intra-oral delivery, said suspension comprising at 37 °C solid particles of said drug, a concentration of said drug greater than 2 M, and a viscosity of greater than 100

Poise wherein said suspension remains free of sedimented solid drug for 6 months or more, wherein said drug is levodopa, a levodopa prodrug, baclofen, or a pharmaceutically acceptable salt thereof, and wherein said suspension comprises a non-aqueous carrier fluid, an oil, or an edible oil.

10. The pharmaceutical composition of claim 9, wherein said solid particles of said drug comprise an average diameter of less than 100 micrometers; or wherein the volume fraction of said solid drug is greater than 0.2; or wherein said suspension comprises an emulsion; or wherein said solid drug particles comprise (i) levodopa or a pharmaceutically acceptable salt thereof or a prodrug thereof and (ii) carbidopa, a carbidopa prodrug, benserazide, or a pharmaceutically acceptable salt thereof; or wherein said pharmaceutical composition comprises more than 500 mg levodopa per mL, or more than 500 mg of levodopa and carbidopa per mL; or wherein said fluid comprises baclofen or a pharmaceutically acceptable salt thereof.

11. A stable, infusible pharmaceutical composition comprising a suspension of carbidopa particles in a fluid at a concentration of 50 mg/mL to 500 mg/mL, wherein the amount of hydrazine is less than 1 mg per 500 mg CD after storage at 5 °C for a period of 1 year, or at 25 °C for a period of 3 months, and wherein said fluid comprises a non-aqueous carrier fluid, an oil, or an edible oil.

12. The use of the pharmaceutical composition of any one of claims 9-11, wherein the pharmaceutical composition is delivered to a patient by removably attaching the device of any one of claims 1-8 to an intraoral surface of said patient or by continuous or semi-continuous administration into the mouth of said patient.

13. The use according to claim 12, wherein the pharmaceutical composition is delivered to said patient for a period of not less than 4 hours and not more than 7 days; or wherein said pharmaceutical composition is delivered to said patient continuously or at least once every 30 minutes; or wherein the fluctuation index of said drug is less than or equal to 2.0, 1.5, 1.0, 0.75, 0.50, 0.25, or 0.15 during the delivery period; or wherein said pharmaceutical composition comprises baclofen or a pharmaceutically acceptable salt thereof and said patient has spasticity; or wherein said pharmaceutical composition comprises levodopa, a levodopa prodrug, or a pharmaceutically acceptable salt thereof and said patient has Parkinson's disease, the use optionally including: (a) inserting the drug delivery device into said patient's mouth, said device having a drug reservoir comprising levodopa, a levodopa prodrug, or a pharmaceutically acceptable salt thereof; (b) the use of said levodopa, a levodopa prodrug, or a pharmaceutically acceptable salt thereof, wherein said levodopa, levodopa prodrug, or a pharmaceutically acceptable salt is delivered to said patient's mouth for a period of at least 8 hours at an hourly rate in the range of 10 – 125 mg/hour; and (c) removing said drug delivery device from the mouth.

14. Use of a drug delivery device inserted into a subject’s mouth to deliver a drug, said device having

(i) a fastener to removably secure said drug delivery device to a surface of said patient's mouth; (ii) a mechanical pump selected from a spring, an elastomer, compressed gas, and a propellant-driven pump; (iii) an oral liquid impermeable drug reservoir having a volume of from 0.1 ml to 5 ml comprising a suspension or solid containing drug prepared to be administered into said patient's mouth continuously or semi-continuously; and (iv) a flow restrictor for controlling the flow of said pharmaceutical composition from said drug reservoir; and removing said drug delivery device from the mouth of the subject for treating Parkinson’s disease.

15. The use according to claim 14, wherein said drug is levodopa, a levodopa prodrug, baclofen, or a pharmaceutically acceptable salt thereof; or wherein said suspension is a paste-prepared to be administered into said subject's mouth continuously or at a frequency of at least once every 30 minutes; or wherein said composition comprises a nonaqueous carrier fluid, an oil, or an edible oil; or wherein the drug delivery device comprises an automatic stop/start; or wherein the drug delivery device comprises a suction-induced flow limiter; or wherein the drug delivery device comprises a temperature-induced flow limiter; or wherein the drug delivery device comprises bite-resistant structural supports; or wherein the subject has delayed gastric emptying or retarded gastrointestinal transit.

16. The use according to claim 14 or 15, wherein the drug is levodopa or a levodopa prodrug and (i) wherein one or more of said drug delivery devices are inserted into said subject’s mouth and the suspension or solid is prepared to be administered to the subject for a period of at least 8 hours at an hourly rate in the range of 10 - 125 mg/hour; or wherein the drug reservoir comprises a composition comprising a suspension of solid particles of said levodopa or levodopa prodrug, wherein the composition has a concentration of said levodopa or levodopa prodrug greater than 2 M and a viscosity of greater than 100 Poise.