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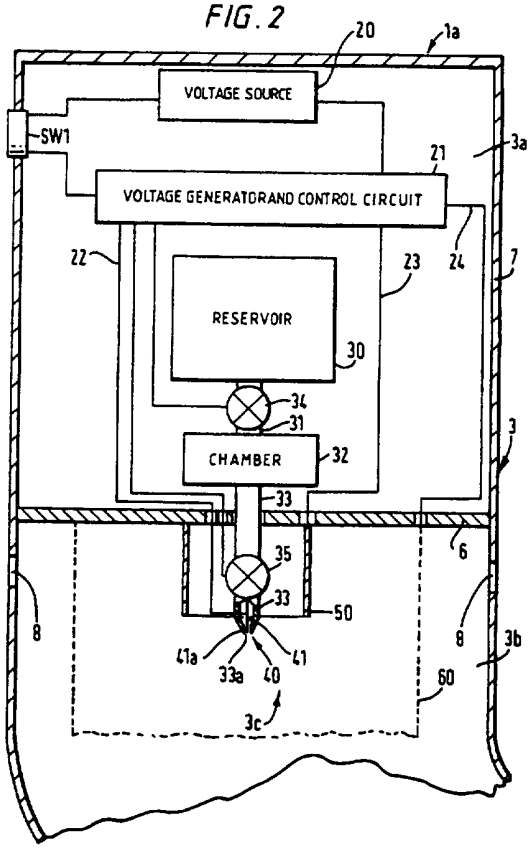
(54) Abstract Title
A dispensing device

(57) Liquid to be dispensed passes down pipe 32 to comminution site 40 where it is atomised by use of an electric field supplied to the electrode 41. A discharge electrode 50 provides oppositely-charged ions from the atmosphere to neutralise at least some of the charged droplets. A further electrode 60 attracts ions produced by the electrode 50 away from the site 40 until a sufficient space charge is built up to attract them to the droplets.

In other embodiments, means are described for pumping doses of the fluid from reservoir 30, and also means for controlling movement of the electrode 41 so that it acts as a valve for the exit 33a.

FIG. 2



GB 2 327 895 A

FIG. 1

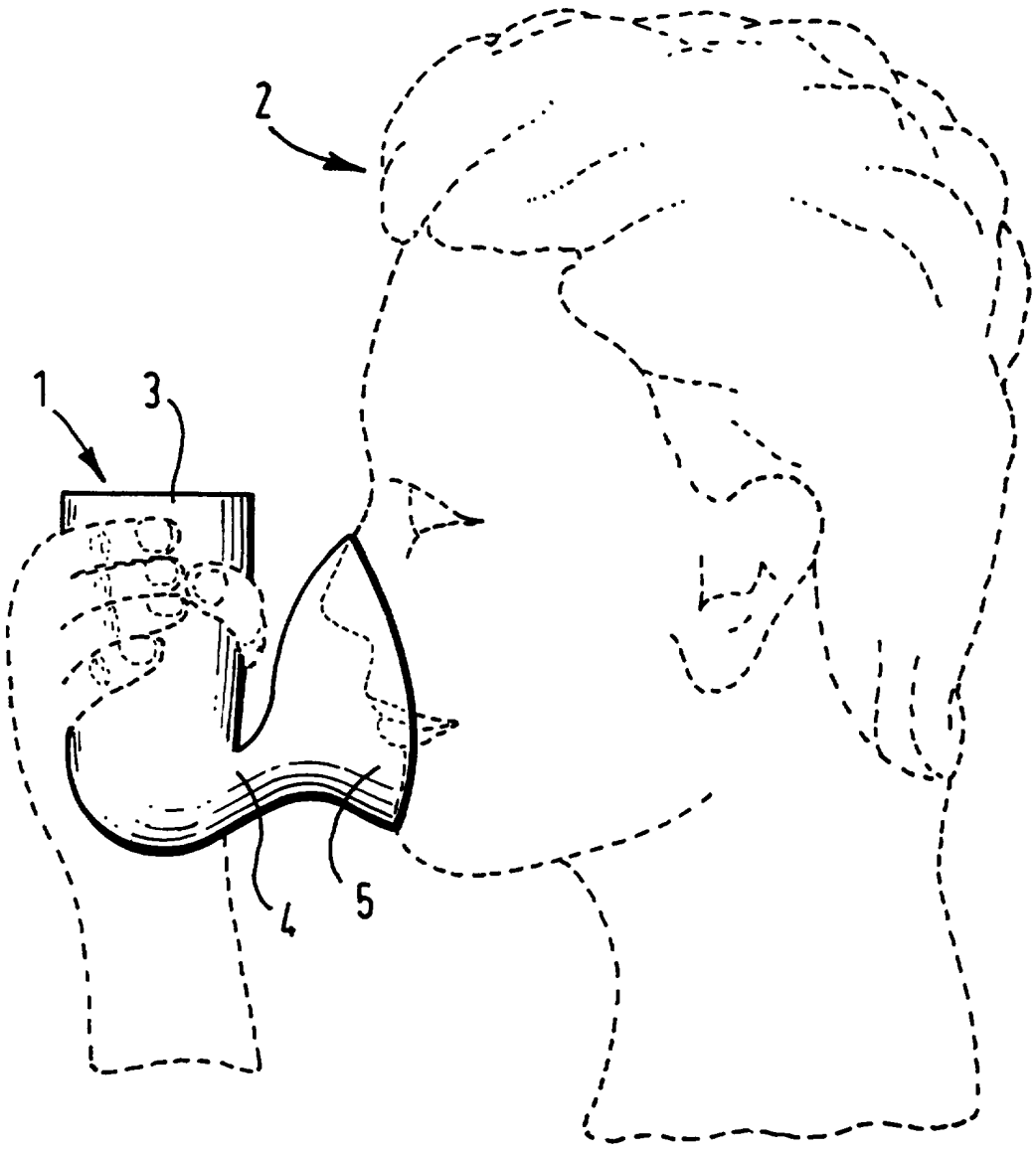
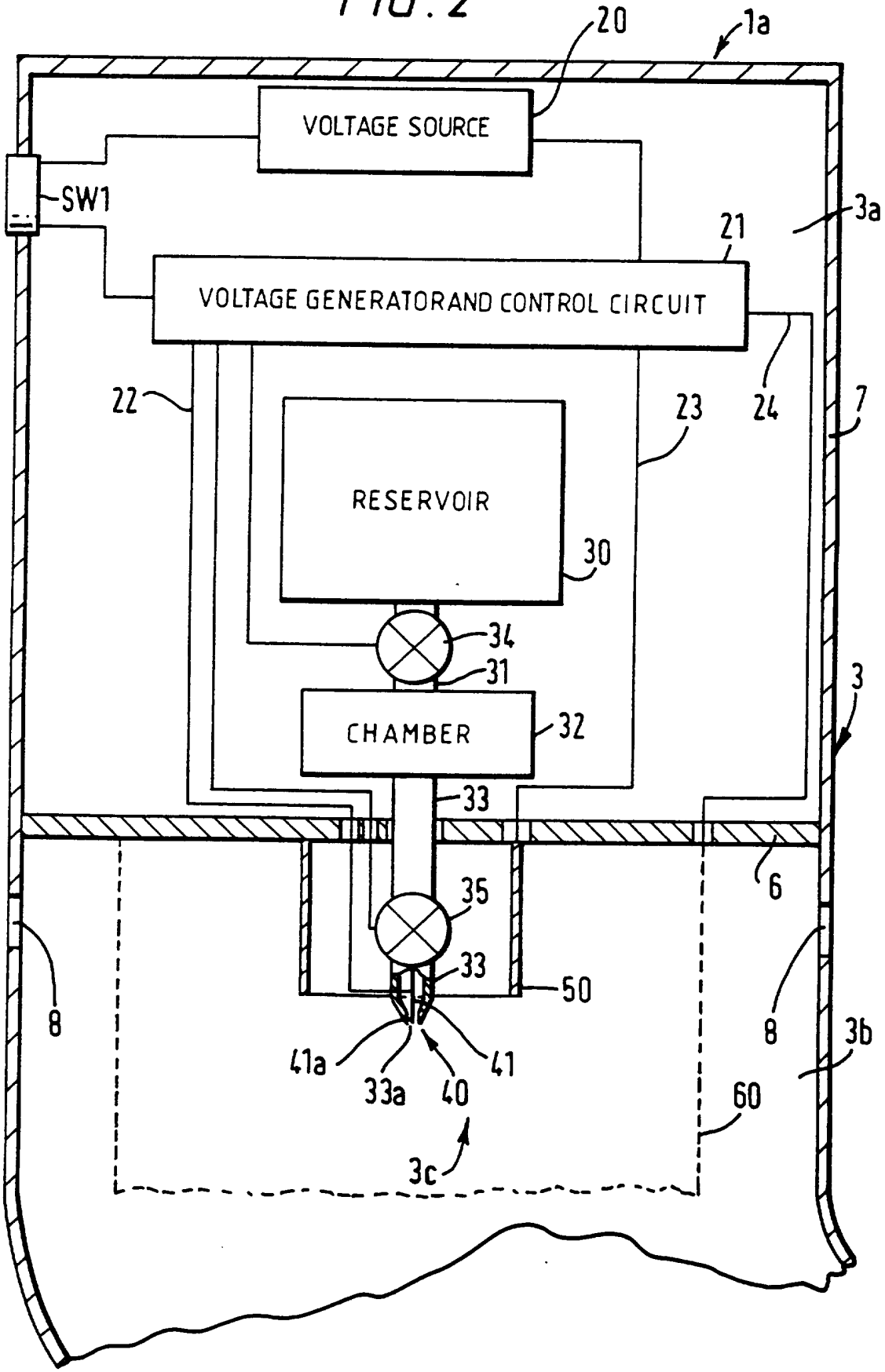


FIG. 2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1a
VOLTAGE SOURCE
SW1
3a
21
VOLTAGE GENERATORAND CONTROL CIRCUIT
22
23
24
7
RESERVOIR
30
34
31
3
CHAMBER
32
33
6
35
33
50
8
8
3b
41a
41
33a
40
60
3c

FIG. 3a

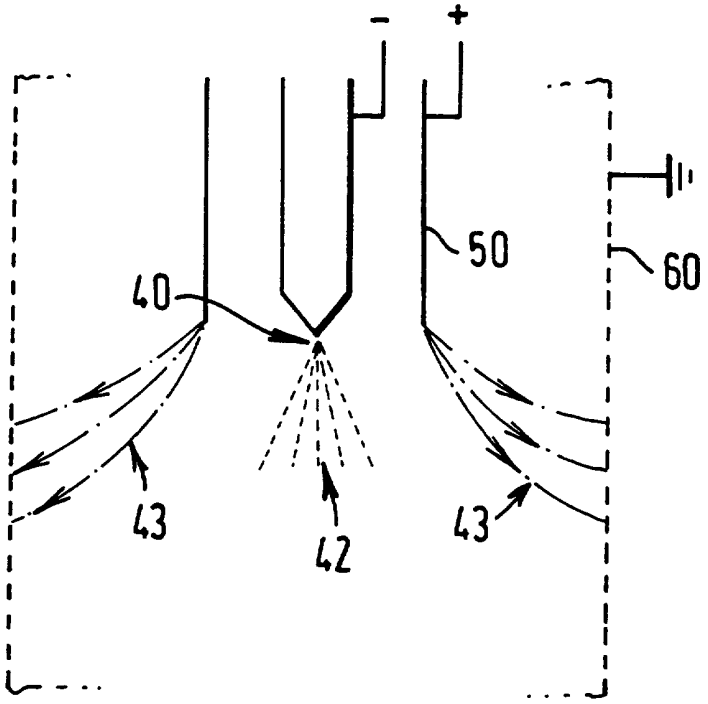


FIG. 3b

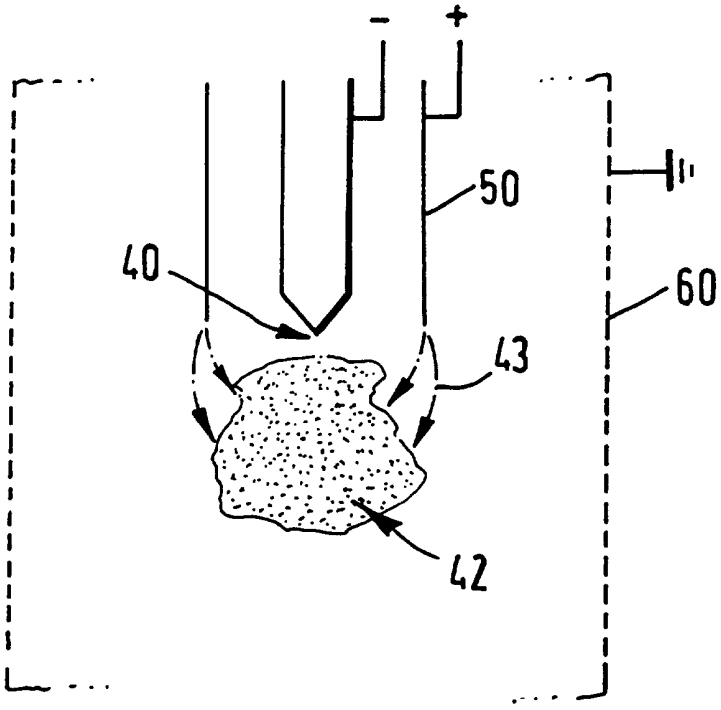
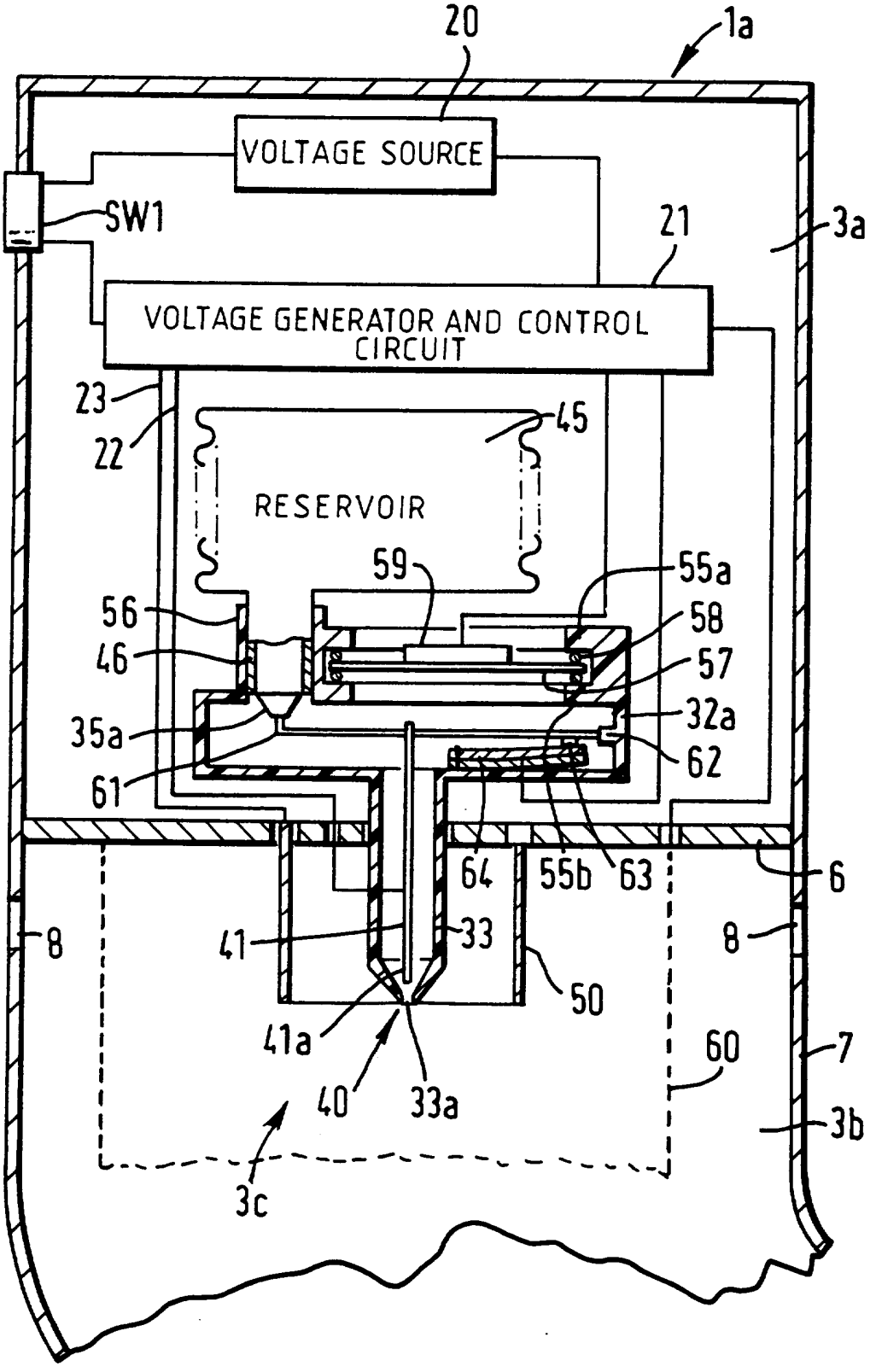


FIG. 4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1a
VOLTAGE SOURCE
SW1
21
3a
VOLTAGE GENERATOR AND CONTROL CIRCUIT
23
22
45
RESERVOIR
59
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46
57
35a
32a
61
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7
40
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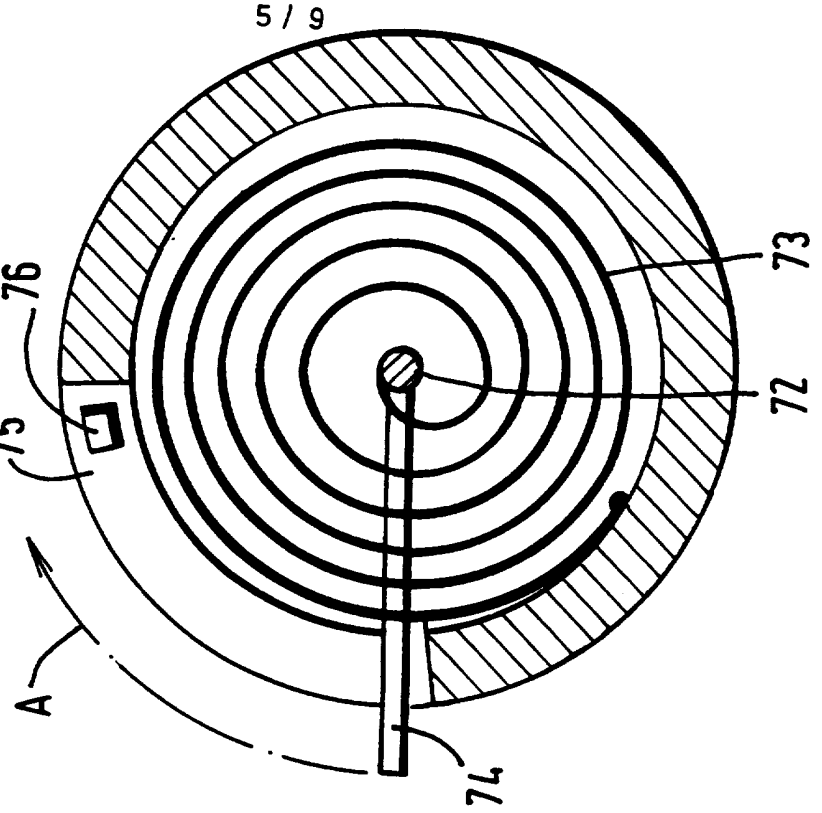
3b
3c

FIG. 6b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73
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74
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FIG. 5

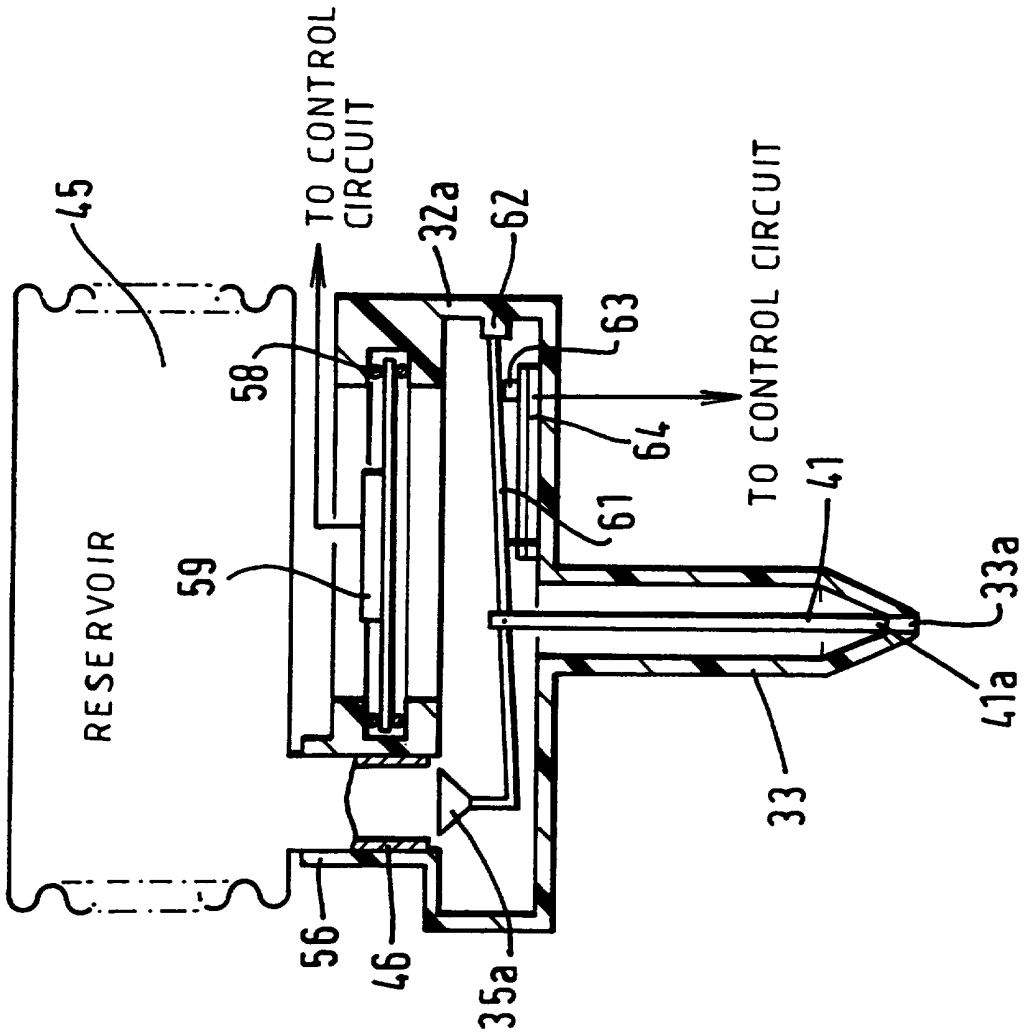

RESERVOIR
45
TO CONTROL CIRCUIT
32a
62
63
58
64
61
59
TO CONTROL CIRCUIT
41
33a
41a
33
56
46
35a

FIG. 6a

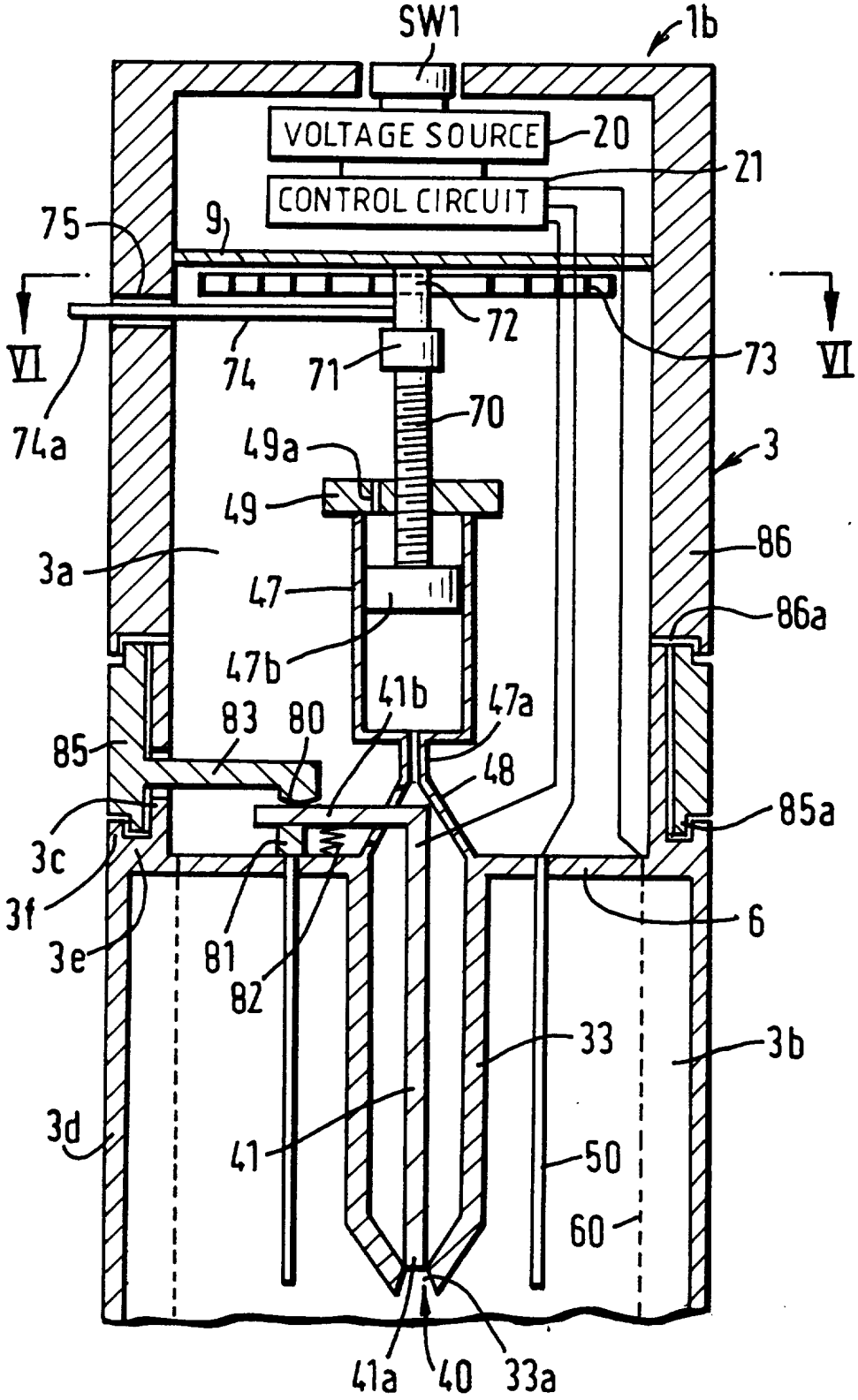

SW1
1b
VOLTAGE SOURCE
20
21
CONTROL CIRCUIT
75
9
72
73
VI
VI
74
71
74a
70
49a
3
49
86
3a
47
86a
47b
41b
47a
83
80
85
48
85a
3c
3f
6
3e
81
82
33
3b
3d
41
50
60
41a
40
33a

FIG. 7

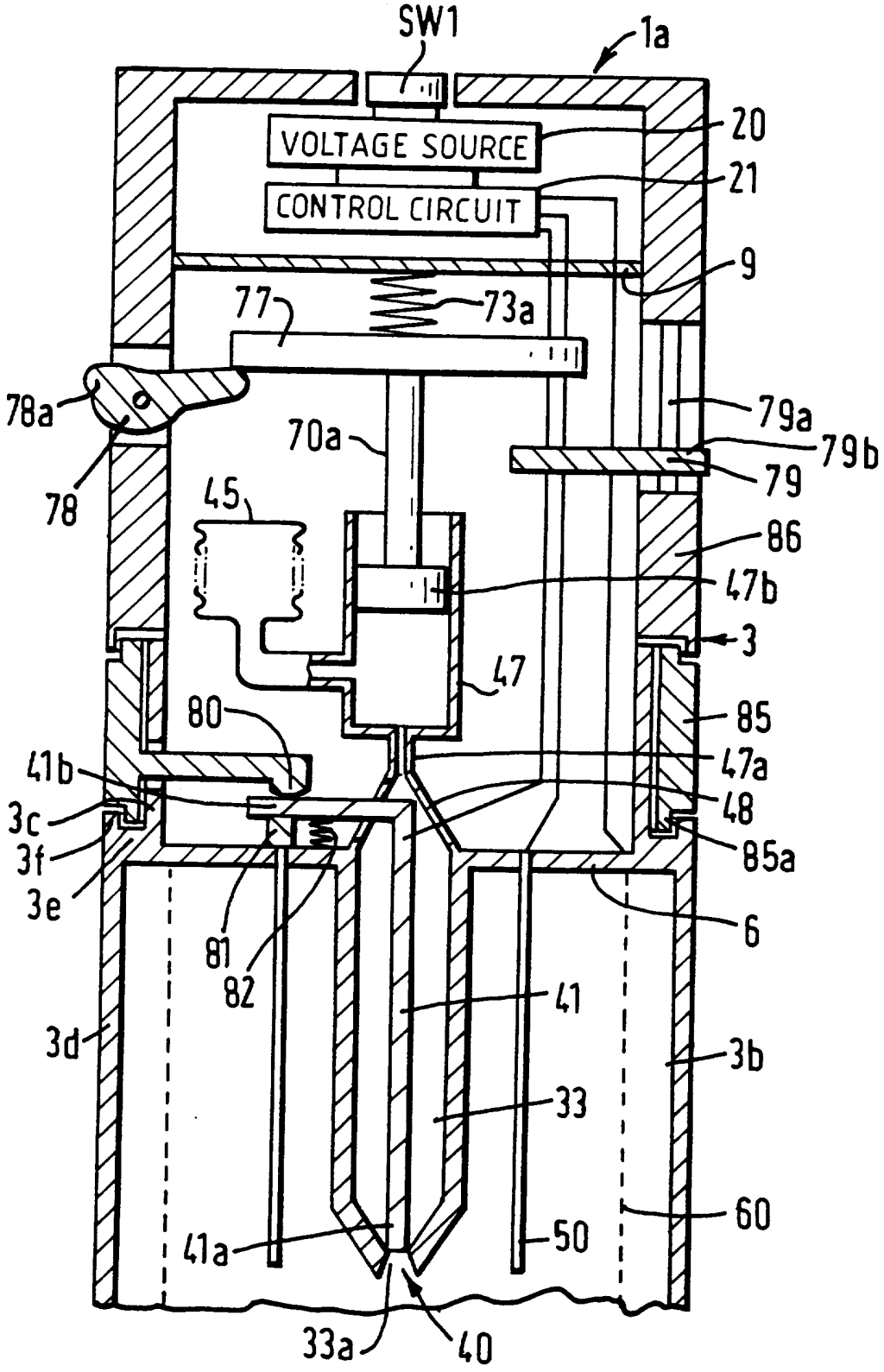

SW1
1a
VOLTAGE SOURCE
20
CONTROL CIRCUIT
21
9
77
73a
78a
79a
79b
70a
79
78
45
86
47b
3
47
80
85
41b
47a
3c
48
3f
85a
3e
6
81
82
41
3d
3b
33
60
41a
50
33a
40

FIG. 8

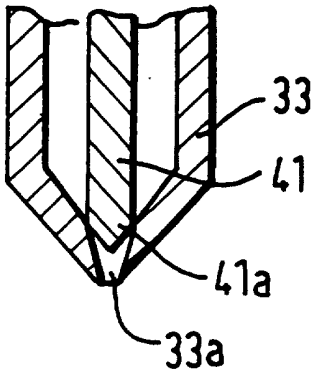


FIG. 10

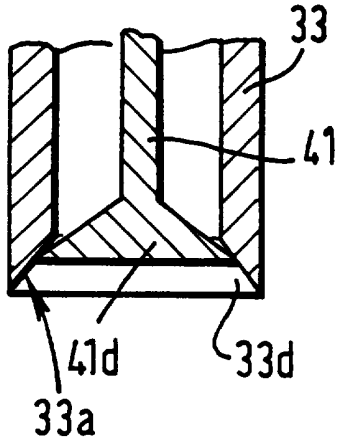


FIG. 9

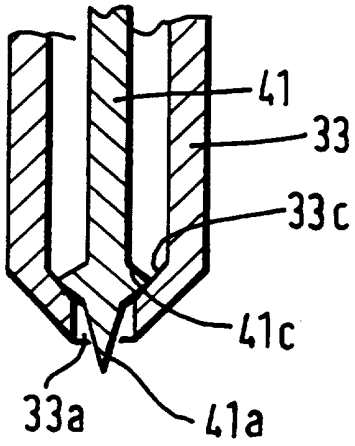


FIG. 11

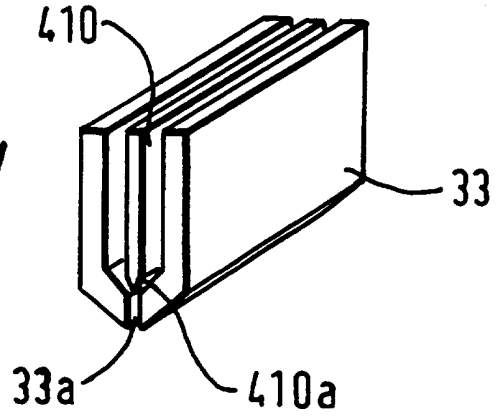


FIG. 12

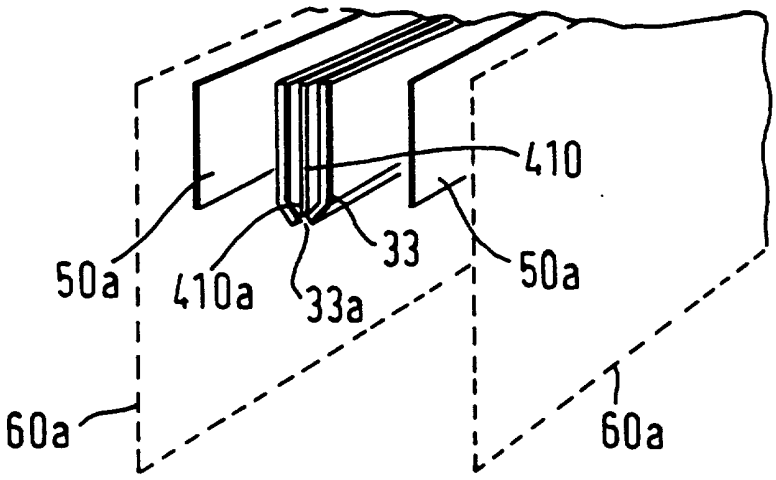
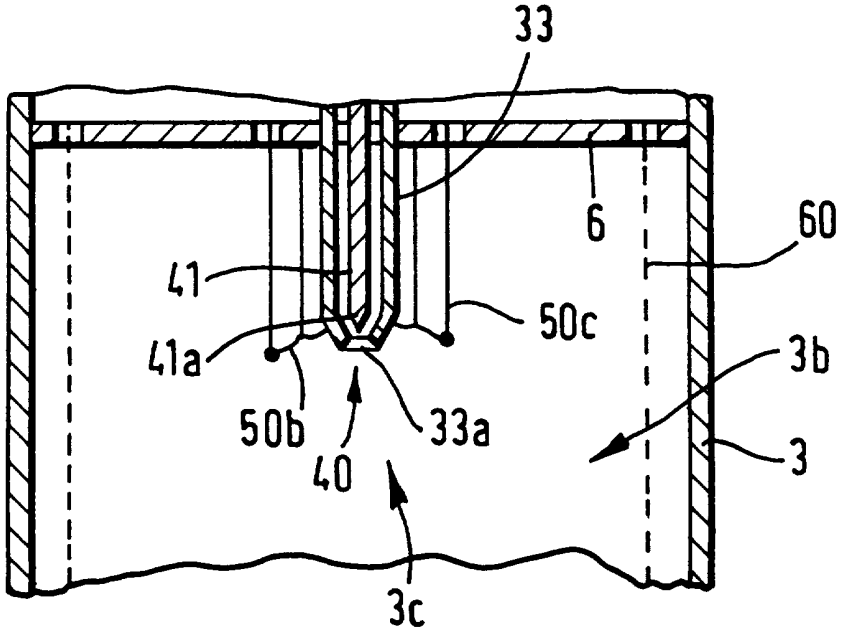

410
50a
410a
33a
33
50a
60a
60a

FIG. 13


33
6
60
41
50c
41a
3b
50b
33a
40
3
3c

A DISPENSING DEVICE

This invention relates to a dispensing device and a method of dispensing comminuted material to, particularly but not exclusively, the respiratory system of an animal such as a mammal or a bird.

As described in for example GB-A-1569707, dispensing devices are known which produce a monodispersed spray or cloud of liquid droplets by an electrohydrodynamic process in which a liquid emerging from an outlet is charged sufficiently that the net electric charge in the liquid as the liquid emerges into free space counteracts the surface tension forces of the liquid and the repulsive forces generated by the like electrical charges cause the liquid to be comminuted so producing an electrohydrodynamic cone or jet of liquid droplets. This process is generally referred to as electrohydrodynamic comminution. The particular device described in GB-A-1569707 is intended primarily for crop spraying and is an inherently bulky, though portable, device. The droplets produced by this device are charged close to their Rayleigh Limit and thus in use migrate quickly toward wet conductive surfaces. Accordingly, such a device would not be suitable for delivery of liquid droplets to an animal respiratory system because the charge on the droplets would cause them to migrate

quickly toward the wet conductive surfaces in the mouth rather than to pass to the upper respiratory tract.

GB-A-2018627 describes an electrohydrodynamic spray device wherein a charged droplet spray produced at a comminution site is fully or partially electrically discharged by means of a discharge electrode in the form of a sharp or pointed edge which is located downstream of the comminution site. Thus, in operation of this device, an electrical potential applied to the discharge electrode causes the discharge electrode to generate gaseous ions by corona discharge, which gaseous ions are then attracted to the oppositely charged droplets of the spray produced by the comminution site and therefore fully or at least partially discharge the liquid droplets. GB-A-2018627 thus effects at least partial discharging of the liquid droplets by ion bombardment.

Unfortunately, ion bombardment discharging may interfere with the comminution process and may reduce the quality and reliability of the liquid droplet spray. Indeed, the detrimental affect of ion bombardment on the comminution spray has been observed in laboratory experiments. In order to counteract these detrimental effects, EP-A-0234842 proposes the use of an annular shield electrode which is positioned between the comminution site and the discharge electrode and aims to maintain a steady

electrical field at the comminution site and to shield the comminution site and resulting liquid droplet spray from ions created at the discharge electrode downstream of the comminution jet or spray. The central aperture of the shield electrode needs, of course, to be sufficiently large to allow free passage of the charged droplets but also small enough to hinder ions from travelling around the spray cloud and interfering with the electrohydrodynamic cone or jet. Experiments have, however, shown that using liquid formulations compatible with human physiology such as water, ethanol and polyethylene glycol, for example, the aperture in the shield electrode must be so large that it is not capable efficiently of hindering the passage of ions as required.

An electrohydrodynamic liquid droplet dispensing device of the kind described in EP-A-0234842 is discussed in a paper entitled "Generation of Micron Sized Droplets from the Taylor Cone" by Meesters et al published in the Journal of Aerosols Science 23 (1992) at pages 37 to 49. The device described in that paper is relatively large being of the order of approximately 150mm high and 50mm in diameter. Experiments have shown that if the dimensions of this device are reduced serious stability problems arise. For example, if the current from the discharge electrode is of the same order as the current produced by the charged liquid droplet spray, droplets

inevitably impact on the tip of the discharge electrode so seriously reducing the ion current, leading to further droplet impaction and rapid reduction in the overall efficiency of this device. Although such problems could be overcome by increasing the ion current with respect to the electronic current produced by the electrohydrodynamic spray, the ionic wind resulting from air entrainment by the rapidly moving ions produced by the discharge electrode would either cause excessive air turbulence within the device resulting in an unacceptably large proportion of droplets impacting on the interior surfaces of the device or interfere with the electrohydrodynamic cone or jet of the liquid droplet spray causing it to become unstable as well as reducing the monodispersed nature of the spray.

According to one aspect of the present invention, there is provided a dispensing device particularly suitable for use for delivering comminuted material such as liquid droplets to the respiratory system of an animal such as human being, having electrohydrodynamic comminution means for generating charged comminuted material from liquid supplied to the comminution means and electrical discharge means for at least partially discharging the comminuted material wherein an ion migration path is provided which does not include the comminution means so that ions produced by the electrical discharge means do

not travel to the comminution means until there is a space charge built up by the production of a charged comminuted material spray by the comminution means.

In another aspect, the present invention provides a dispensing device having a geometry such that when a charged spray of comminuted material is produced by electrohydrodynamic comminution means, the resulting space charge diverts ions of opposite charge to the comminuted material away from a path away from the comminution means back towards the comminution means so that the ions may at least partially discharge the spray.

In another aspect, the present invention provides a dispensing device having air-permeable electrically conductive or semi-conductive internal walls through which air is drawn into a comminution area when comminuted material are sucked from the device, so reducing impact of comminuted material within the device enabling the amount of comminuted material which may be inhaled by a user to be increased.

In another aspect, the present invention provides an electrohydrodynamic dispensing device comprising a flexible or collapsible liquid reservoir which inhibits contact of air with the liquid to be dispensed and acts to retard evaporation of, for example, solvents during

storage, thereby increasing the useful lifetime of the device.

In another aspect, the present invention provides a dispensing device which uses a piezoelectric diaphragm pump coupled to an electrical control circuit to provide a steady flow of liquid to electrohydrodynamic comminution means.

In another aspect, the present invention provides a dispensing device wherein valve means are provided at an electrohydrodynamic comminution site to inhibit liquid evaporation when the device is not in use. The valve means may be actuable by, for example, a piezoelectric element and/or by a mechanically, magnetically or electrostatically coupled lever system.

In another aspect, the present invention provides a dispensing device having means for pumping liquid to electrohydrodynamic comminution means. The pumping means may be in the form of a hydraulic syringe having a user-operable piston which may be acted upon by a steady mechanical force provided by, for example, spring biasing means, or may be in the form of, for example, an electrohydrodynamic pump as described in EP-A-0029301 or an electroosmotic pump such as described in WO94/12285.

In another aspect, the present invention provides a dispensing device arranged to produce comminuted material by electrohydrodynamic comminution of liquid supplied to electrohydrodynamic comminution means, wherein means are provided for controlling the flow of liquid to the comminution site, for example the amount of liquid or the rate at which it is supplied, so as to control the amount or dose of comminuted material produced in operation.

In another aspect, the present invention provides a dispensing device having means for applying voltages to electrohydrodynamic comminution means and electrical discharge means in the form of an electromagnetic high voltage multiplier of the type manufactured by Brandenburg or Start Spellman or a piezoelectric high voltage source such as described in, for example, WO94/12285.

The present invention also provides a dispensing device having control means for enabling liquid to be supplied to electrohydrodynamic comminution means prior to actuation of the comminution means and for delaying production of ions from electric discharge means for a predetermined time until a cloud of charged comminuted material has been produced by the comminution means.

The present invention also provides an inhaler having the

features of any one or more of the preceding aspects.

The present invention also provides a method of supplying a medicament to the respiratory system of an animal such as a mammal or a bird using a device having the features of any one or more of the preceding aspects.

The present invention also provides a dispensing device for delivering electrohydrodynamically comminuted material comprising an olfactory stimulant such as an aroma or perfume or an insectide, biocide, pesticide, insect repellent or other airborne product.

Embodiments of the present invention will now be described, by way of example, with reference to the accompanying drawings, in which:

Figure 1 is a diagrammatic drawing showing a person using a dispensing device embodying the present invention as an inhaler;

Figure 2 shows a part-sectional view through one example of a dispensing device embodying the invention illustrating block schematically functional components of the dispensing device;

Figures 3a and 3b are schematic diagrams for illustrating

the production of charged comminuted material and its subsequent discharge during use of a dispensing device in accordance with the invention;

Figure 4 shows a part-sectional view similar to Figure 2 through part of another example of a dispensing device embodying the invention;

Figure 5 shows a part-sectional view of part of the dispensing device shown in Figure 4 for illustrating its operation;

Figure 6a shows a part-sectional view similar to Figure 2 of part of another example of a dispensing device embodying the invention;

Figure 6b is a schematic diagram for illustrating operation of a portion of the device shown in Figure 6;

Figure 7 shows a part-sectional view similar to Figure 6a of part of another example of a dispensing device embodying the invention;

Figures 8 to 11 illustrate diagrammatically various forms of comminution site suitable for use in a dispensing device embodying the invention;

Figure 12 illustrates one possible configuration or arrangement for a comminution site and discharge and further electrodes suitable for a dispensing device embodying the invention; and

Figure 13 illustrates another possible configuration for a comminution site and dispensing and further electrodes for use in a dispensing device embodying the invention.

As illustrated schematically in Figure 1, a dispensing device 1 embodying the invention is intended primarily for use as a pocket-size, hand-held inhaler which is actuated manually by a user 2 to enable, for example, delivery of a medicament or drug to the upper respiratory tract or lung, for example for delivery of a bronchodilator such as salbutamol or albuterol or steroids such as busenoide for the treatment of, for example, asthma, emphysema or bronchitis.

The dispensing device 1 comprises a housing 3 made of an electrically insulative material such as a plastics material. The inhaler has an outlet 4 through which liquid droplets to be inhaled are supplied to a user. The outlet 4 may be coupled, as shown in Figure 1, to a mask 5 which covers the nose and mouth of the user to enable both oral and nasal inhalation or may, for example, be coupled to an outlet tube to be received in

the mouth of the user where oral rather than nasal inhalation is required.

Figure 2 illustrates a part-sectional view through one example of a dispensing device embodying the invention.

As shown in Figure 2, the housing 3 of the dispensing device 1a has an internal wall 6 which separates first and second chambers 3a and 3b of the housing. The first chamber 3a accommodates a voltage source 20 which may be, for example, a conventional electromagnetic high voltage multiplier of the type manufactured by Brandenburg, Astec Europe, of High Street, Wollaston, Stourbridge, West Midlands DY8 4PG, UK, or Start Spellman of Unit 1, Broomers Park, Broomers Hill Lane, Pulborough, West Sussex RH20 2RY, UK or a piezoelectric high voltage source such as described in, for example, WO95/32807. The voltage source 20 is coupled to a voltage generator and control circuit 21 which is arranged to derive from the voltage source the various voltages required by the dispensing device as will be described below. Although it may be possible to use microprocessor or similar control circuit so as to determine the exact value and timings of the various voltages to be described below, in practice a relatively simple control circuit may be used in which one or more resistor-capacitor integrator networks and/or potential dividers are used to smoothly

ramp up the voltage to that required. Of course, other forms of voltage ramping arrangements may be used.

A reservoir 30 of the liquid to be dispensed is coupled via an electrically insulating supply pipe 31 to a chamber 32. The pipe should be made of an insulating material which does not retain charge for any significant length of time. A suitable material is, for example, polyacetyl or Delrin (trade mark). The reservoir may be a collapsible reservoir, for example the liquid may be contained within a flexible collapsible bag, or may have an internal wall arranged to move with the liquid to avoid or at least reduce air contact with the liquid. Liquid may be supplied to the chamber 32 from the reservoir 30 by, for example, gravity feed. Alternatively, the chamber 32 may comprise a pump such as an electrohydrodynamic pump as described in EP0-A-0029301 or an electroosmotic pump of the type described with reference to Figures 6 and 7 of WO94/12285 or any other suitable form of electrically operated pump operable under the control of the control circuit 30 so as to enable a steady flow of liquid from the chamber 32.

The chamber 32 is coupled to a liquid supply pipe 33 which passes from the first chamber 3a and through the wall 6 into the second chamber 3b of the dispensing device.

A comminution site 40 is provided at the end of the supply pipe 33. In this example, the comminution site is provided by the tip 41a of an electrically conductive rod 41 which extends axially through the liquid supply pipe 33 so that the tip 41a is located adjacent the outlet 33a of the supply pipe 33.

A discharge electrode arrangement 50 is mounted to the wall 6 so as to extend into the second chamber 3b and so as to be spaced from the comminution site 40 in a direction which is generally transverse to the general direction in which liquid issues from the supply pipe 33. The discharge electrode arrangement 50 provides, as will be described below, one or more discharge points or a discharge line which are or is spaced from the comminution site in a direction radially of the supply pipe 33 but located at about the same location as the comminution site in the axial direction of the supply pipe 33. The discharge points may be arranged so as to point in the same direction as the comminution site or may be angled towards the comminution site.

A further electrode 60 is positioned so as to be separated from the comminution site 40 by the discharge electrode 50. In the arrangement shown in Figure 2, the discharge electrode 50 and further electrode 60 are concentrically disposed with respect to the comminution

site so that the discharge electrode 50 surrounds the comminution site 40 and is in turn surrounded by the further electrode 60. The further electrode may extend as far as the outlet 4 of the housing.

The further electrode 60 comprises a perforate electrically conductive or semiconductive body which may, effectively, form an inner wall of the second chamber 3b so as to bound a comminution chamber or area 3c of the device. For example the further electrode 60 may comprise a tube or cage of wire mesh. The wall 7 of the second chamber 3b is formed with one or more apertures 8 to allow air to enter the second chamber 3b. The apertures may be symmetrically disposed around the comminution site so as to facilitate a symmetrical air flow.

The comminution site 40, discharge electrode 50 and further electrode 60 are connected to respective voltage outputs 22, 23 and 24 of the voltage generator and control circuit 21 which is arranged to provide respective voltages so that the voltage applied to the further electrode 60 is intermediate the voltages applied to the comminution site 40 and the discharge electrode 50. In this example, the circuit 21 is arranged to supply a negative voltage to the comminution site 40, a positive voltage to the discharge electrode 50 and earth

or ground potential to the further electrode 60. The further electrode 60 has the further advantage of shielding the comminution chamber 3c from external electromagnetic fields so that the electrical fields within the device are not detrimentally affected when, for example, the device is held by a user.

The voltage source 20 is coupled to the voltage generator and control circuit 21 by means of a user operable switch SW1 which may be, for example, a conventional toggle or push button switch.

Where desirable, to control dispensing of liquid from the reservoir to the chamber 32, the supply pipe 31 from the reservoir 30 may be coupled to the chamber 32 by means of a valve 34. A further valve 35 may be provided in the supply pipe 33 adjacent the comminution site 40 to inhibit loss of liquid by (which may occur by evaporation if the liquid being dispensed is volatile) when comminution is not occurring.

In the arrangement shown in Figure 2, the valves 34 and 35 are electrically operated valves, for example solenoid or piezoelectric valves which are operated under the control of the control circuit 21. However it may be possible to use simple one-way mechanical valves and, as will be described below, other mechanical valve

arrangements are also possible.

In order to use the dispensing device shown in Figure 2 as an inhaler, the user 2 places the mask over their nose and mouth, grasps the housing 3 of the dispensing device in their hand as shown schematically in Figure 1 and actuates the switch SW1 with their thumb or a finger and then breaths in. As will be appreciated, if the device is designed for only oral inhalation, the user will insert the inhalation tube into their mouth. Actuation of the switch SW1 couples the voltage source 20 to the voltage generator and control circuit 21 which supplies a voltage signal to open the valve 34 to allow liquid to be supplied via the chamber 32 and the supply pipe 33 to the comminution site 40. If as discussed above, the liquid is to be pumped from the chamber 32, then the control circuit 21 also supplies the required voltage signals to activate the pump to supply the liquid to the supply pipe 33. At the same time or slightly thereafter, the voltage generator and control circuit 21 outputs the negative and positive voltages on the voltage supply lines 22 and 23 and couples the further electrode 60 to, in this example, earth.

Initially, as shown schematically in Figure 3a, the electric field adjacent the comminution site 40 causes atomization of the liquid supplied to the comminution

site so resulting in a spray or jet 42 of charged droplets. As the user breaths in, air is entrained through the apertures 8 in the second chamber 3b and through the perforate further electrode 60 into the comminution chamber bounded by the further electrode 60. This general movement of air through the perforate electrode 60 hinders or inhibits charged liquid droplets or other charged comminution products from impacting on the electrode 60. The voltage applied to the discharge electrode 50 results, by corona discharge, in ionization of air or other gas molecules within the second chamber 3b to produce ions oppositely charged to the liquid droplets. As shown schematically by the dot-dash lines 43 in Figure 3a, initially the oppositely charged air or gas ions are attracted away from the liquid spray 42 toward the more negatively charged (in this case earthed) further electrode 60. However, as shown in Figure 3b, the space charge resulting from the generation of the liquid droplet spray 42 eventually becomes sufficient to attract the ions away from their normal path and towards the liquid droplet spray 42 so enabling the charge on the liquid droplets to be at least partially discharged by the oppositely charged air or gas molecules produced by the discharge electrode 50 so that the liquid droplets breathed in by the user are at least partially discharged.

The use of the further electrode 60 spaced from the comminution site 40 by the discharge electrode 50 enables the discharge electrode 50 to be placed relatively close to the comminution site 40 without the gaseous ions produced by the discharge electrode interfering with the comminution process. Typically, the discharge electrode 50 may be as close as 6-12mm from the comminution site. This allows the device structure to be particularly compact so that the comminution and discharging arrangement may have, for example, a height of about 40mm and a diameter of about 30mm making it particularly suitable for hand-held use and for transportation in a handbag or a user's pocket. Generally, the distance between the discharge electrode and the comminution site will be greater than, for example about twice, the distance between the discharge electrode and the further electrode 60. In practice, the actual relative distances are selected in combination with the respective voltages applied to the electrodes 50 and 60 and the comminution site 40 so as to ensure that gaseous ions are diverted toward the further electrode 60 until a sufficient cloud of charged liquid droplets has been generated and to ensure efficient discharge.

Experiments were carried out using a liquid formulation of 20% by volume polyethylene glycol and 80% by volume ethanol containing typically 2% by mass per volume of

Salbutomol with the comminution site 40 being supplied with liquid at a flow rate of 1.33 μL/s (microlitres per second) and being held at a potential of -2.3 kilovolts, with four discharge electrodes 50 held at a potential of +2 kilovolts spaced at 90° intervals around the circumference of a 15mm diameter circle centred on the comminution site 40 and an earthed 25mm diameter cylindrical perforate electrode 60 concentrically arranged with respect to the comminution site. The liquid droplets emerging from the outlet 4 of the device were found to be substantially uncharged and a device efficiency of over 97% (that is the percentage of the mass of drug supplied to the comminution site that is actually delivered to the outlet 4 of the device) was observed.

Charged liquid droplets produced by electrohydrodynamic comminution have a charge-to-mass ratio corresponding roughly to the Rayleigh Criterion for charged droplet stability, namely:

$$r = \left[\frac{q^2}{32\pi^2\epsilon\gamma}\right]^{1/3}$$

where r is the droplet radius in metres, ϵ is the relative permittivity, γ is the liquid's surface tension, and q the charge on the droplet. Accordingly by controlling the voltage applied to the comminution site,

the charge and thus the radius of the liquid droplet can be controlled.

The discharge electrode arrangement may be arranged either to fully or partially electrically discharge the charged liquid droplets by adjusting the voltage applied to the discharge electrode in accordance with the voltages applied to the comminution site, the resistivity and flow rate of the liquid being comminuted so that the number of ionised air molecules produced by the discharge electrode is sufficient to either fully or partially discharge the comminuted material.

Figure 4 is a part-cross sectional view similar to Figure 2 showing part of another example of a dispensing device 1a embodying the invention.

The dispensing device shown in Figure 4 has a voltage source 20, voltage generator and control circuit 21, comminution site 40, discharge electrode 50 and further electrode 60 which are arranged in and operate in a similar manner to the corresponding components described with reference to Figure 2 when the switch SW1 is operated by a user in the manner discussed above.

The dispensing device shown in Figure 4 differs from that shown in Figure 2 in the manner in which a liquid to be

dispensed is supplied to the comminution site 40. In the arrangement shown in Figure 4, liquid to be dispensed is retained in a collapsible reservoir 45 which may be in the form of a flexible bag or may have a bellows type arrangement. The collapsible reservoir 45 has an outlet pipe 46 which is received in a fluid-tight manner within an inlet pipe 56 of a pump chamber 32a which may be integrally formed with, for example moulded with, the supply tube 33 for supplying liquid to the comminution site 40.

A flexible diaphragm 57 is mounted in a fluid-tight manner into an aperture in an upper portion of the pump chamber 32a. The periphery of the flexible diaphragm 57 is, in the arrangement shown, held between twin flanges 55a and 55b bounding the aperture. O-ring or similar seals 58 may be provided to ensure a fluid-tight seal. In an alternative arrangement, where the pump chamber 32a is moulded from a plastics material, for example, the flexible diaphragm may be positioned in place during the moulding process.

The flexible diaphragm is caused to flex under the control of a diaphragm control member 59 when the voltage supplied by the control circuit 21 reaches a predetermined value. The diaphragm control member 59 may be, for example, a piezoelectric element formed by a

ceramic disc on a metal plate such as is available commercially from Morgan Matroc Ltd., of Bewdley Road, Stourport-on-Severn, Worcestershire DY13 7QR, UK. Of course, other means for causing the diaphragm 57 to flex, for example, a piston arrangement or a magnetically or electrostatically coupled lever system may be used.

As shown in Figure 4, the conductive rod 41 which provides the comminution site 40 is pivotally mounted to and depends from a support arm 61 which is pivotally mounted at one end to a pivot mount 62 provided on an inner wall of the pump chamber 32a. The other end of the support arm 61 carries a valve member 35a for closing the outlet pipe 46 from the flexible reservoir 45. The support arm 61 is supported adjacent the pivot mount 62 by a support bar 63 which itself is mounted at one end of a piezoelectric element 64 having its other end fixedly secured to a base wall of the pump chamber 32a. In this case, the piezoelectric element 64 will normally have a thin and flexible resistive coating to insulate it from the liquid in the pumping chamber. The piezoelectric element 64 preferably comprises a piezoelectric bimorph formed of a plurality of layers of ceramic which provides a greater degree of movement for a given applied voltage than a single piezoelectric ceramic layer. Such piezoelectric bimorphs are also commercially available from Morgan Matroc.

Prior to use of the dispensing device shown in Figure 4, no voltage is applied to either of the piezoelectric elements 59 and 64. In this state, as shown in Figure 5, the free end 41a of the conductive rod 41 cooperates with a narrowing portion of the insulative supply pipe 33 to form a valve head closing the outlet 33a of the insulative supply pipe to prevent loss of liquid by evaporation. The valve head 35a is spaced away from the outlet 46 of the flexible reservoir 45 allowing the pump chamber 32a to be filled with liquid.

When the switch SW1 is actuated by the user and the voltage supplied by the control circuit reaches the required value, the piezoelectric element 64 flexes or bends so raising the rod 41 to cause the valve head 35a to close the outlet pipe 46 of the reservoir 45 and to move the free end of the rod 41 away from the outlet 33a of the supply pipe 33 to bring the device into the condition shown in Figure 4. When the voltage supplied to the piezoelectric element 59 reaches a predetermined value, the piezoelectric element 59 causes the diaphragm 57 to flex downwardly in Figure 4 so forcing the liquid in the pump chamber 32a to flow toward the outlet of the supply pipe 33 at a steady flow rate. The voltage generator and control circuit 21 applies voltages as described with reference to Figure 2 to the comminution site 40, discharge electrode 50 and further electrode 60

in the same manner as described with reference to Figures 2, 3a and 3b so resulting in a spray of charged droplets which are then discharged by the discharge electrode 50 and pass, by the action of the user breathing in, through the outlet 4 of the device into the upper respiratory system of the user. As discussed above, the control circuit may be a microprocessor or resistor-capacitor RC network.

Figure 6a shows a part-cross sectional view similar to Figures 2 and 4 of part of another dispensing device embodying the invention.

In the arrangement shown in Figure 6a, liquid to be dispensed is contained in a syringe 47 having its capillary tube outlet 47a coupled to a liquid guiding funnel arrangement 48 for guiding liquid to the liquid supply pipe 33 which is, in this example, mounted to or integrally formed with the wall 6 dividing the first chamber 3a from the second chamber 3b.

The syringe body 47 is mounted to a nut 49 provided with an air vent 49a. The nut is itself secured in a manner not shown to the wall of the upper or first chamber 3a. The syringe piston 47b is carried by a screw-threaded rod 70 which extends through and cooperates with the nut 49.

The other end of the screw-threaded rod 70 is coupled by a uni-directional coupling 71 of conventional form to a shaft 72 rotatably mounted to a internal wall 9 of the housing which separates the voltage source 20 and control circuit 21 from the remainder of the device. A flat coil spring 73 which has one end secured to shaft 72 and the other end secured to the inner surface of the housing. A lever 74 is fixed to and extends from the shaft 72. A free end 74a of the lever extends through a slot 75 provided in the housing so that the free end 74a of the lever 74 can be gripped by a user. The lever 74 is movable within the slot 75 as will be described below to enable a user to wind up the spring 73.

A cam surface 80 retains an end 41b of the rod 41 on a support 81 against the action of a biasing spring 82 so as bias the other end 41a of the rod 41 into a position closing the outlet 33a of the liquid supply pipe 33.

The cam surface 80 is provided on a rod 83 which extends through an aperture in the housing 3 from an outer rotatable sleeve 85.

The portion 3c of the housing forming part of the side walls of the first chamber 3a is recessed with respect to the portion 3d forming the side walls of the housing forming the second chamber 3b and has at its lower end

a radially outwardly extending flange 3e provided with a lip 3f which receives an axially extending rim 85a of the sleeve 85.

The upper end of the sleeve 85 is held in place by a separate cap member 86 forming a top part of the upper chamber and having a recess 86a for receiving an axially extending circumferential projection of the sleeve. The cap member may for example be secured to the housing portion 3c by adhesive.

Operation of the device shown in Figure 6a will now be described with the aid of Figure 6b which shows very schematically a cross-sectional view of the device of Figure 6a taken along line VI-VI in Figure 6b. For simplicity Figure 6b omits all components of the device apart from the coil spring 73, the shaft 72 to which one end of the spring 73 is attached, the lever 74 and its associated aperture 75 and a stop 76. The user first primes the device by rotating the lever 74 in its slot 75 in the direction of the arrow A in Figure 6b and against the biasing force of the coil spring 73 so winding up the coil spring. The unidirectional coupling 71 prevents rotation of the piston rod 70 as the spring is being wound up. The stop 76 is mounted within the aperture 75 so as to engage the lever when the lever meets the stop. For example, the stop 76 may comprise

a spring-biassed detent which engages the lever as it rides over the stop. Once the spring has been wound up, the user rotates the sleeve 85 causing the cam surface 80 to move relative to the end 41b of the rod 41 to allow the biasing spring 82 to move the rod 41 upwardly in Figure 6a so as to open the outlet 33a of the liquid supply pipe 33. An opening is provided in the funnel arrangement 48 to enable movement of the rod 41.

Actuation of the switch SW1 provided in the top of the cap 86 of the housing causes the control circuit to supply the required voltages to the electrodes 41, 50 and 60, as discussed above, the user then depresses a button (not shown) to release the engagement between the detent 76 and the lever 74 allowing the coil spring 73 to twist the threaded shaft of the piston rod 70 through a set angle at a set rate so that the cooperation between the piston rod 70 and nut 49 causes the piston 47b to move through the syringe 47 so that a metered amount of liquid is supplied at a steady rate from the syringe to the liquid supply pipe 33. The air vent 49a in the nut 49 enables air to enter the syringe to allow movement of the piston 47b.

Liquid passing from the outlet 33a of the supply pipe 33 is atomized or comminuted by the electric field at the comminution site 40 and, once sufficient space charge has

built up, the charge on the thus produced droplets is electrically discharged by ions generated by the discharge electrode 50 as described above so providing a cloud or spray of discharged droplets which can then be inhaled by the user.

The lever 74 may be mechanically and/or electrically connected to the switch SW1 so that depression of the switch SW1 also causes the lever to be released to allow the spring 73 to move the piston, so obviating the need for a separate button.

Once the dose of liquid has been supplied from the outlet 33a of the supply pipe 33, the user rotates the sleeve 85 to return the rod 41 to its position closing the outlet 33a of the liquid supply pipe 33.

The above described actions are repeated each time the user wishes to use the device and with each use the piston 47b moves further down the syringe delivering a metered dose each time to the supply pipe 33.

It will of course, be appreciated that alternative ways of priming the coil spring or biassing the piston to cause a metered does to be delivered to the supply pipe 33 may be used.

Figure 7 is a part cross-sectional view similar to Figure 6a of part of a further example of a device embodying the invention.

The device shown in Figure 7 is identical in operation to that shown in Figure 6a except in the manner in which liquid is supplied to the supply pipe 33. In the device shown in Figure 7, the syringe 47 has a reciprocable piston 47b. The free end of the piston rod 70a is mounted to a support plate 77 which is held in a first position against the biassing action of a spring 73a by a spring-biassed latch 78. The latch 78 is pivotally mounted to the housing 3 and has a portion 78a extending through an aperture is in the housing 3 to form a user operable switch so that when the user presses downwardly, after having rotated the rotatable sleeve 85 to open the outlet 33a and actuated the switch SW1, the portion 78a the latch 78 is pivoted upwardly past the edge of the support plate 77 thus freeing the support plate and allowing it to move downwardly under the action of the spring 73a until the plate 77 meets a support member 79. This causes the piston to supply a metered dose of liquid to the outlet 33a where the liquid is electrohydrodynamically comminuted as described above. The actual amount of the dose supplied is determined by the location of the support member 79.

The support member 79 is slidably mounted in a slideway 79a defined in the wall of the housing 3 and in order to reprime the device, the user grasps a free end 79b of the support member 79 and moves it upwardly in the slideway 79a so causing the support plate 77 to move upwardly in Figure 7 forcing the latch 78 to pivot upwardly against its spring biassing so that the support plate 77 comes to rest on the latch 78 as shown in Figure 7. During this return movement, the liquid in the syringe is replenished by supply through a one-way valve (not shown) from a collapsible reservoir 45 of similar type to that shown in Figure 4.

It will be appreciated that any suitable form of biassing and latching mechanism may be used to control movement of the piston in the device shown in Figure 7. In addition, the device shown in Figure 6a may be modified so as to provide a reciprocating piston arrangement by removing the uni-directional coupling and providing the collapsible reservoir 45.

It will, of course, be appreciated that other mechanical lever arrangements may be used to control opening of the liquid supply valve and priming and releasing of the spring mechanism for rotating the piston rod. Also a magnetically coupled or electrostatically coupled lever system may be used.

A combination of electrically and mechanically operated arrangements may be used so that, for example, a mechanical outlet valve of the type shown in Figures 6a and 7 may be used in combination with an electrically operated outlet valve or alternatively an electrical pumping arrangement may be used with a mechanical outlet valve.

In the arrangements shown in Figures 2, 4, 6a and 7, the comminution site is provided by a rod 41 which extends through the liquid supply pipe 33 and cooperates with the liquid supply pipe so as to form a valve closing the liquid supply pipe opening 33a when supply of liquid from the liquid supply pipe is not required.

The end 41a of the rod 41 and the opening 33a of the liquid supply pipe 33 may be shaped so as to improve the liquid tightness of the valve when closed. For example, as shown in Figure 8, the rod 41 may be provided with a conical, i.e. sharpened or pointed, end 41a and the opening 33a of the liquid supply pipe may be arranged to be frusto-conical, narrowing towards the exterior so that, when the valve is closed, the conical end or tip 41a of the rod extends into the outlet opening of the liquid supply pipe.

Figure 9 shows a further alternative arrangement wherein

the rod 41 is provided with a radially extending flange 41c which, when the valve is closed, rests on a cooperating surface 33c of the outlet of the liquid supply pipe.

Figure 10 shows a further possible arrangement which may be used in the devices shown in Figures 2, 6a and 7 wherein the rod 41 carries a conical valve head 41d which cooperates with a frusto-conical valve seat 33d provided by the opening 33a of the liquid supply pipe 33. In this arrangement, the rod 41 is raised so as to close the valve and lowered to open the valve, and so would require the operation of the cam surface 80 on the biasing spring 82 shown in Figure 6a or 7 to be reversed.

In the arrangements described above, the comminution site is provided as a point by a cylindrical rod 41. However, other forms of comminution site may be used as described in, for example, WO95/26235, WO95/26234 or WO95/32807. As one example, the comminution site may be provided as a ring or annulus of spaced-apart comminution points each similar to the one shown in Figure 1 as described with reference to Figure 5 of WO95/32807. As another possibility, as illustrated schematically in Figure 11, the comminution site 40 may be provided as a line rather than a point or series of points by replacing the rod 41 described above by a planar member 410 providing at its

lower end a comminution site in the form of a knife edge 410a along which multiple jets will be formed in use. As another possibility an annular comminution site may be used by providing a hollow cylinder in place of the rod 41.

Where the comminution site itself is rotationally symmetrical, for example where the comminution site comprises a rod or cylinder, then the discharge electrode or electrodes and the further electrode will preferably be rotationally symmetric and concentrically arranged with respect to the comminution site. Where, however, the comminution site is provided as a linear edge as shown in Figure 11, then the discharge electrode may similarly be provided as two elongate edges 50a as shown in Figure 12 and the further electrodes may be provided by two perforate planar members 60a disposed either side of the comminution site so as to ensure that, in use, the generated electric fields are symmetric with respect to the comminution site.

As discussed above, the discharge electrode may be formed as a single discharge point or may be formed by a number of discrete discharge points which may be provided by, for example, separate discharge needles or may be provided by a discharge wire 50b held in place by conductive restraints 50c as shown schematically in

Figure 13.

In the arrangements described above, liquid is supplied to the comminution site by gravity feed or by a pumping mechanism such as a flexible diaphragm or a syringe pump. As discussed above, other pumping mechanisms may be used, for example, an electrohydrodynamic pump such as that described in EP-A-0029301 or an electroosmotic pump as described with reference to Figures 6 and 7 of WO94/12285 may be used or other forms of pump which allow a metered dose to be supplied may be used.

In the examples described above, the further electrode 60 is perforate and is spaced from the interior wall of the housing so as to enable air flow through the further electrode to inhibit impact of comminuted material or product on the further electrode. It may, however, be possible to provide the further electrode by providing an electrically conductive or semiconductive coating on the interior wall of the housing and to rely on air flow over the coating to inhibit impact of comminuted product on the further electrode. In such an arrangement, at least a major part of the interior wall of the housing may be coated and earthed which should enable particularly efficient electromagnetic shielding but at the expense of there being an increased likelihood of deposition of comminuted product onto the further

electrode and thus less efficient delivery of the comminuted product.

The dose delivered by a device embodying the invention may be adjustable. For example, in the devices shown in Figures 2 and 4, the relative times at which the valves 34 and 35 in Figure 2 and 35a and 41a in Figure 4 are opened may be used to control the amount of liquid delivered to the comminution site. This may be achieved by, for example, adjusting the rates at which the respective voltages are ramped up to the required voltages to actuate the valves by appropriate adjustment of the control circuit. Such adjustment may be carried out at a factory level by adjusting the values of the resistors and capacitors in the ramp circuit or may be controllable by a pharmacist or an end user by providing switch means for switching in or out additional resistors and capacitors to adjust the voltage ramp rates.

In the device shown in Figures 6a and 6b, the amount by which the spring is wound up or allowed to unwind, and so the amount by which the piston moves within the syringe cylinder, may be selected by determining the circumferential extent of the slot 75 and/or the location of the abutment 76. The location of the abutment 76 may be selectable by a pharmacist or a doctor to adapt the device for the particular requirements of a particular

patient or may be selectable by a patient to enable the patient to select the number of doses required. For example, the slot 75 may be provided with a number of different discrete locations to which the abutment 76 may be moved with each location being identified by a scale on the housing as providing a given multiple of a basic dose. Where the location of the abutment 76 and therefore the dose is selectable by the pharmacist or doctor, then the abutment may be designed so as to be fixed in position once inserted into the slot and may be, for example, colour coded to enable easy identification of the dose the device is designed to delivery.

In the device shown in Figure 7, the delivery dose may be adjusted by, for example, adjusting the length of the slideway 79a in the factory or by providing on the slideway an abutment similar to the abutment 76 shown in Figure 6b which may be located as discussed above.

Enabling the dose of liquid delivered to the comminution site to be controlled allows the device to be adapted for different patient requirements. Thus, for example the device may be adapted for use by an adult or a child and also for use with different drugs which may require different liquid dosages.

Typically, liquids with resistivities in the range of

from 10^2 to 10^8 ohm-metres and viscosities in the range of from 1 to 250 centipoise may be comminuted by a device embodying the present invention. The liquid may be a melt, solution, suspension, emulsion microsuspension or microemulsion or even a gel provided that the liquid can be caused to flow at an adequate flow rate to the comminution site.

The size of the comminuted liquid droplets produced depends on, for a given liquid, the electric field used to cause comminution and the flow rate. In the example given above, the electric field used for causing comminution and the flow rate of the liquid being comminuted are selected to produce droplets of a size suitable for delivery to the upper respiratory tract. However by appropriately selecting the flow rate and the electric field for a given liquid, droplets of a size suitable for delivery to the mouth cavity and throat area or to the nasal passages or even the small bronchi of the lungs may be provided.

As discussed above, a dispensing device embodying the invention is primarily intended for use as a hand held portable device suitable for use as an inhaler for supplying a medicament to the respiratory system. Medicaments suitable for delivery by a device embodying the invention include bronchodilators or steroids as

discussed above and others for treatment of disorders of the upper respiratory tract including disorders of the nasal mucosa and congestion and disorders of the upper respiratory tract associated with hayfever.

Particular medicaments for use as nasal decongestants include as oxymetazoline, xylometazoline, phenylephrine, propylhexadrine, nephazoline and tetrahydrozoline and as appropriate salts thereof such as the hydrochloride salt, and formulations thereof.

A device embodying the invention may also be suitable for oral or nasal delivery of drugs which are currently being tested as anti-migraine agents such as the triptans (for example almotriptan, eletriptan, naratriptan, rizatriptan, sumatriptan and zolmitriptan) or CP-122, 288 produced by Pfizer and Lanepitant produced by E. Lilley. A device embodying the invention is suitable for use as a pocket-size hand held inhaler for, for example, the occasional delivery of a medicament because its design enables the electrical discharge means and comminution site to be brought close together without impeding their function so allowing the device to be compact. The device should also be user friendly in that it is simple to operate, particularly for unskilled users and the infirm, because the liquid droplet spray is delivered under the control of the inhalation of the user and not

with the force of a gas discharge as in conventional aerosol systems.

A device embodying the invention may however also be used for dispensing droplets of other liquids, for example as a desktop or hand-held dispenser for dispensing olfactory stimuli such as aromas and perfumes, insect repellents, biocides or insecticides, pesticides and other airborne products.

CLAIMS

1. A dispensing device, comprising:

means for subjecting liquid to an electric field for causing comminution of the liquid to produce charged comminuted material;

means for supplying liquid to the comminution means;

electrical discharge means for producing ions to at least partially electrically discharge comminuted material produced by the comminution means and means spaced from the comminution means by the electrical discharge means for electrically attracting ions produced by the electrical discharge means away from the comminution means until comminuted material produced by the comminution means builds up sufficient space charge to divert the ions towards the charged comminuted material to enable the ions at least partially to discharge the comminuted material.

2. A device according to claim 1, wherein the electrical discharge means are spaced from the comminution means in a direction transverse to the general direction in which comminuted material is supplied from the comminution means.

3. A device according to claim 1, wherein the electrical discharge means surround or are provided on either side of the comminution means.

4. A device according to claim 1, 2 or 3, wherein the ions attracting means surround or are provided on either side of the electrical discharge means.

5. A dispensing device, comprising:

a housing having an outlet for supplying comminuted material, the housing containing:

means for subjecting liquid to an electric field for causing comminution of the liquid to produce a cloud of charged comminuted material in a comminution chamber within the housing;

means for supplying liquid to the comminution means;

electrical discharge means at least partially surrounding the comminution means for producing ions to at least partially electrically discharge comminuted material produced by the comminution means;

means spaced from the comminution means by the electrical discharge means and bounding the comminution chamber for electrically attracting ions produced by the electrical discharge means away from the comminution means until comminuted material produced by the comminution means builds up sufficient space charge to divert the ions towards the cloud of charged comminuted material to enable the ions to at least partially discharge the comminuted material;

means for allowing air to enter the comminution chamber; and

voltage supply means for supplying electrical potentials for causing the ion attracting means to be at a potential between that of the comminution means and the electrical discharge means.

6. A device according to any one of the preceding claims, wherein the ion attracting means comprises an electrically conductive or semiconductive perforate wall.

7. A device according to any one of the preceding claims, wherein the ion attracting means comprises an electrically conductive or semiconductive coating provided on an inner surface of a housing of the device.

8. A device according to claim 5, wherein the ion attracting means comprises an electrically conductive or semiconductive inner wall spaced from an inner surface of the housing which wall is perforate and together with at least one air inlet provided in the housing provides the means for allowing air to enter the comminution chamber for reducing impact of comminuted material on the electrically conductive or semiconductive inner wall.

9. A device according to any one of the preceding claims, wherein, in a general direction of production of comminuted material from the comminution means, the electrical discharge means is located at about the same

position as the comminution means.

10. A device according to any one of the preceding claims, wherein the electrical discharge means comprises a plurality of electrical discharge sites symmetrically located with respect to the comminution means.

11. A device according to any one of the preceding claims, wherein the comminution means comprises a plurality of comminution sites.

12. A device according to any one of the preceding claims, wherein the arrangement of the comminution means, the electrical discharge means and the ion attracting means is rotationally symmetric with the electrical discharge means and the ion attracting means being located on respective circles concentric with the comminution means.

13. A device according to any one of claims 1 to 11, wherein the comminution means comprises an array of comminution sites and the discharge means and ion attracting means each comprise a pair of elongate electrodes or arrays of electrodes disposed on either side of the comminution site array.

14. A device according to any one of the preceding

claims, wherein the liquid supply means comprises a liquid reservoir and pump chamber for supplying liquid from the reservoir to the comminution means.

15. A device according to claim 14, wherein the pump chamber comprises a pump selected from the following types: a diaphragm pump; an electrohydrodynamic pump; an electroosmotic pump; and an electrohydrodynamic pump.

16. A device according to claim 14, wherein the pump chamber comprises a flexible diaphragm arranged to flex in response to application of a control signal to diaphragm control means.

17. A device according to claim 16, wherein the diaphragm control means comprises a piezoelectric element.

18. A device according to claim 14, wherein the pump chamber comprises a syringe body and a syringe piston and means operable by a user are provided for moving the piston to cause a dose of liquid to be dispensed to the comminution means.

19. A device according to claim 18, wherein the user-operable means comprises a spring biassing mechanism.

20. A device according to any one of the preceding claims, further comprising means for controlling the amount of liquid supplied to the comminution means.

21. A device according to claim 18 or 19, comprising means for controlling the amount of movement of the piston to control the amount of liquid supplied to the comminution site.

22. A device according to claim 20 or 21, wherein the controlling means are adjustable to enable the amount of liquid supplied to the comminution means to be manually adjustable.

23. A device according to any one of claims 16 to 22, further comprising valve means for controlling supply of liquid from the reservoir to the pump chamber.

24. A device according to any one of the preceding claims, wherein valve means are provided for controlling a liquid outlet to the comminution means.

25. A dispensing device, comprising:

means for subjecting liquid to an electric field for causing comminution of the liquid to produce a comminuted material;

liquid supply means having a liquid supply outlet

for supplying liquid to the comminution means; and

valve means for closing the outlet to inhibit evaporation of liquid when the comminution means is not in use.

26. A device according to claim 24 or 25, wherein the comminution means comprises a rod having at least an electrically conductive end, the rod extending through an electrically insulative liquid supply tube and cooperating with an outlet of the liquid supply tube to form the valve means, means being provided for moving the rod relative to the tube to open the valve means to enable supply of liquid for comminution.

27. A device according to claim 25 or 26 when dependent on claim 25, further comprising:

electrical discharge means for producing ions to at least partially electrically discharge liquid droplets produced by the comminution site.

28. A device according to claim 27, further comprising means spaced from the comminution means by the electrical discharge means for electrically attracting ions produced by the electrical discharge means away from the comminution means until charged comminuted material produced by the comminution means builds up sufficient space charge to divert the ions towards the charged

comminuted material to enable the ions to at least partially electrically discharge the charged comminuted material.

29. A device according to any one of the preceding claims, comprising control means for causing liquid to be supplied to the comminution means prior to actuation of the comminution means.

30. A dispensing device substantially as hereinbefore described with reference to the accompanying drawings.

31. An inhaler comprising a device in accordance with any one of the preceding claims and means for delivering at least partially electrically discharged comminuted material to the respiratory system of an animal.

32. A method of delivering a medicament to the respiratory system of an animal which comprises using a device in accordance with any one of claims 1 to 29 to deliver comminuted material to the respiratory system of the animal.

33. An olfactory stimulant delivery device comprising a device in accordance with any one of the preceding claims having a supply of an olfactory stimulant such as an aroma or perfume.

34. A dispensing device in accordance with any one of claims 1 to 30 adapted for the delivery of insect repellant, a biocide, an insecticide, pesticide or other airborne product.

The Patent Office

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Application No: GB 9716888.4
Claims searched: 1-24

Examiner: John Warren
Date of search: 4 November 1997

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.O): B2F (FGB)

Int Cl (Ed.6): B05B 5/025, 5/053, 5/16

Other: ONLINE Databases: WPI and CLAIMS

Documents considered to be relevant:

Category	Identity of document and relevant passage	Relevant to claims
	None	

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.