rate of 0.125 cm^3/s in order to be fully emitted during a 5 second inhalation, which is 25 times greater than that required in the example provided above for lactose blends.

[0010] Small diameter pins or staples can readily pierce a capsule without causing undue material deformation, such as collapse of the capsule's walls or domes. For higher density lactose blends, use of small diameter pins or staples does not present an issue. In particular, the low volumetric flow rates required for these products allows for the total hole area to be small. The hole made by, for example, a 1 mm diameter round pin will have an area of about 0.008 cm^2. In the first (i.e., high density powder) example above, 25 mg of the 1 g/cm^3 lactose blend powder emitted from a hole of this size in 5 seconds will have a volumetric flux of about 0.625 $cm^3/[cm^2s]$. This level of flux is readily obtainable in capsule-based inhalers. In the second (i.e., low density powder) example above, though, 25 mg of the 0.04 g/cm^3 powder emitted from a 1 mm diameter hole in 5 seconds would require a volumetric flux of about 15.625 $cm^3/[cm^2s]$. In practice, a volumetric flux of this magnitude is not achievable. This can be remedied by increasing the hole area, but piercing a large hole through the capsule requires high force loading which will, without more, collapse the capsule before the puncture is created. Improving the sharpness of the piercing mechanism can also provide some relief, but this is limited by the nature of the metals and forming processes used.

[0011] Accordingly, a need exists for improved devices and methods for puncturing a capsule to release a powdered medicament therefrom. In particular, an improved approach is required in order to produce enough hole area in a capsule to allow for a full dose emission of a low density powder without the capsule being collapsed.

Summary ~~of the Invention~~

[0012] Various embodiments of the inhalation device described herein allow for high doses of low-density inhalation powders to be delivered. In one embodiment, the inhalation device accomplishes this by strategically piercing the highest strength region of the capsule (i.e., the domes) and by positioning the piercing elements towards the perimeter of the domed regions. In other words, the piercing elements (e.g., the individual prongs or tines) are placed far apart and at the point where most of their force is transmitted to the cylindrical wall of the capsule, thus placing as little force as possible on the dome. Such a design allows for relatively large pins or staple tines to produce large openings in the capsule's dome without collapsing the capsule. In particular, the inhalation device can incorporate pins or staples with large cross-

sectional areas, which results in a substantial increase in the total hole area available for dose emission from the capsule.

[0012a] In one aspect of the present disclosure, there is provided a device for puncturing a capsule to release a powdered medicament therefrom, the device comprising:

a chamber for receiving a capsule comprising opposing domes and a cylindrical wall portion defined by a capsule wall radius r; and

a mechanism for puncturing at least one hole in at least one dome, a center of each hole located within an annular puncture region situated at no less than 0.4r,

wherein a total surface area of all puncture holes is between about 0.5% and about 2.2% of a total surface area of the capsule.

[0012b] In another aspect of the present disclosure, there is provided a punctured capsule, comprising:

opposing domes and a cylindrical wall portion defined by a radius r, at least one dome being punctured with at least one hole, a center of each hole located within an annular region situated at no less than 0.4r,

wherein a total surface area of all puncture holes is between about 0.5% and about 2.2% of a total surface area of the capsule.

[0012c] In a further aspect of the present disclosure, there is provided a method for puncturing a capsule to release a powdered medicament therefrom, the method comprising:

receiving, within a chamber, a capsule comprising opposing domes and a cylindrical wall portion defined by a capsule wall radius r; and

puncturing at least one hole in at least one dome, a center of each hole located within an annular puncture region situated at no less than 0.4r,

wherein a total surface area of all puncture holes is between about 0.5% and about 2.2% of a total surface area of the capsule.

[0013] In one embodiment, the preferred location for the center of each puncture hole is in an annular region on the dome's surface that is positioned at no less than 40% (e.g., between about 40% and about 80%, or between about 40% and about 60%) of the dome's radius away from a central axis of the dome. In addition, in one such embodiment, the preferred total surface area of all puncture holes is between about 0.5% and about 2.2% of the total surface area of the capsule, or between about 3% and about 15% of the total surface area of a single dome. It has been determined that these particular combinations of puncture hole location and

puncture hole surface area advantageously avoid the capsule collapsing upon itself when punctured. Moreover, it has been determined that such a puncture hole surface area allows for a full dose of a low-density (i.e., below 0.10 g/cm^3) powder to be emitted from a capsule at a sufficient volumetric flow rate and an achievable magnitude of volumetric flux so as to be consumed in a single breath by a typical adult patient.

[0014] In general, ~~in one aspect,~~ embodiments of the ~~invention~~ present disclosure feature a device for puncturing a capsule to release a powdered medicament therefrom. The device includes a chamber for receiving the capsule. The capsule includes opposing domes and a cylindrical wall portion defined by a capsule wall radius r. The device further includes a mechanism for puncturing at least one hole in at least one dome. A center of each hole is located within an annular puncture region situated at no less than 0.4r, and a total surface area of all puncture holes is between about 0.5% and about 2.2% of a total surface area of the capsule. The annular puncture region may, for example, be situated between about 0.4r and about 0.8r, or between about 0.4r and about 0.6r.

[0015] Additioanlly, i~~I~~n general, ~~in another aspect,~~ embodiments of the present disclosure ~~invention~~ feature a method for puncturing a capsule to release a powdered medicament therefrom. The method includes receiving, within a chamber, a capsule that itself includes opposing domes and a cylindrical wall portion defined by a capsule wall radius r. The method also includes puncturing at least one hole in at least one dome. A center of each hole is located within an annular puncture region situated at no less than 0.4r, and a total surface area of all puncture holes is between about 0.5% and about 2.2% of a total surface area of the capsule. The annular puncture region may, for example, be situated between about 0.4r and about 0.8r, or between about 0.4r and about 0.6r.

[0016] In various embodiments, the puncturing mechanism (which may include a plurality of prongs and which may be moveable between a non-puncturing position and a puncturing position) is configured to puncture only a single dome. In such instances, the total surface area of all puncture holes is between about 3% and about 15% of a total surface area of the single dome. In one embodiment, the capsule has a volume of at least 0.50 cm^3. The capsule may house a powdered medicament, which may have a density below 0.10 g/cm^3 and/or contain levodopa as an active drug. Puncturing the capsule's dome causes the powdered medicament to be released from the capsule.

[0017] In certain embodiments, an outer surface of the capsule is between about 0.08 mm and about 0.12 mm thick. The capsule (i.e., the opposing domes and the cylindrical wall portion thereof) may be made from a material such as, for example, hydroxy propyl methyl cellulose or gelatin.

[0018] In one embodiment, the device further includes an inhalation portion that is coupled to the chamber. The inhalation portion may define, for example, at least one aperture for emitting the powdered medicament therethrough. For its part, the chamber may include a wall defining a plurality of vents for introducing air into the chamber to disperse the powdered medicament released from the capsule.

[0019] Additionally, ~~In~~ in general, ~~in yet another aspect,~~ embodiments of the present disclosure ~~invention~~ feature a punctured capsule. The punctured capsule includes opposing domes (at least one of which is punctured with at least one hole) and a cylindrical wall portion defined by a radius r. A center of each hole is located within an annular region situated at no less than 0.4r, and a total surface area of all puncture holes is between about 0.5% and about 2.2% of a total surface area of the capsule. The annular region may, for example, be situated between about 0.4r and about 0.8r, or between about 0.4r and about 0.6r.

[0020] In various embodiments, only a single dome of the capsule is punctured. In such instances, the total surface area of all puncture holes is between about 3% and about 15% of a total surface area of the single dome. In one embodiment, the punctured capsule has a volume of at least 0.50 cm^3. The punctured capsule may include therein a powdered medicament, which may have a density below 0.10 g/cm^3 and/or contain levodopa as an active drug. In addition, an outer surface of the punctured capsule may be between about 0.08 mm and about 0.12 mm thick. The opposing domes and the cylindrical wall portion of the punctured capsule

may each be made from a material such as, for example, hydroxy propyl methyl cellulose or gelatin.

[0021] These and other objects, along with advantages and features of the embodiments of the present ~~invention~~ disclosure herein disclosed, will become more apparent through reference to the following description, the accompanying drawings, and the claims. Furthermore, it is to be understood that the features of the various embodiments described herein are not mutually exclusive and can exist in various combinations and permutations.

Brief Description of the Drawings

[0022] In the drawings, like reference characters generally refer to the same parts throughout the different views. Also, the drawings are not necessarily to scale, emphasis instead generally being placed upon illustrating the principles of the invention. In the following description, various embodiments of the present invention are described with reference to the following drawings, in which:

[0023] FIG. 1 schematically illustrates a front view of an inhalation device in accordance with one embodiment of the invention;

[0024] FIG. 2 is a cross-sectional view of the exemplary device depicted in FIG. 1 along the line 2–2;

[0025] FIG. 3 is a table of standard capsule sizes;

[0026] FIG. 4 schematically illustrates a side view of a capsule in accordance with one embodiment of the invention;

[0027] FIG. 5 schematically illustrates a top view of a capsule's dome in accordance with one embodiment of the invention;

[0028] FIG. 6 is a table showing the percentage of powder emitted for various surface areas of puncture holes in a capsule;

[0029] FIG. 7 is a graph illustrating the percentage of powder emitted for various surface areas of puncture holes in a capsule;

[0030] FIG. 8 is a table showing the amount of deflection in a capsule's dome for various locations of a puncture hole's center in the capsule's dome; and

[0031] FIG. 9 is a graph illustrating the amount of deflection in a capsule's dome for various locations of a puncture hole's center in the capsule's dome.