

METHOD AND APPARATUS FOR DRIVING A TRANSDUCER OF AN INHALATION DEVICE

The present invention relates generally to the field of inhalation devices, and more specifically, to inhalation devices that utilize vibration to facilitate suspension of particles of a medication into an inhaled gas stream (e.g., of inhaled air). The invention will be described in detail in connection with delivery of powdered medication to a patient, and will be described in connection with such utility, although other utilities, including specifically delivery of liquid droplets is contemplated.

Certain diseases of the respiratory tract are known to respond to treatment by the direct application of therapeutic agents. As these agents are most readily available in dry powdered form, their application is most conveniently accomplished by inhaling the powdered material through the nose or mouth. This powdered form results in the better utilization of the medicament in that the drug is deposited exactly at the site desired and where its action may be required; hence, very minute doses of the drug are often equally as efficacious as larger doses administered by other means, with a consequent marked reduction in the incidence of undesired side effects and medicament cost. Alternatively, the drug in this form may be used for treatment of diseases other than those of the respiratory system. When the drug is deposited on the very large surface areas of the lungs, it may be very rapidly absorbed into the blood stream; hence, this method of application may take the place of administration by injection, tablet, or other conventional means.

It is the opinion of the pharmaceutical industry that the bioavailability of the drug is optimum when the drug particles delivered to the respiratory tract are between 1 to 5 microns in size. When the drug particles need to be in this size range the dry powder delivery system needs to address a number of issues:

(1) Small size particles may develop an electrostatic charge on themselves during manufacturing and storage. This may cause the particles to agglomerate or aggregate, resulting in clusters of particles which have an effective size greater than 5 microns. The probability of these large clusters making it to the deep lungs then decreases. This in turn results in a lower percentage of the packaged drug being available to the patient for absorption.

1 (2) The amount of active drug that needs to be delivered to the patient may be
2 of the order of 10s of micrograms. For example, in the case of albuterol, a drug used
3 in asthma, this is usually 25 to 50 micrograms. Current manufacturing equipment can
4 effectively deliver aliquots of drugs in milligram dose range with acceptable accuracy.
5 So the standard practice is to mix the active drug with a filler or bulking agent such as
6 lactose. This additive also makes the drug "easy to flow". This filler is also called a
7 carrier since the drug particles also stick to these particles through electrostatic or
8 chemical bonds. These carrier particles are very much larger than the drug particles in
9 size. The ability of the dry powder inhaler to separate drug from the carrier is an
10 important performance parameter in the effectiveness of the design.

11 (3) Active drug particles with sizes greater than 5 microns will be deposited
12 either in the mouth or throat. This introduces another level of uncertainty since the
13 bioavailability and absorption of the drug in these locations is different from the
14 lungs. Dry powder inhalers need to minimize the drug deposited in these locations to
15 reduce the uncertainty associated with the bioavailability of the drug.

16 Prior art dry powder inhalers (DPIs) usually have a means for introducing the
17 drug (active drug plus carrier) into a high velocity air stream. The high velocity air
18 stream is used as the primary mechanism for breaking up the cluster of micronized
19 particles or separating the drug particles from the carrier. Several inhalation devices
20 useful for dispensing this powder form of medicament are known in the prior art. For
21 example, in U.S. Pat. Nos. 3,507,277; 3,518,992; 3,635,219; 3,795,244; and
22 3,807,400, inhalation devices are disclosed having means for piercing of a capsule
23 containing a powdered medicament, which upon inhalation is drawn out of the
24 pierced capsule and into the user's mouth. Several of these patents disclose propeller
25 means, which upon inhalation aid in dispensing the powder out of the capsule, so that
26 it is not necessary to rely solely on the inhaled air to suction powder from the capsule.
27 For example, in U.S. Pat. No. 2,517,482, a device is disclosed having a powder
28 containing capsule placed in a lower chamber before inhalation, where it is pierced by
29 manual depression of a piercing pin by the user. After piercing, inhalation is begun
30 and the capsule is drawn into an upper chamber of the device where it moves about in
31 all directions to cause a dispensing of powder through the pierced holes and into the
32 inhaled air stream. U.S. Pat. No. 3,831,606 discloses an inhalation device having

1 multiple piercing pins, propeller means, and a self-contained power source for
2 operating the propeller means via external manual manipulation, so that upon
3 inhalation the propeller means aids in dispensing the powder into the stream of
4 inhaled air. See also U.S. Pat. No. 5,458,135.

5 These prior art devices present several problems and possess several
6 disadvantages which are remedied by the inhalation devices of the present invention.
7 For instance, these prior art devices require that the user exert considerable effort in
8 inhalation to effect dispensing or withdrawal of powder from a pierced capsule into
9 the inhaled air stream. With these prior art devices, suction of powder through the
10 pierced holes in the capsule caused by inhalation generally does not withdraw all or
11 even most of the powder out of the capsule, thus causing a waste of the medicament.
12 Also, such prior art devices result in uncontrolled amounts or clumps, of powdered
13 material being inhaled into the user's mouth, rather than a constant inhalation of
14 controlled amounts of finely dispersed powder.

15 The above discussion of the prior art is taken largely from U.S. Pat. No.
16 3,948,264 to Wilke et al, who discloses a device for facilitating inhalation of a
17 powdered medication that includes a body portion having primary and secondary air
18 inlet channels and an outlet channel. The secondary inlet channel provides an
19 enclosure for a capsule containing the powdered medication and the outlet channel is
20 formed as a mouthpiece protruding from the body. A capsule piercing structure is
21 provided, which upon rotation puts one or more holes in the capsule so that upon
22 vibration of the capsule by an electro-mechanical vibrator, the powdered drug may
23 be released from the capsule. The piercing means disclosed in Wilke et al includes
24 three radially mounted, spring-biased piercing needles mounted in a trochoidal
25 chamber. Upon hand rotation of the chamber, simultaneous inward radial motion of
26 the needles pierces the capsule. Further rotation of the chamber allows the needles to
27 be retracted by their spring mountings to their original positions to withdraw the
28 needles from the capsule.

29 The electromechanical vibrator includes, at its innermost end, a vibrating
30 plunger rod which projects into the intersection of the inlet channel and the outlet
31 channel. Connected to the plunger rod is a mechanical solenoid buzzer for energizing
32 the rod to vibrate. The buzzer is powered by a high energy electric cell and is

1 activated by an external button switch. According to Wilke et al, upon inhalation
2 through an outlet channel and concurrent pressing of a switch to activate the
3 electromechanical vibrating means, air is sucked through inlet channels and the air
4 stream through a secondary inlet channel raises the capsule up against a vibrating
5 plunger rod. The capsule is thus vibrated rapidly with powder being fluidized and
6 dispensed from the pierced holes therein. (This technique is commonly used in
7 manufacturing for dispensing powder through a hopper where the hopper is vibrated
8 to fluidize the powder and move it through the hopper outlet. The pierced holes in the
9 capsule represent the hopper outlet.) According to Wilke et al, the air stream through
10 the inlet channels aids in withdrawal of powder from the capsule and carries this
11 powder through the outlet channel to the mouth of the user. (Wilke et al, column 3,
12 lines 45-55). Wilke et al further discloses that the electromechanical vibrator means
13 may be placed at a right angle to the inlet chamber and that the amplitude and
14 frequency of vibration may be altered to regulate dispensing characteristics of the
15 inhaler.

16 Prior art devices such as above described have a number of disadvantages
17 which makes them less than desirable for the delivery of dry powder to the lungs.
18 Some of these disadvantages include:

- 19 • The performance of the prior art inhalers depends on the flow rate
20 generated by the user. Lower flow rate does not result in the powder
21 being totally deaggregated and hence adversely affects the dose
22 delivered to the patient.
- 23 • Inconsistency in the bioavailability of the drugs from dose-to-dose
24 because of lack of consistency in the deaggregation process.
- 25 • Large energy requirements for driving the electromechanical based
26 inhalers which increases the size of the devices making them
27 unsuitable for portable use.
- 28 • Loss of medication from opened or topped capsules.
- 29 • Deterioration of medication in open or topped capsule due to exposure
30 to oxygen or moisture.

31 In prior U.S. Patent Nos. 7,318,434 and 7,334,577 incorporated herein by
32 reference, and assigned to the common assignee MicroDose Technologies, Inc., there

1 is provided an improvement over prior art inhalers that utilize vibration to facilitate
2 suspension of powder into an inhaled gas stream and which utilizes a synthetic jet to
3 aerosolize drug powder from a blister pack or the like. As taught in the aforesaid U.S.
4 Patent Nos. 7,318,434 and 7,334,577 there is provided a dry powder inhaler having a
5 first chamber such as a blister pack or other container, for holding a dry powder, and a
6 second chamber connected to the first chamber via a passageway for receiving an
7 aerosolized form of the dry powder from the first chamber and for delivering the
8 aerosolized dry powder to a user. A vibrator is coupled to the dry powder in the first
9 chamber. The vibrator is energized and coupled to the first chamber and drives the
10 powder from the chamber by synthetic jetting.

11 The medicament for dry powder inhalers is commonly contained in a blister
12 pack or other flat bottom container that is placed in contact with the face of a
13 piezoelectric transducer or vibrator, whereupon the vibration energy of the transducer
14 is transferred to the medicament particles. However, frictional losses between the
15 engaging surface of the blister pack or other container and the face of the transducer
16 may constrain movement of the transducer face and reduce the overall efficiency of
17 the device.

18 The present invention provides an improvement over the prior art devices such
19 as discussed above by providing an inhaler having a piezoelectric transducer for
20 aerosolizing medicament contained in a blister pack or other flat bottom container,
21 wherein the drive signal to the transducer has a waveform that excites both a primary
22 and a secondary resonant frequency of the piezoelectric transducer. The preferred
23 drive signal to the transducer should be one that comprises a waveform that has a
24 fundamental frequency equal to the primary resonance frequency of the transducer
25 and, in addition, significant energy at harmonics of the fundamental frequency.

26 Secondary resonant frequencies of the transducer are excited by the harmonics
27 of the drive signal resulting in a more complex motion of the transducer face. The
28 transducer face moves similar to the vibrating surface of a drum. This includes a
29 considerable number of modes of vibration. The more complex movement of the
30 transducer face causes the contact area between the engaging surface of the blister
31 pack or other flat bottom container and the transducer face to be reduced, and in turn,
32 the friction between the two surfaces also is reduced. This occurs primarily because

1 of the tendency of the blister or container bottom to ride on the peaks of the deflection
2 pattern of the transducer face and not to follow the complexity of its deformation due
3 to the complex movement. A portion of the relative motion between the blister or
4 container bottom and the transducer face is in the radial direction, necessitated by the
5 changing radial dimension of the transducer face as it vibrates in a direction
6 perpendicular to the plane of the face. This relative motion is necessary to avoid the
7 significant energy loss that is associated with trying to periodically stretch the
8 material that comprises the bottom surface of the container or blister pack such that it
9 conforms to or remains firmly adhered to, i.e. in contact with the transducer face
10 during vibration.

11 Further features and advantages of the present invention will be seen from the
12 following detailed description, taken in conjunction with the accompanying drawings,
13 wherein:

14 FIG. 1 is a cross-sectional view of a piezoelectric actuator made in accordance
15 with the present invention;

16 FIG. 2 is a graph showing the waveform of a drive signal for a piezoelectric
17 transducer in accordance with the present invention;

18 FIG. 3 is a graph showing the harmonic energy of the piezoelectric transducer
19 generated by the waveform shown in FIG. 1;

20 FIG. 4 is a graph showing the admittance of a piezoelectric transducer at
21 various harmonic frequencies; and

22 FIG. 5 is a schematic showing a drive circuit for a piezoelectric transducer in
23 accordance with the present invention.

24 In the following description, reference is made to the accompanying drawings,
25 which form a part hereof, and in which is shown, by way of illustration, various
26 embodiments of the present invention. It is understood that other embodiments may
27 be utilized and changes may be made without departing from the scope of the present
28 invention.

29 The present invention provides a method and device for delivering
30 medicament to the lungs of a patient from an inhaler by using a piezoelectric
31 transducer to deaggregate and aerosolize the medicament contained in a blister pack
32 or the like. The piezoelectric transducer is activated by a drive signal which excites

1 the transducer to vibrate at two or more different frequencies including its primary
2 resonance frequency and at least one secondary frequency which is near a harmonic
3 of the primary resonance frequency.

4 That is to say, the drive signal is chosen to excite secondary resonance
5 frequencies of the piezoelectric transducer resulting in a complex pattern of
6 deformation on the face of the transducer. Without being bound by theory, our
7 observations suggest that the complex movement of the transducer face causes the
8 surface area of the contact between the flat surface of the blister bottom in contact
9 with the transducer face to be reduced, and by such a reduction, the friction between
10 the two surfaces correspondingly reduced. This may occur because of the tendency of
11 the blister bottom to ride on the peaks of the deflection pattern of the transducer face
12 and not follow the complexity of its deformation due to the complex movement. This
13 enables relative motion between the blister bottom and the transducer face in the
14 radial direction, something that we have found necessary because of the changing
15 radial dimension of the transducer face as it vibrates due to the elasticity of the
16 material comprising the transducer face, such elasticity enabling the vibrating motion
17 of the transducer. While not wishing to be bound by theory, our observations support
18 the notion that such relative motion is necessary to avoid the significant energy loss
19 that is associated with trying to periodically stretch the polymeric material that
20 comprises the bottom of the blister bottom such that it conforms to or remains firmly
21 adhered to, i.e. in contact with the transducer face during vibration.

22 According to an exemplary embodiment of the present invention, the
23 piezoelectric transducer is driven by a signal having a waveform as shown by in FIG.
24 2. This waveform is preferred for driving the motion described above in a
25 piezoelectric transducer used in a dry powder inhaler by the assignee company. The
26 piezo-electric transducer (FIG. 1) is a purpose designed transducer comprising an
27 aluminum cylinder 20 that is 12.24 mm tall, and has an o.d. of 13.32 mm, that is
28 closed at one end with a 0.25 mm thick piezoelectric disc 22 that in turn is attached to
29 the flat surface of a cap 24 that is press-fitted into and that closes the cylinder 20. A
30 positive lead wire 26 is soldered to the inside surface of the piezoelectric disc 22 and
31 is adhered to the interior wall surface of the cap 24 using a silicone adhesive to
32 provide strain relief. A negative lead wire 28 is attached to the aluminum cylinder 20.

FIG. 3 is a plot of the harmonic energy of the waveform shown in FIG. 2. As can be seen, there is a considerable amount of harmonic energy generated by this waveform at each of the harmonics.

FIG. 4 shows the electrical admittance of the piezoelectric transducer used in the dry powder inhaler. The peaks in the admittance response indicate frequencies of mechanical resonance for the transducer. As can be seen, there are several points of significant mechanical resonance in addition to the primary resonance frequency of 35 kHz. Different piezoelectric transducers, however, may have different resonance frequencies. In our observations, we found that the aforesaid piezoelectric transducer was greatly excited at 285 kHz, which corresponds to the 8th harmonic of the drive waveform. Other transducers, however, may resonate strongly near other harmonics (2nd, 4th, 6th, etc.) of the drive waveform, thereby performing in a manner similar to that found with the example transducer. Importantly, our experiments have consistently found that a drive signal with a high amount of harmonic energy is necessary to reliably create a strong synthetic jet for all combinations of transducer types and flat bottom blisters types that have been examined.

FIG. 5 is an example of a drive circuit that is capable of generating the preferred waveform of FIG. 2. The transducer 5 receives power from power supply 10. The field effect transistors 22, 23 comprise an electronic switch that is opened and closed at the primary resonance frequency of the transducer. Alternatively, the drive circuit may be constructed with a single transistor. Inductor 12 stores energy when the electronic switch is closed. When the electronic switch is open, all of the energy in the inductor 12 is transferred to the piezoelectric transducer 5. The diode 15 effectively disconnects the inductor from the transducer after the energy of the inductor has been transferred to the transducer, thereby insuring the maximum energy transfer during a cycle.

Other waveforms may also be used. The primary requirement is that the drive waveform produce sufficient harmonic energy such that a secondary resonant frequency of the piezoelectric transducer is excited whereby a mechanical oscillation at the secondary resonance occur. It also is possible to generate a waveform comprising two sinusoidal signals at two different frequencies corresponding to the primary and a secondary resonance frequency of the transducer. Any signal that has

1 sufficient energy at both the primary and a secondary resonance frequency such that
2 significant mechanical motion of the transducer face is created at both frequencies
3 creates the motion of the piezoelectric transducer face that has the desired effect of
4 minimizing the friction between the transducer face and the blister bottom.

5 It should be emphasized that the above-described embodiments of the present
6 device and process, particularly, and “preferred” embodiments, are merely possible
7 examples of implementations and merely set forth for a clear understanding of the
8 principles of the invention. Many different embodiments of the invention described
9 herein may be designed and/or fabricated without departing from the spirit and scope
10 of the invention. All these and other such modifications and variations are intended to
11 be included herein within the scope of this disclosure and protected by the following
12 claims. Therefore the scope of the invention is not intended to be limited except as
13 indicated in the appended claims.

14

1 **CLAIMS**

- 2 1. In an inhaler using a piezoelectric transducer as a vibrator, a method of
3 driving the transducer, including providing a signal to the transducer to produce
4 oscillations, the signal exciting a primary resonant frequency of the transducer and at
5 least one secondary resonant frequency of the transducer.
- 6 2. The method of claim 1, wherein the signal is a waveform comprising two
7 sinusoidal signals at two frequencies corresponding to the primary resonant frequency
8 and the secondary resonant frequency.
- 9 3. The method of claim 1, wherein the transducer is used to aerosolize
10 medicament contained in a blister pack.
- 11 4. The method of claim 3, wherein friction between the blister pack and the
12 transducer due to the oscillations is minimized.
- 13 5. The method of claim 3, wherein the medicament is a dry powder.
- 14 6. The method of claim 3, wherein the medicament is a liquid.
- 15 7. The method of claim 1, wherein the transducer resonates at an nth
16 harmonic of its primary resonance frequencies, wherein n is a whole number selected
17 from the group consisting of 2, 4, 6 and 8.
- 18 8. A circuit for driving a piezoelectric transducer in an inhaler that uses a
19 flat bottomed medicament container substantially in contact with the face of the
20 transducer comprising: a power supply; a diode; an inductor; and an electronic switch,
21 wherein the power supply, diode, inductor, and electronic switch are connected in
22 series, the piezoelectric transducer is connected across the switch, and wherein the
23 switch opens and closes at the lowest resonance frequency of the piezoelectric
24 transducer.
- 25 9. The circuit of claim 8, wherein the electronic switch is comprised of at
26 least one transistor.
- 27 10. The circuit of claim 9, wherein the electronic switch is comprised of two
28 field effect transistors that open and close at the primary resonance frequency of the
29 piezoelectric transducer.
- 30 11. The circuit of claim 9, wherein the inductor is sized to dump
31 substantially all of its energy into the transducer when the switch is open.

1 12. The circuit of claim 9, wherein the circuit delivers substantial energy at
2 harmonics of the lowest resonant frequency of the transducer and at least one
3 secondary resonant frequency of the transducer.

4 13. In an inhaler comprising a piezoelectric transducer for facilitating
5 suspension of particles of a medicament into an inhaled gas stream, a circuit for
6 driving the piezoelectric transducer as claimed in claim 9.

7 14. The inhaler as claimed in claim 13, wherein the medicament is a dry
8 powder.

9 15. The inhaler as claimed in claim 13, wherein the medicament is a liquid.

10 16. A method for minimizing friction between an oscillating transducer face
11 and an element in contact therewith, which comprises driving the transducer at two or
12 more frequencies corresponding to a primary resonant frequency and at least one
13 secondary resonant frequency thereof.

14 17. The method of claim 16, wherein the transducer is driven at an nth
15 harmonic of its primary resonance frequency, wherein n is a whole number selected
16 from the group consisting of 2, 4, 6 and 8.

17