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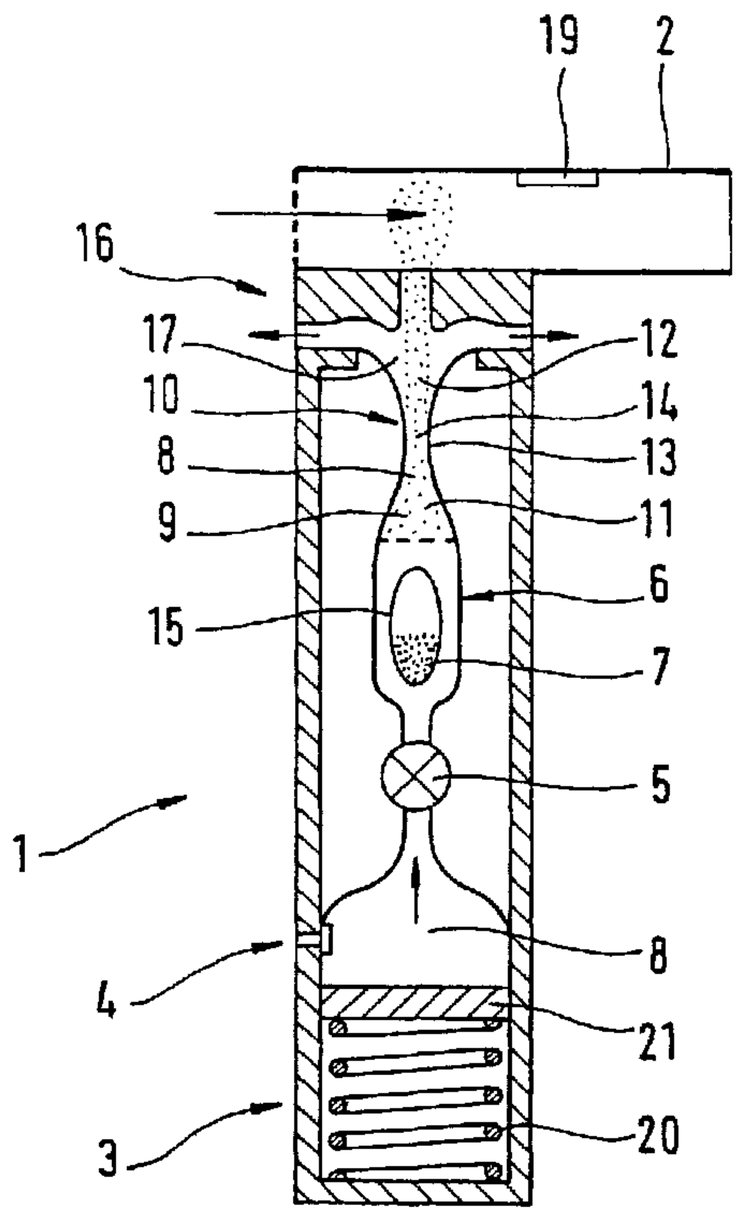

(57) Abrégé/Abstract:
The invention relates to a powder inhaler (1) comprising a mouthpiece (2) for dispersing pharmaceutical medicinal formulations. Said powder inhaler (1) comprises an auxiliary source of energy in the form of a pressurized medium system (3) and a device for storing (6) a powdered formulation (7). A gaseous pressurized medium (8) released by the pressurized medium system (3) forms an aerosol together with the powdered formulation (7) such that the powder particles are supplied in a dispersed manner in the gaseous pressurized medium (8) when said pressurized medium system is actuated. The aim of the invention is to create a powder inhaler (1), by means of which a particle size and particle size distribution that are preferred for the inhalation as well as the highest possible proportion of fine particles are obtained. Said aim is achieved by a powder inhaler (1) that is characterized by the fact that a nozzle (10) through which the aerosol (9) flows before leaving the inhaler (1) is provided within the inhaler (1).

Abstract

The invention relates to a powder inhaler (1) with mouthpiece (2) for dispersing pharmaceutical medicament formulations, which comprises an auxiliary energy source in the form of a pressure medium system (3), having a device for supplying (6) a powder formulation (7), while on activation of the pressure medium system a gaseous pressure medium (8) released by the pressure medium system (3) forms an aerosol (9) with the powder formulation (7) such that the powder particles are present in the gaseous pressure medium (8) in dispersed form.

A powder inhaler (1) is to be provided by means of which a particle size and particle size distribution which are preferred for inhalation are to be achieved and with which the highest possible fine particle content is achieved.

This is achieved by means of a powder inhaler (1) which is characterised in that a nozzle (10) is provided in the inhaler through which the aerosol (9) flows before leaving the inhaler (1) and in that the nozzle (10) is a multi-channel nozzle the channels of which are inclined to one another at an angle such that the aerosol jets flowing through them meet one another downstream behind the nozzle (10).

See also Fig. 1

87097pct

Powder inhaler

The invention relates to a powder inhaler with mouthpiece for dispersing pharmaceutical medicament formulations, which has an auxiliary energy source in the form of a pressure medium system, with a device for supplying a powder formulation, wherein on activation of the pressure medium system a gaseous pressure medium released by the pressure medium system forms an aerosol with the powder formulation such that the powder particles are present in dispersed form in the gaseous pressure medium.

Powder inhalers of this kind are needed for preparing inhalable medicaments. For diseases of the pulmonary and bronchial region, in particular, the medicaments are required and provided as inhalable pharmaceuticals (inhalants).

Within the scope of the present invention the term "medicament" refers to the active ingredient of a pharmaceutical which is usually also known as a drug or active substance.

The term "medicament formulation" basically covers not only powdered formulations but also solution formulations and suspension formulations. Different inhalation systems have been developed for each type of formulation. The solution or suspension formulations are formulated in a pharmacologically suitable solvent. Suitable solvents are basically water or liquefied propellant gases, for example. In the past, chlorofluorohydrocarbons were preferably used and more recently fluorohydrocarbons. In the case of inhalers operated with highly volatile propellant gases of this kind, the pharmaceutical composition is also formulated as a solution or

suspension in the propellant. Within the scope of the present invention, the powdered formulation or the powder inhaler required to disperse it is pre-eminent. However, it should be mentioned at this point that the three different drug formulations with their special properties make completely different demands of the inhaler.

In inhalers the formulations are normally stored or kept in a reservoir and for this reason the formulations used must have sufficient stability on storage. Excipients may be added to the medicament for this purpose, to adjust the physico-chemical properties which affect the quality-determining parameters such as availability and durability in a desirable manner.

The medicament formulation stored in a powder inhaler is nebulised and breathed in by the patient as an aerosol. The medicament is prepared in an inhalable form.

However, in this process, it is not usual for the entire **measured dose** to be expelled as an aerosol but only part of it. This is due to the fact that some of the powder formulation is left behind in the storage container, merely subjected to turbulence and then re-deposited elsewhere in the inhaler.

The proportion of the measured dose which leaves the mouthpiece of the powder inhaler is referred to as the **delivered dose**.

Powder particles can only enter the lungs during the inhaling process if the aerodynamic particle diameter is less than 5 µm. The result of this is that only a proportion of the delivered dose can actually reach the lungs. This proportion can only be determined by laborious tests on the patient. For this reason *in vitro*

tests have been developed in which a simple laboratory experiment is used to determine the **aerodynamic fine content**, which corresponds to the lung-bound part of the delivered dose. The aerodynamic fine content is defined as the proportion of the measured dose in percent which has an aerodynamic particle diameter of less than 5.8 µm.

Within the scope of the present invention the aerodynamic particle diameter is the particle diameter which corresponds to the equivalent diameter of a ball of density 1g/cm^3 which has the same sedimentation speed in air as the examined particle.

To achieve the highest possible aerodynamic fine particle content, the following considerations are crucial.

First of all, a powder formulation must be prepared which contains the medicament in micronised form. The majority of all medicament particles should range from 1-5 µm in size. As micronised powders, being bulk materials, exhibit a high tendency to form particle agglomerates, the powder formulation usually contains excipients which make it easier to break up the micronised medicament particles and also increase their flow properties. Another parameter which is relevant to the quality of the powder formulation is its chemical and physical stability. Chemical stability is ensured if the medicament does not change into breakdown products on storage. Physical stability indicates that the aerodynamic fine content measured does not change during the storage period.

A suitable powder inhaler must convert a defined quantity of the powder formulation, the measured dose, into an aerosol during the inhaling process by the patient, while the highest possible values must be achieved for the

delivered dose and the aerodynamic fine particle content. To achieve this, an important function of the powder inhaler is to break up the particle agglomerates of the medicament contained in the bulk powder formulation as efficiently as possible, as larger particles are deposited in the mouth and throat when breathed in and only particles with aerodynamic particle diameters of less than 5 µm reach the lungs. Thus, there is a more or less great difference between the proportion of the delivered dose based on the measured dose and the aerodynamic fine particle content, which is critically influenced by the efficiency of nebulisation.

Against the background of the above remarks the particle size must be reproducible within narrow limits so as to prevent fluctuations in the delivered dose and the aerodynamic fine content. On each actuation of the inhaler roughly the same amount of medicament should be administered, while the delivered doses should have roughly the same size distributions of the particles of medicament.

However, from the point of view of efficiency and the most economical use of medicaments it is also desirable to produce the largest possible aerodynamic fine particle content, as defined above.

In the prior art, there are basically two different systems of powder inhalers.

The so-called **passive inhalers** generally use the air breathed in by the patient to nebulise the powder formulation without any additional auxiliary energy sources - for example in the form of compressed air. These powder inhalers are designed so that powder is either contained in a prefabricated capsule in the form

of a single dose (premetered dose), for example, or a number of premetered doses are held in readiness in a multi-dose container inserted in the inhaler. During use, the capsule or one of the multi-dose containers is pierced and the powder is emptied out and nebulised using the air breathed in by the patient.

The powder may also be present in the inhaler as a powder supply (bulk powder), an individual dose being prepared by means of a metering device before being transported out of the inhaler in the patient's air stream.

It is obvious that, with the powder inhalers described, the aerodynamic fine particle content is highly dependent on the patient's breathing manoeuvre.

Against the background of the above remarks it is now common to use so called **active powder inhalers** which use stored energy, e.g. pressurised gas. By using the pressurised gas for controlled expulsion and nebulisation of the powder formulation the process is made independent of the patient's breathing.

In order to achieve the break up of lumps and efficient nebulisation and obtain the desired particle size and particle size distribution, essentially two methods have been used in the prior art.

In the case of some inhalers described in the literature the breaking up of the powder is assisted by the impact of the particles on so called impact surfaces. Using pressure, for example, the powder particles are deliberately directed against these impact surfaces to break up the particles. However, the result of this is that some of the powder particles striking the impact surface remain stuck to it and are deposited thereon. As

a result, it is not possible to achieve a highly accurate and reproducible dosage.

One disadvantage is that when pressurised gases are used to break up the lumps in powder formulations very high aerosol speeds are reached. Very high aerosol speeds in turn mean that the proportion of the dose that reaches the lungs is reduced. Therefore, for powder inhalers operating with pressurised gases, additional spacers/ separators are provided which have the task of reducing the speed of the aerosol particles formed.

These spacers/separators (or break up chambers) in which the speed of the powder particles is decelerated are arranged in front of the mouthpiece of the inhaler and make the inhaler bulky and awkward to use. Inhalers for the pharmaceutical field should however be small and convenient so that the patient can carry the inhaler about with them at all times.

Against this background the aim of the present invention is to provide a powder inhaler for dispersing pharmaceutical powder formulations with which the problems of conventional powder inhalers known from the prior art are eliminated but at the least are reduced and with which, in particular, a high content of solid particles less than 5.8 µm in size is produced.

This objective is achieved by means of a powder inhaler of the generic type which is characterised in that in the inhaler there is provided a nozzle through which the aerosol flows before leaving the inhaler.

In the powder inhaler according to the invention the pressure medium carries the powder from the powder supply and transports it through the nozzle.

The gaseous pressure medium is accelerated more and the powder particles container therein are carried along, as a result of which the clumps of powder particles are broken up. The shear forces exerted on the particles by the gaseous pressure medium as a result of the higher speeds of the gas molecules cause the clumps of particles to break up.

In the simplest embodiment of the nozzle it is a so-called perforated screen. The efficiency of break-up is measured by the aerodynamic particle size distribution of the particles using a cascade impactor. The critical measured variable determined was the fine particle content as a percentage of the pre-metered powder quantity. To do this, 5 mg of micronised fenoterol HBr was used as the pharmaceutical substance. The Fine Particle Fraction for this nozzle variant is specified below.

Table 1

nozzle	diameter [mm]	compressed air		fine particle fraction [%]
		volume [ml]	pressure [bar]	
perforated screen	0.4	12	4	44
perforated screen	0.6	7.5	4	34
perforated screen	0.8	12	0.5	42

An inhaler known by the trade mark HandiHaler® was used as reference. A device of this kind is described for example in EP 0911047. This inhaler (Handihaler) is intended for the inhalation of powdered pharmaceuticals from capsules. It is characterised by a housing containing two ports, a deck in which there are air inlet

holes and which is provided with a screen secured via a screen housing, an inhalation chamber attached to the deck on which is provided a push button having two sharp pins which is movable counter to a spring and a mouthpiece foldably connected to the housing, the deck and a cap by means of a spindle. This device delivers a fine particle fraction of 18-20% of a pre-metered amount of 5 mg fenoterol HBr with a quantity of 4 l of air and a pressure drop of 4 kPa. The values in Table 1 thus show that the system described according to the invention has a significantly greater break-up efficiency.

If a perforated screen is used as the nozzle, holes with a diameter of 0.1 to 3 mm, preferably 0.3 to 2 mm, particularly 0.5 to 1.5 mm are preferred.

In another embodiment of the powder inhaler, the nozzle is not just a simple perforated screen: rather, the screen has a tapering entry section. This nozzle can be further developed such that the exit section also widens out, so that the nozzle is shaped like a tube tapering in the middle, in which the angles of the tapering tube sections produced by the constriction may be identical or different. A continuously tapering entry section or flaring exit section ensures that the aerosol flow is accelerated or slowed down at a constant rate. There is laminar flow against the inner wall of the nozzle and the formation of turbulent zones and so-called "dead water areas" in which the aerosol flow is stagnant and no longer flowing, i.e. the flow comes to a standstill to some extent, is prevented. The avoidance of "dead water areas" is to be regarded as advantageous, particularly in the light of the depositing of powder particles.

In nozzles with a convergent entry section and hole-type exit, i.e. without a divergent exit, holes with a

diameter of 0.1 to 3 mm, preferably 0.3 to 2 mm, more particularly 0.5 to 1.5 mm are preferred.

In nozzles with a convergent entry section and divergent exit section, very small cross-sections with a diameter of 0.1 to 3 mm, preferably 0.3 to 2 mm, more particularly 0.5 to 1.5 mm are preferred.

When the nozzle is constructed with a convergent entry section and divergent exit section, the entry opening of the nozzle has a diameter of preferably 2 to 6 mm, particularly 3 to 5 mm. The entry section has a concave or linear configuration with an opening angle of preferably 10 to 50°. The entry section is preferably from 3 to 10 mm long, preferably 5 to 8 mm long.

In nozzles with a divergent exit, the opening of the exit section has a diameter of preferably 0.1 to 10 mm, particularly preferably 0.3 to 7.5 mm, most preferably 0.4 to 5 mm. The angle of opening of the exit section is 7 to 15°, preferably 8 to 12°. However, the shape of the exit section may be characterised by a linear divergence, followed by a tubular section. It is preferably 3 to 50 mm long, more preferably 5 to 15 mm long.

Embodiments of the powder inhaler in which the nozzle is a Laval nozzle are advantageous.

In this embodiment of the powder inhaler, the aerosol flows through the nozzle, first entering the tapering entry section, then passing through the middle section in which the cross-section of the nozzle is at is smallest, and finally passing through the flaring exit section.

The aerosol is accelerated in the tapering entry section, and in turn the gaseous pressure medium is accelerated more, picking up the powder particles contained therein,

thereby transporting the powder particles. The shear forces exerted on the particles by the gaseous pressure medium as a result of the higher speeds of the gas molecules cause the aggregates or clumps of particles to break up into smaller particles of smaller diameter, thereby achieving disaggregation. The aerosol reaches its maximum speed in or after the narrowest cross-section of the nozzle, which is in the middle part.
Depending on the pressure prevailing, gas speeds above or below the speed of sound are produced in the Laval nozzle.

The gas speed in relation to the speed of sound is known as the Mach number (Ma). The **Mach number** is calculated as the quotient of the gas speed and the speed of sound. Thus, Ma = 1 when the speed of the gas achieves the speed of sound. The term supersonic speed is used when Ma > 1.

In advantageous embodiments of the nozzle, the pressure medium is accelerated to supersonic speed in the exit section.

This presupposes that the aerosol flow in the narrowest cross-section of the nozzle has already reached the speed of sound. In this case, where the aerosol has reached the speed of sound in the middle part, i.e. Ma = 1, the aerosol flow in the flaring exit section of the nozzle is additionally accelerated to supersonic speed.

The speed actually achieved in the flaring exit cross-section of the nozzle, i.e. the Ma speed, depends crucially on the pressure produced upstream of the nozzle. The powder particles are not accelerated to supersonic speed like the gas molecules, with the result that there is a difference in speed, which in turn means

that shear forces are exerted on the powder particles and these are disaggregated.

In this embodiment, a so-called Mach shock is produced in the region of the flaring exit section. As they pass through this Mach shock the gas molecules are sharply decelerated to subsonic speed within a short distance of a few millimetres. The powder particles which were slower than the gas molecules before passing through the Mach shock are decelerated less sharply than the gas molecules, so that after the Mach shock the powder particles have a higher speed than the gas molecules. This results in extremely high friction or shear forces which attack the powder particles. The consequence of this is further disaggregation of the particles, leading to even better inhalability because of the particle sizes and size distributions achieved. The Fine Particle Fraction for 5 mg of fenoterol HBr, micronised, for some Laval nozzle variants is given below.

Table 2

nozzle	diameter [mm]	compressed air		fine particle fraction [%]
		volume [ml]	pressure [bar]	
Laval nozzle	0.5	7.5	4	30
Laval nozzle	0.8	7.5	4	26
Laval nozzle	1.5	7.5	4	32

For reference values: cf. Table 1

As an excessively high flow speed reduces the fine particle content which is capable of reaching the patient's lungs during the inhalation process, the speed at the exit from the mouthpiece should be not more than

20 m/s, preferably not more than 10 m/s, more particularly not more than 5 m/s.

As high flow speeds have to be produced for breaking up the powder as it passes through a nozzle it is generally necessary to reduce the aerosol speed along the path between the nozzle and mouthpiece. This can be achieved in various ways, so that there is no need to use the powder inhaler according to the invention together with a spacer. Specifically, the following results are preferably obtained:

The aerosol leaving the nozzle outlet can be mixed in various ways with the patient's breath as it travels between the nozzle and mouthpiece.

The production of a turbulent flow of the patient's breathed-in air is a suitable measure for this purpose. The aerosol cloud passing through the nozzle is injected into the turbulence of the breathed-in air, thereby reducing the forward component of the speed of the aerosol cloud.

Designing the nozzle so that the breathed-in air and the aerosol flow emerging from the nozzle are directed against each other, again resulting in deceleration, is another measure for reducing the flow rate of the aerosol cloud.

In an alternative embodiment the entry opening for the breathed-in air is located askew or perpendicular to the direction of flow of the nozzle.

The aerosol speed measured for the fine particle fraction at a distance of 10 cm behind the nozzle will now be given for two different measures and different nozzles (Table 3):

Table 3

nozzle	diameter [mm]	compressed air		fine particle fraction [%]
		volume [ml]	pressure [bar]	
perforated screen	0.8	2.5	4	19
perforated screen	0.6	6.7	1.5	12
perforated screen	0.6*	5.4	1.5	5
perforated screen	0.6**	5.4	1.5	2
perforated screen	0.4	16.7	0.5	3
Laval nozzle	0.5	5.4	1.5	2

* production of a turbulent flow in the patient's breathed-in air

** breathed-in air and the aerosol flow leaving the nozzle are in opposite directions

In order to reduce the speed of the aerosol cloud leaving the nozzle in the inhaler it has proved advantageous to mix this aerosol cloud with an air current in counter current thereto. It is advantageous if this contrary air current is produced by the breathing in process of the user. Usually, in a powder inhaler, provision is made for the patient to breathe in air as well when breathing in the cloud of powder in order to ensure an inspiration process free from complications. For this purpose, air slots may be formed in the mouthpiece, for example, through which the patient automatically breathes in air at the same time as the cloud of particles. Within the scope of the powder inhaler according to the invention these air inlet openings may be formed so that the

inflowing air meets the aerosol cloud either as a simple counter current or as an air current striking the aerosol cloud, thereby reducing its speed. This objective can be achieved in terms of construction by having the mouthpiece located perpendicular to the path travelled by the aerosol cloud as it leaves the nozzle openings. The air inlet slots are then also perpendicular to the mouthpiece and are formed in a line with the exit path of the aerosol cloud from the nozzle, but precisely opposite the nozzle. Expressed in simple terms this construction would be in the form of a T-shaped member, with the nozzle for the aerosol cloud and the air inlets for the counter current of air determining the end points of the crosspiece of the T while the mouthpiece corresponds to the base of the T.

In an alternative embodiment the nozzle and the air inlet holes open into a turbulence chamber, are spun around with one another therein and then leave through a mouthpiece.

A turbulence chamber of this kind may, in the simplest case, be a hollow chamber into which the nozzle opens at one point: the air inlet can then open into the chamber precisely opposite the nozzle or preferably perpendicular thereto or at least offset at an angle. The chamber then has an exit to the mouthpiece. An imaginary line leaving the nozzle opening and a line from the mouthpiece into the chamber form a straight line or meet at an angle or are colinear with one another.

In the simplest case the powder inhaler according to the invention consists of a housing with a mouthpiece. In front of the mouthpiece and inside the housing is the nozzle described above. Also on the inside is a chamber for accommodating the powder formulation which is to be nebulised.

Preferably, the powder inhaler comprises a pressure system which directs a pressurised gas on to the quantity of powder formulation to be dispersed so that the latter is dispersed and the resulting aerosol is conveyed through the nozzle system described above into the mouthpiece, while coarser particles are broken up. The powder inhaler has channels inside it which define the path of the pressurised gas released through the inhaler into the mouthpiece. In the chamber for accommodating the powder formulation intended for dispersion the powder may be loose or may be in a container, e.g. in a capsule or blister which is opened before the pressurised gas passes through, such that the pressurised gas is able to carry the powder along leaving substantially no residues. In the case of a single-use inhaler this device does not have any other supply for further doses of the powder formulations. In the case of a device intended for repeated use the inhaler may have one or more reservoirs for the powder formulation. Thus, the reservoir may simply be a chamber containing the powder mixture in loose form and from there measured quantities are carried into the nebulising chamber. Alternatively, the reservoir may be a collection of capsules which are filled with the powder formulation and introduced mechanically or manually into the nebulising chamber. Finally, the reservoir may also be a blister with a plurality of pouches for the powder formulation, in which case one of these pouches is introduced into the nebulising chamber. Reservoir systems of this kind and the transfer of the powder formulation from the reservoir into the nebulising chamber are known from the prior art and will therefore not be discussed in detail at this point.

As the pressure medium system the powder inhaler according to the invention may have a cartridge of

compressed air, a cartridge filled with a gas other than air, e.g. nitrogen, carbon dioxide, a noble gas such as helium or argon or even a fluorohydrocarbon, an alkane and the like. In advantageous embodiments of the powder inhaler, the pressure medium system is a system which takes in air from the environment and then releases the air in controlled manner under compression and under pressure in the direction of the formulation which is to be nebulised. On the one hand air is the most acceptable medium for the patient as a carrier for the powder particles. On the other hand it is freely available. The preferred embodiment of the powder inhaler takes the required amount of air from the atmosphere, compresses it and then uses it as a carrier medium for the powder formulation. There is no need to change the pressure medium system as would be the case with a pressure medium stored in a cartridge.

However, in other advantageous embodiments of the powder inhaler the pressure medium system comprises a cartridge which supplies a pressure medium under pressure. In contrast to the powder inhaler described previously, this embodiment is less complex in structure and therefore cheaper and smaller in size.

In any case the pressure medium system is such that the user of the inhaler can achieve a controlled delivery of pressure medium.

There are advantageous embodiments of the powder inhaler which are characterised in that the device for supplying the powder formulation is arranged between the pressure medium system and the nozzle such that the pressure medium has to go past the device, while preferably the device for supplying the powder formulation comprises a powder-filled capsule. Preferred embodiments of the powder inhaler are those wherein the capsule is

replaceable as the consumable material. A mechanism is provided on the powder inhaler by means of which the capsule can be changed.

In this embodiment the pressure medium flows through the device for supplying the powder formulation and distributes or picks up the powder, so that after flowing through the supply chamber the desired aerosol is formed.

In advantageous embodiments of the powder inhaler, the device for supplying the powder formulation comprises a multi-dose blister container. Multi-dose blister containers of this kind may be linear as a blister strip, flat as a blister disk or blister rings or three-dimensional as cylindrical or polygonal bodies. Multi-dose systems of this kind may contain 2 to 90 doses, preferably 5 to 60 doses, more particularly 7 to 30 doses, each dose being stored in a separate pocket or pouch which is opened by suitable means on use.

As already stated, powder inhalers in which air is provided as the pressure medium are preferred.

If the pressure medium system is not manually operated by its nature, but comprises a control means, e.g. in the form of an actuator valve, which has to be operated, and which releases the pressure medium by opening or closing, it is advantageous to have embodiments of the powder inhaler which provide a throughflow sensor in the mouthpiece to measure the flow of breath of the patient and, on reaching a certain value, generate an input signal for the pressure medium system or its control member.

The throughflow sensor measures the air current as the patient breathes in and generates an input signal which acts upon the control member. This opens and allows the

pressure medium to flow out when the throughflow rate is in a range suitable for inhalation, but the control member does not release the pressure medium system if this throughflow rate is outside the preferred range. This automatic opening and closing does away with the need to provide an additional actuating device and makes the inhaler more user friendly and easier to handle.

The powder inhaler according to the invention has the following advantages over the prior art:

- an aerosol is produced from bulk powder premetered in a suitable container, while the energy available in the form of a pressurised gas is used to overcome the forces of agglomeration of the micronised powder particles with one another so as to produce an aerosol with a comparatively above-average content of solid particles less than 5.8 µm in size.
- the system described here does not need fluorinated propellant gases or chlorofluorohydrocarbons.
- the production of the aerosol and the particle size distribution achieved are independent of the patient's breathing manoeuvre.
- the powder residues in the device are kept to a minimum by the construction as the breaking up of the clumps of powder is achieved by the action of flowing gases in a nozzle and not by impacting on impact surfaces.
- the inhaler described is small and can easily be carried around by the patient.
- there is no need to use the device with a "spacer" as in other "active" powder systems (WO 99/6249) as a slowly moving aerosol cloud is produced in the device by suitable measures.

The invention will now be described in more detail with reference to several embodiments shown in the two figures of drawings. In these drawings:

Fig. 1 is a diagrammatic view of a first embodiment of a powder inhaler, in side view, in section,

Fig. 2 is a diagrammatic representation of a nozzle of a second embodiment of a powder inhaler in side view, in section,

Fig. 3a is a diagrammatic representation of a first embodiment of a multi-dose blister container for supplying the powder formulation, in side view,

Fig. 3b is a diagrammatic representation of a second embodiment of a multi-dose blister container for supplying the powder formulation, in side view,

Fig. 3c is a diagrammatic representation of a third embodiment of a multi-dose blister container for supplying the powder formulation, in side view,

Fig. 3d is a diagrammatic representation of a fourth embodiment of a multi-dose blister container for supplying the powder formulation, in perspective view,

Fig. 3e is a diagrammatic representation of a fifth embodiment of a multi-dose blister container for supplying the powder formulation, in perspective view,

Fig. 4 is a diagrammatic representation of a nozzle of a third embodiment of a powder inhaler in side view, in section,

Fig. 5 is a diagrammatic representation of a nozzle of a fourth embodiment of a powder inhaler in side view, in section,

Fig. 6 is a diagrammatic view of a first embodiment of a device for delaying the aerosol flow in side view and in section, and

Fig. 7 is a diagrammatic view of a second embodiment of a device for delaying the aerosol flow in side view and in section.

In the description that follows, identical parts have been given the same reference numerals.

Figure 1 is a diagrammatic representation of a first embodiment of a powder inhaler 1 for dispersing pharmaceutical medicament formulations, in side view and in section.

The powder inhaler 1 has at its top end a mouthpiece 2. It has an auxiliary energy source in the form of a pressure medium system 3, the pressure medium system 3 being equipped with a pump which is connected to the atmosphere through a valve 4 and uses the ambient air as the pressure medium 8. The air acts as a carrier medium for the powder particles 7 and is taken in through the valve 4 by a piston 21 acted upon by a spring 20 during the expansion phase and is compressed as the piston travels up. There is no need to replace the pressure medium system as would be the case when using a pressure medium stored in a cartridge.

The pressure medium 8 leaves the pressure medium system 3 through a control member or actuator valve 5. In the embodiment shown in Fig. 1 a throughflow sensor 19 is provided in the mouthpiece 2. The throughflow sensor 19

measures the air current as the patient breathes in - the throughflow rate - and generates an input signal which acts upon the actuator valve 5. This opens and allows the pressure medium 8 to flow out when the throughflow rate is in a range suitable for inhalation, while the control member 5 closes the pressure medium system 3 if this throughflow rate is outside this preferred range. This automatic opening and closing makes the device more user friendly and achieves optimum conditions during inhalation.

After leaving the pressure medium system 3 the pressure medium 8 flows through a device for supplying 6 the powder formulation 7. The device for supplying 6 the powder formulation 7 comprises a capsule 15 filled with powder 7. The mechanism by which the capsule can be changed is not shown.

In this embodiment the pressure medium 8 flows through the device for supplying 6 the powder formulation 7 and picks up some of the powder 7, so that after flowing through the supply chamber the desired aerosol 9 is obtained such that the powder particles 7 are dispersed in the gaseous pressure medium 8.

The aerosol 9 then flows through the nozzle 10, first entering the tapering entry section 11, passing through the middle part 13 in which the cross-section 14 of the nozzle 10 is at its smallest, and then flowing through the flaring exit section 12. This embodiment thus uses a Laval nozzle.

The aerosol 9 is accelerated in the tapering entry section 11, the gaseous pressure medium 8 being accelerated more and carrying with it the powder particles 7 contained therein, thus transporting the powder particles 7. The shear forces exerted on the

particles 7 by the gaseous pressure medium 8 as a result of the higher speeds of the gas molecules 8 cause the particle aggregates or clumps 7 to be broken up into smaller particles of smaller diameter, thereby producing disaggregation. The aerosol 9 attains its maximum speed in or after the narrowest cross-section 14 of the nozzle 10, which is located in the middle part 13.

Fig. 2 shows a diagrammatic representation of a nozzle 10 in a second embodiment of a powder inhaler, in side view and in section.

The aerosol produced, which consists of the powder particles dispersed in the pressure medium as carrier medium, and the pressure medium itself, enters the continuously tapering entry section 11 of the nozzle 10, is accelerated, passes through the narrowest cross-section 14, which is located in the middle part 13, in order to flow through the flaring exit section 12 thereafter and leave the nozzle 10 through the exit 17.

The Laval nozzle 10 shown in Fig. 2 is characterised in that it has a comparatively long exit section which has only a small angle of opening (in this case about 11°).

Nozzles 10 of this kind are used in powder inhalers in which the aerosol flow in the nozzle 10 is accelerated to supersonic speed, while a so-called Mach shock (not shown) is produced in the flaring exit section 12 of the nozzle 10. The shape of the nozzle 10 described above is necessary in order to accelerate the aerosol flow to supersonic speed and ensure that the Mach disc is formed in the exit section 12.

As they pass through this Mach shock zone the gas molecules are sharply decelerated from supersonic to subsonic speed within a short distance of a few

millimetres. The powder particles, which were slower than the gas molecules before the Mach shock, are decelerated less sharply than the gas molecules, so that after the Mach shock the powder particles have a higher speed than the gas molecules. This results in extremely high friction or shear forces which attack the powder particles and break up any clumps.

Fig. 3a shows a diagrammatic representation of a first embodiment of a multi-dose blister container 22 for supplying the powder formulation, in side view. The multi-dose blister container 22 is of linear construction in the form of a blister strip 23 and comprises a number of capsules 26 arranged in a row, each capsule 26 containing a single dose, while the capsule 26 in use is opened by suitable means (not shown).

Fig. 3b shows a diagrammatic representation of a second embodiment of a multi-dose blister container 22 for supplying the powder formulation, in side view. The multi-dose blister container 22 is of flat construction in the form of a blister disk 24 and comprises a plurality of capsules 26 arranged in a circle.

Fig. 3c is a diagrammatic view of a third embodiment of a multi-dose blister container 22 for supplying the powder formulation, in side view. The multi-dose blister container 22 is constructed flat as a blister ring 25 and comprises a plurality of capsules 26 arranged in a circle.

Fig. 3d shows a diagrammatic representation of a fourth embodiment of a multi-dose blister container 22 for supplying the powder formulation, in perspective view. The multi-dose blister container 22 is of three dimensional construction in the form of a cylindrical body. Multi-dose systems of this kind may contain 2 to

90 doses, preferably 5 to 60 doses, in particular 7 to 30 doses, each dose being stored in a separate capsule 26 which is opened by suitable means on use.

Fig. 3e shows a diagrammatic representation of a fifth embodiment of a multi-dose blister container 22 for supplying the powder formulation, in perspective view. The multi-dose blister container 22 is of three-dimensional construction, as in Fig. 3d, in the form of a polygonal body.

Fig. 4 shows a diagrammatic representation of a nozzle 10 of a third embodiment of a powder inhaler in side view, in section. It is a perforated screen 28 which has neither a tapering entry section nor a flaring exit section.

Fig. 5 shows a diagrammatic representation of a nozzle 10 of a fourth embodiment of a powder inhaler in side view, in section. It is a perforated screen 28 which has a tapering entry section 11 but not a flaring exit section.

Fig. 6 shows a diagrammatic representation of a first embodiment of a device for delaying the flow of aerosol in side view and in section. The two flows, both the flow of inspired air in the inlet channel 18 and the aerosol flow in the channel 30, initially run parallel in two coaxial tubes, the inspired air being transformed into a turbulent flow. The aerosol flow injected into this turbulent flow has a lower flow velocity.

Fig. 7 shows a diagrammatic representation of a second embodiment of a device for delaying the aerosol flow, in side view and in section. The flow of inspired air and the aerosol flow are directed towards one another. As they come into contact and the flow is deflected the forward speed of the aerosol flow is reduced.

List of Reference Numerals

1 Powder inhaler
2 Mouthpiece
3 Pressure medium system
4 Valve
5 Actuator valve
6 Supply device
7 Powder formulation
8 Gaseous pressure medium
9 Aerosol
10 Nozzle
11 Entry section
12 Exit section
13 Middle part
14 Narrowest cross-section
15 Capsule
16 Device
17 Exit opening of the nozzle
18 Inlet channel
19 Throughflow sensor
20 Spring
21 Piston
22 Multi-dose blister container
23 Blister strip
24 Blister disk
25 Blister rings
26 Capsule
27 Blister body
28 Perforated screen
29 Turbulence chamber
30 Channel

Patent Claims

1. Powder inhaler (1) with mouthpiece (2) for dispersing pharmaceutical medicament formulations, which comprises an auxiliary energy source in the form of a pressure medium system (3), having a device for supplying (6) a powder formulation (7), while on activation of the pressure medium system a gaseous pressure medium (8) released by the pressure medium system (3) forms an aerosol (9) with the powder formulation (7) such that the powder particles are present in the gaseous pressure medium (8) in dispersed form, characterised in that a nozzle (10) is provided in the inhaler (1) through which the aerosol (9) flows before leaving the inhaler (1).

2. Powder inhaler (1) according to claim 1, characterised in that the nozzle (10) is in the form of a perforated screen.

3. Powder inhaler (1) according to claim 1, characterised in that the nozzle (10) has a tapering entry section (11) adjoining which is a perforated screen.

4. Powder inhaler (1) according to claim 1, characterised in that the nozzle (10) has a tapering entry section (11), a middle part (13) and a flaring exit section (12) which is adjacent to the middle part (13).

5. Powder inhaler according to claim 4, characterised in that the narrowest cross-section is arranged in the middle part (13).

6. Powder inhaler (1) according to claim 5, characterised in that the nozzle (10) is a Laval nozzle.

7. Powder inhaler (1) according to claims 4 to 6, characterised in that the narrowest cross-section (14) of the nozzle (10) is 100 µm to 1500 µm, preferably 400 µm to 800 µm, in diameter.

8. Powder inhaler (1) according to one of claims 4 to 7, characterised in that the nozzle (10) has a flaring exit section (12) such that in the exit section (12) the pressure medium (8) is accelerated to supersonic speed.

9. Powder inhaler (1) according to one of the preceding claims, characterised in that the pressure medium system (3) comprises a pump connected to the environment and uses ambient air as the pressure medium (8).

10. Powder inhaler (1) according to one of claims 1 to 8, characterised in that the pressure medium system (3) comprises a cartridge which supplies a pressure medium (8) under pressure.

11. Powder inhaler (1) according to one of the preceding claims, characterised in that air is provided as the pressure medium (8).

12. Powder inhaler (1) according to one of claims 1 to 8 or 10 to 11, characterised in that N_2, CO_2, Ar or He is provided as the pressure medium (8).

13. Powder inhaler (1) according to one of the preceding claims, characterised in that the device for supplying (6) the powder formulation (7) is arranged between the pressure medium system (3) and nozzle (10) such that the pressure medium (8) has to pass the device (6).

14. Powder inhaler (1) according to one of the preceding claims, characterised in that the device for supplying

(6) the powder formulation (7) comprises a capsule (15) filled with powder (7).

15. Powder inhaler (1) according to claim 14, characterised in that the capsule (15) is replaceable as a consumable material.

16. Powder inhaler (1) according to one of claims 1 to 13, characterised in that the device for supplying (6) the powder formulation (7) comprises a multi-dose blister container.

17. Powder inhaler (1) according to one of claims 1 to 8 or 10 to 16, characterised in that a throughflow sensor (19) is provided in the mouthpiece (2), which generates an input signal for the pressure medium system (3).

18. Powder inhaler (1) according to one of the preceding claims, characterised in that between the exit section (12) and the exit of the mouthpiece (2) a turbulent flow is produced in the inspired air sucked in through an inlet channel.

19. Powder inhaler (1) according to one of the preceding claims, characterised in that the nozzle (10) and an inlet channel (18) for the inspired air are arranged so that the aerosol flow emerging from the nozzle (10) and the inspired air are directed counter to one another (Fig. 7).

20. Powder inhaler (1) according to one of claims 1 to 19, characterised in that the nozzle (10) and an inlet channel for the inspired air are arranged so that the aerosol flow leaving the nozzle and the inspired air strike one another at an angle.

21. Powder inhaler (1) according to one of claims 1 to 20, characterised in that the channel (30) carrying the aerosol flow and the inlet channels (18) for the inspired air open into a turbulence chamber (29) from which the aerosol cloud is conveyed to the nozzle (10) (Fig. 6).

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Fig. 1

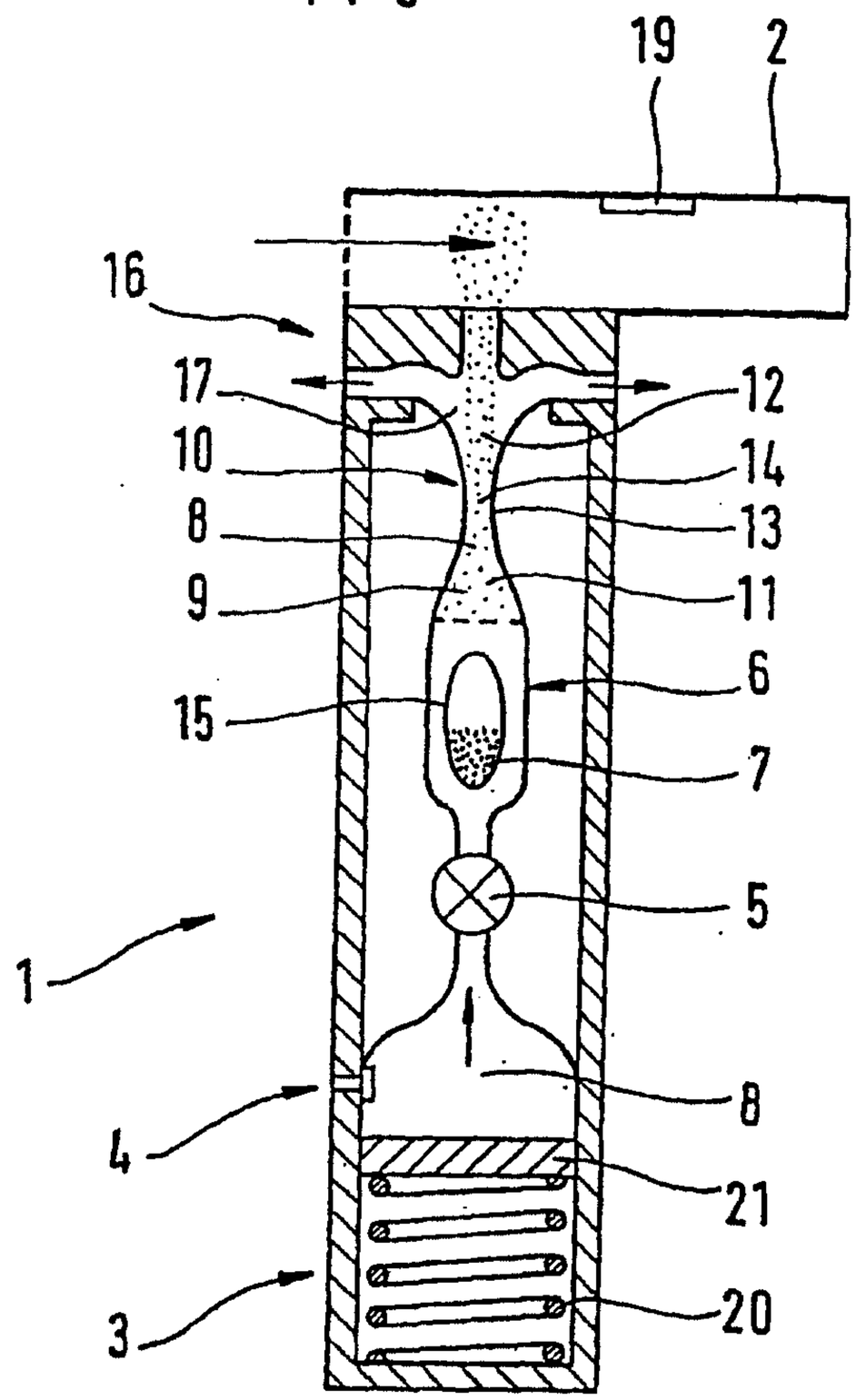


Fig. 2

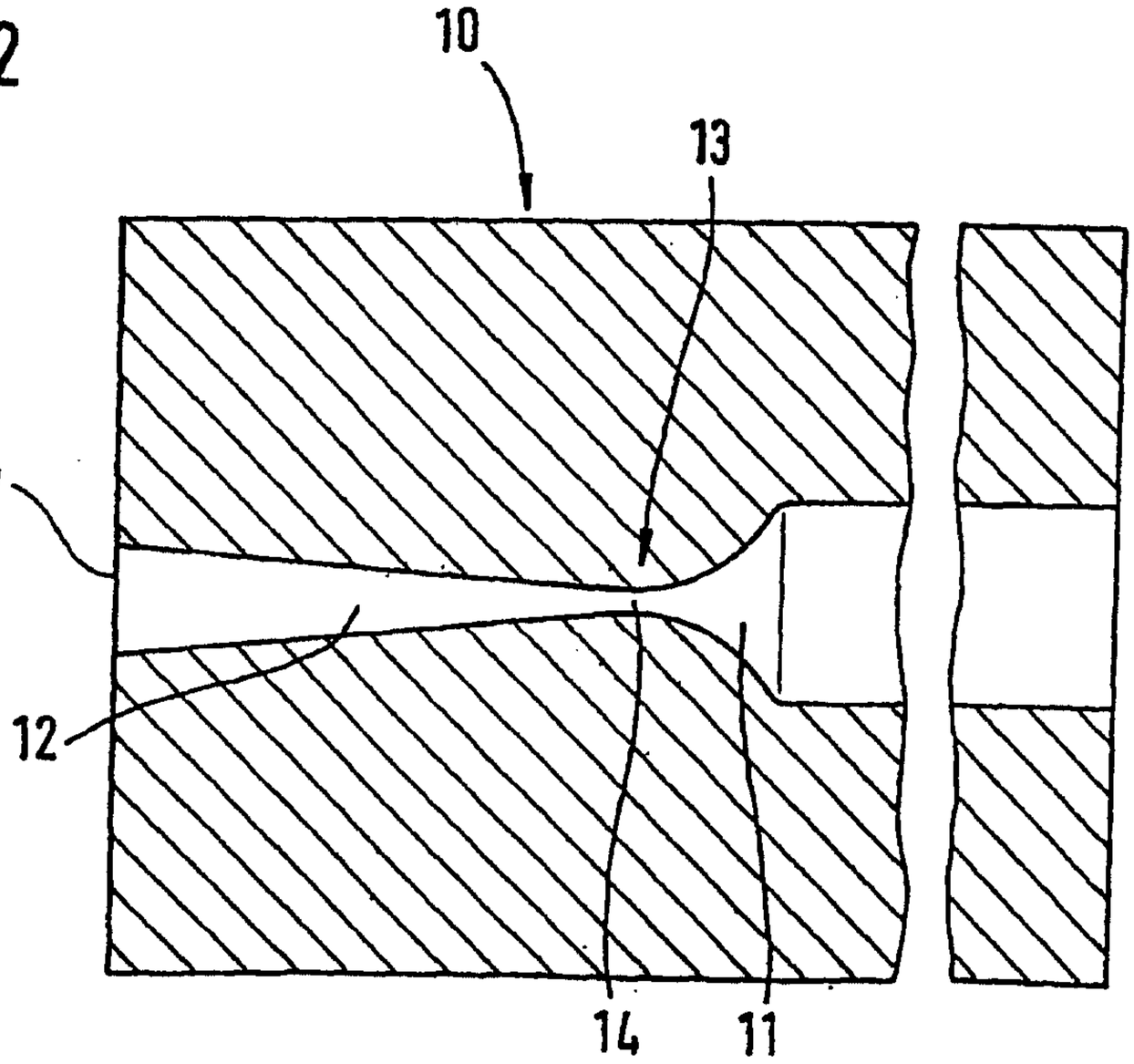
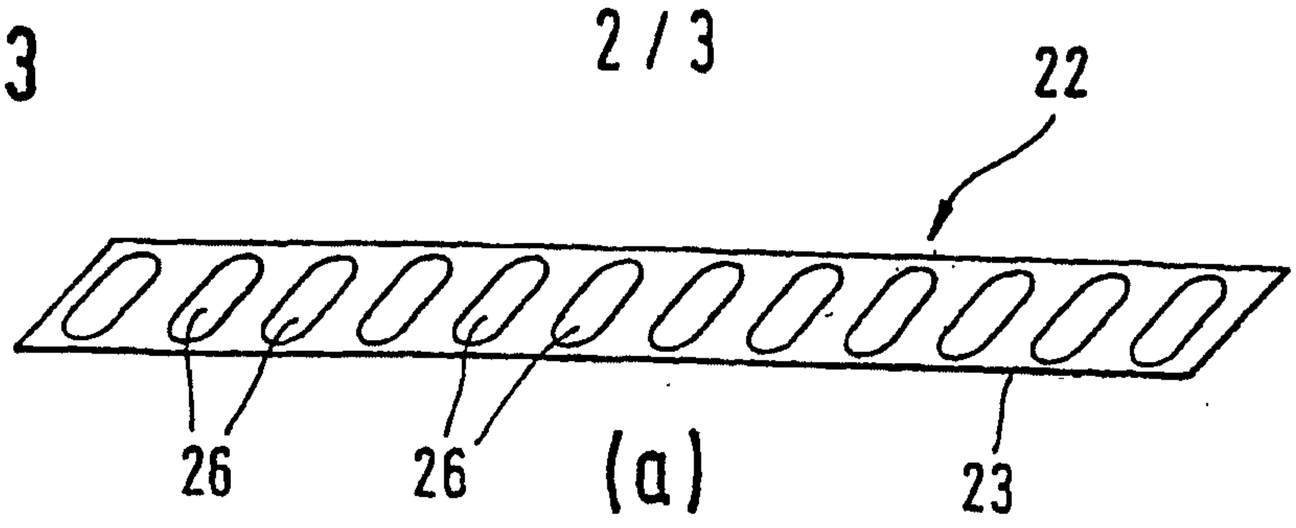


Fig. 3



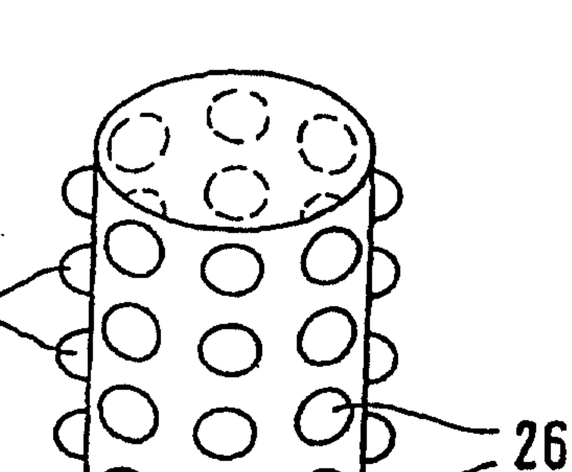


Fig. 4

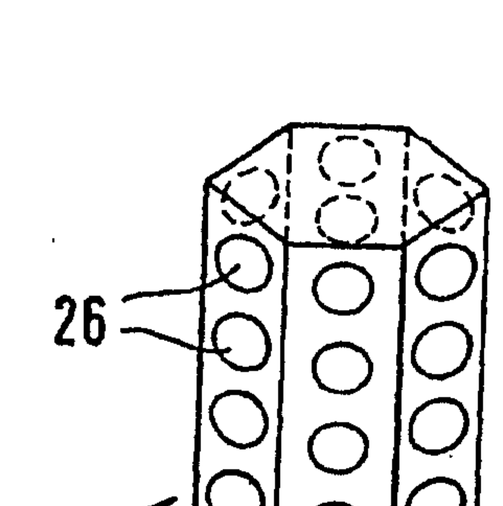


Fig. 5

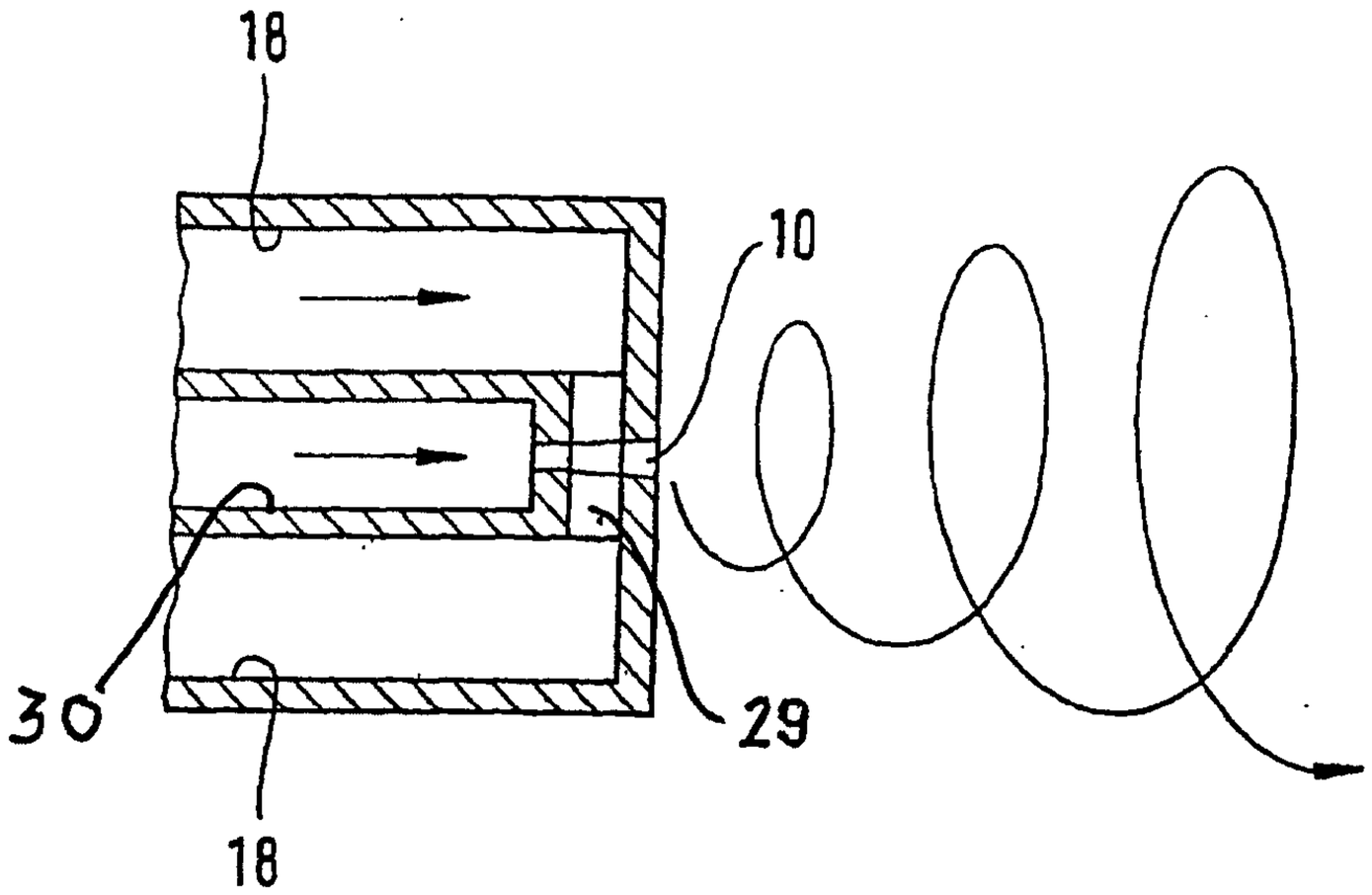


Fig. 6

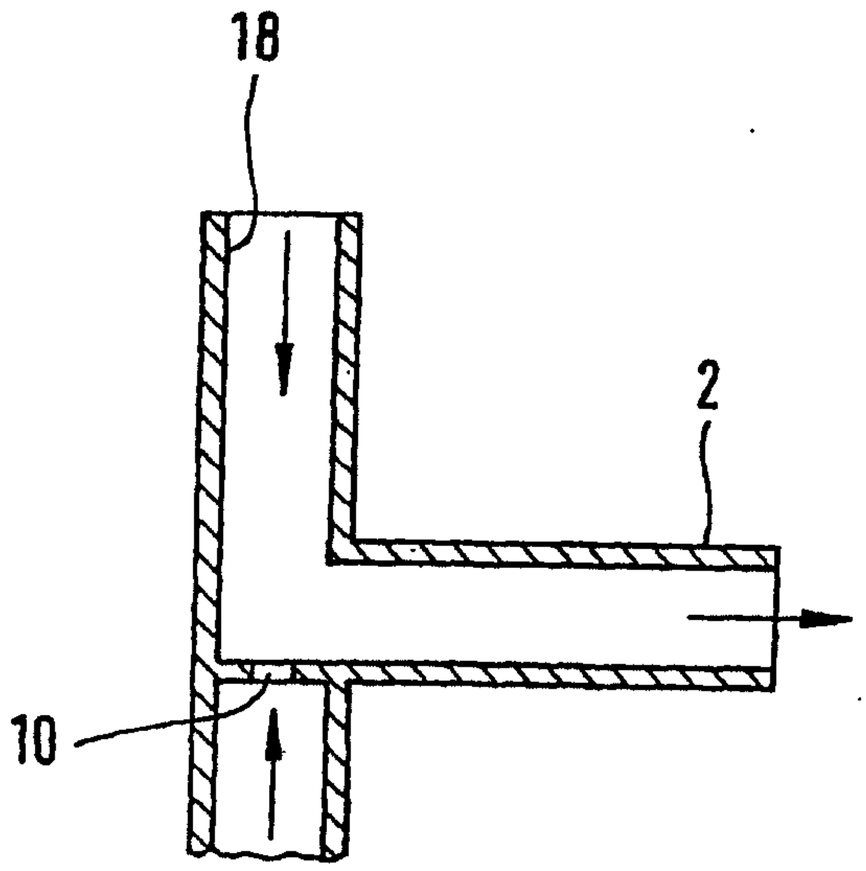
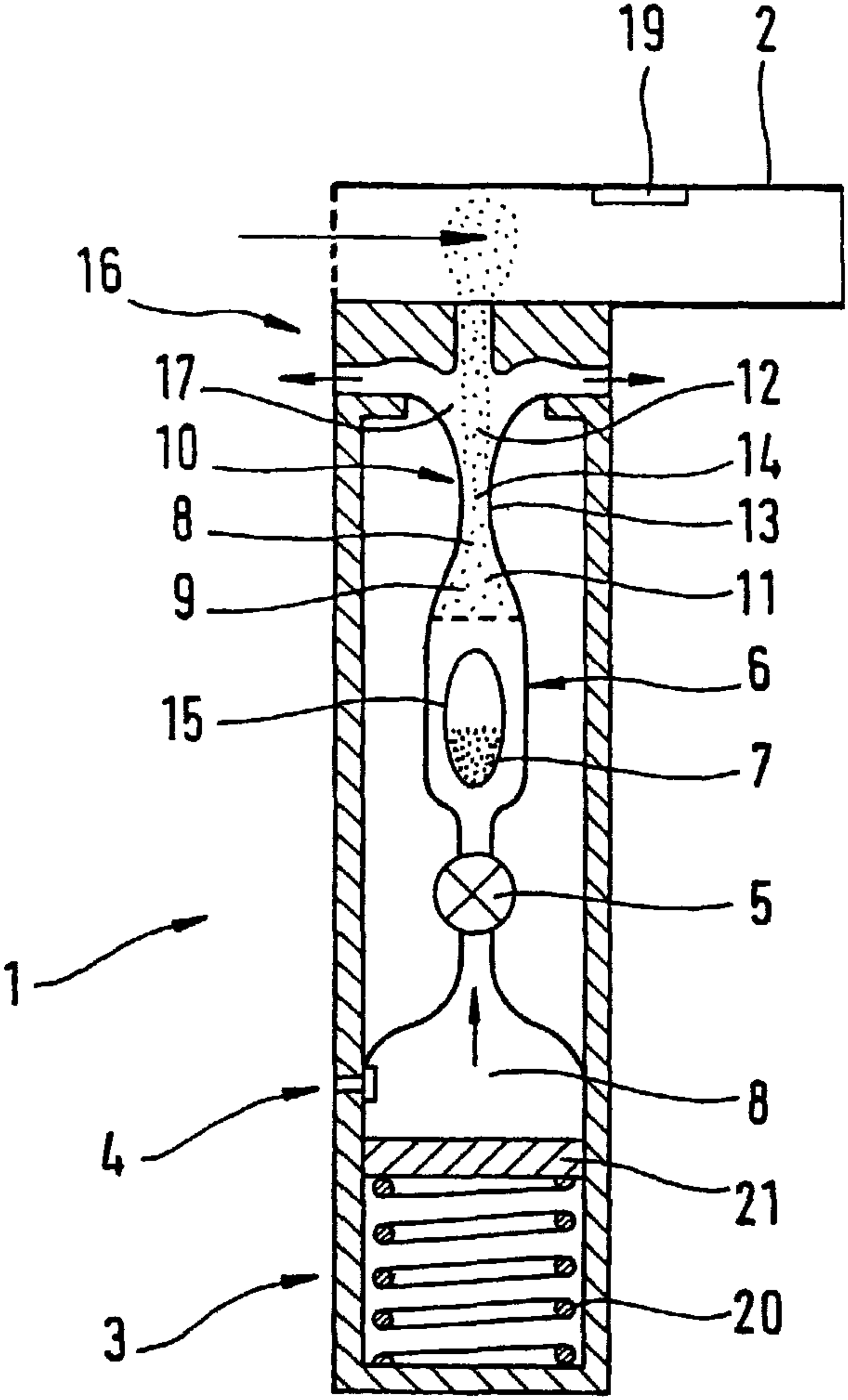


Fig. 7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