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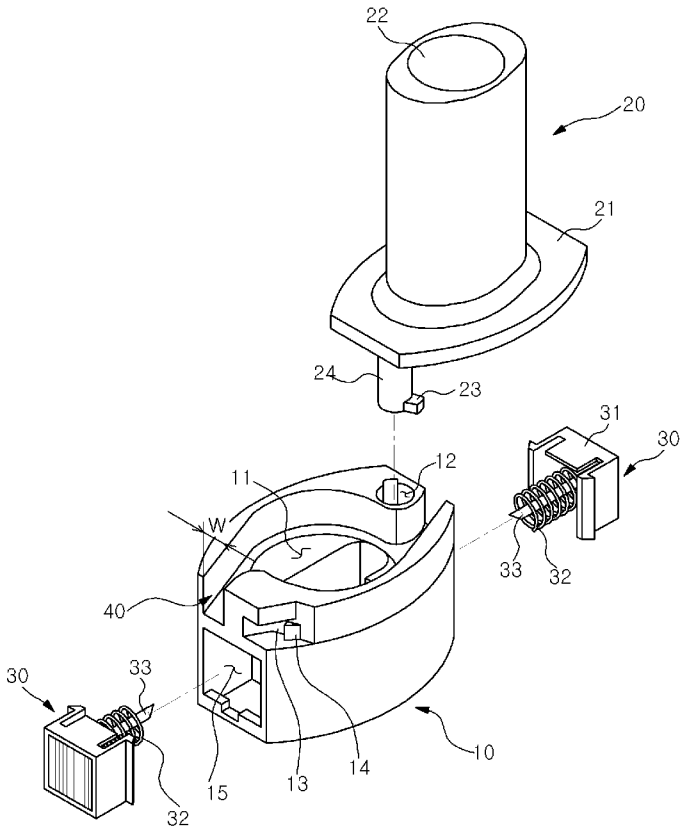
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[Continued on next page]

(54) Title: DRY POWDER INHALER DEVICE



(57) Abstract: Disclosed is a dry powder device which generates little change in the aerodynamic size distribution a pharmaceutically active ingredient with a variation of airflow rates, and shows a high targeting ability to deliver the pharmaceutically active ingredient deep into the lungs. The dry powder inhaler device according to one embodiment of the present invention comprises a main body in which a capsule accommodation portion for accommodating a composition-loaded capsule is formed; an air passage, formed at the main body, for introducing external air into the main body therethrough by patient's suction; and an inhalation portion, combined with the main body, for guiding the external air introduced into the main body, together with the composition, to the patient.

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Description

Title of Invention: DRY POWDER INHALER DEVICE

Technical Field

[1] The present invention relates to an inhaler device for delivering dry powder to the lungs.

Background Art

[2] For the therapy of respiratory diseases such as asthma and chronic obstructive pulmonary disease (COPD), various drugs are used in the form of inhalants. Even at small doses, an inhalant shows strong therapeutic effects. However, because only a part of the dose administered by inhalation reaches the target region, the off-targeted remainder is highly prone to causing side effects.

[3] Thus, a study into exactly directing a pharmaceutically active ingredient toward a target has been conducted so as to prevent it from reaching organs needing no therapy, with the consequent maximization of the intended pharmaceutical effect.

[4] In the therapy of respiratory diseases, the delivery of inhalants is widely dependent on inhaler devices. When inhaled, together with air, with the aid of an inhaler device, an inhalant reaches the airway of the patient. For example, since its approval in 1956, a metered dose inhaler (MDI) has claimed 80 % of the inhaler market. With the use of MDI formulations, however, environmental problems, such as ozone layer depletion, global warming, etc., have arisen, and study has extensively turned toward dry powder inhalers (DPI). Nowadays, DPI formulations are upgraded to overcome the drawbacks of MDI formulations. MDI formulations become poor in stability since a solvent serving as a propellant is compressed together with a pharmaceutically active ingredient. In addition, when delivered by an MDI, the pharmaceutically active ingredient is discharged too fast, and reaches the pharynx too fast, accordingly. In contrast, DPI formulations are easy to handle, and exhibit higher stability because they are composed of solid powders (refer to Martin J Telko and Anthony J Hickey, Dry Powder Inhaler Formulation, Respiratory Care, September 2005, Vol 50, No. 9).

[5] However, DPI formulations are observed to vary in effective dose and effective dose patterns depending on inhaler devices. This seems to be attributed to the fact that expiratory volumes differ from one patient to another, causing the flow rate in the inhaler to vary. In addition, the structural difference of inhalers depending on manufacturers leads to a difference in pressure drop and gas flow pattern from one inhaler to another. Accordingly, there is a need for an inhaler that is convenient for use and that can effectively deliver a pharmaceutically active ingredient and maintain consistent effective dose under various expiratory volumes.

Disclosure of Invention

Technical Problem

[6] It is an object of the present invention to provide a dry powder inhaler which is convenient for use, is highly unlikely to change the aerodynamic size distribution of the pharmaceutically active ingredient, and shows a targeting ability to deliver a pharmaceutically active ingredient deep into the lungs.

Solution to Problem

[7] The dry powder inhaler according to an aspect of the present invention comprises a dry powder inhaler device, comprising: a main body in which a capsule accommodation portion for accommodating a composition-loaded capsule is formed; an air passage, formed at the main body, for introducing external air into the main body therethrough by a patient's suction; and an inhalation portion, combined with the main body, for guiding the external air introduced into the main body, together with the composition, to the patient, wherein said dry powder inhaler device is designed to have an airflow resistance of 0.02 $\sqrt{kPa}$/L/min to 0.03 $\sqrt{kPa}$/L/min within the main body.

[8] In the dry powder inhaler device, the air passage may pass through the main body so that the capsule accommodation portion communicates with an outside of the main body.

[9] In one embodiment, the airflow resistance may be adjusted by adjusting the width of an entrance of the air passage.

[10] Further, the width of the entrance of the air passage may range from 1.5 mm to 3 mm.

[11] In another embodiment, the dry powder inhaler device may further comprise at least one pushbutton assembly disposed at one or more sides of the main body, which is structured to move into and out of the main body to exert an external force on the capsule, whereby the composition is discharged out of the capsule.

[12] In this context, the pushbutton assembly may comprises a needle for perforating the capsule, a pushbutton which is movable into and out of the main body and by which the needle is supported, and an elastic member for elastically supporting the pushbutton and the main body therebetween.

[13] In addition, a grid for filtering impurities may be disposed between the main body and the inhalation portion.

[14] In another embodiment, the inhalation portion may comprise: an inhalation duct communicating with the capsule accommodation portion; and a flange, extended from the inhalation duct, for combining the inhalation portion with the main body.

[15] In another embodiment, the inhalation portion comprises a peg which extrudes from the inhalation portion with a cross tooth laterally directing from an end portion of the

peg, and the main body has an engagement hole corresponding to a figure of the peg and the cross tooth, wherein when the cross tooth is engaged with the engagement hole by inserting the peg into the engagement hole, the inhalation portion can be rotated on the axis made by the peg and the engagement hole to close or open the capsule accommodation portion of the main body.

[16] When the inhalation portion closes the capsule accommodation portion, the inhalation portion is latched onto the main body by engagement between a ridge formed within a latching recess of the main body, and a hook formed in the inhalation portion.

Advantageous Effects of Invention

[17] As described hitherto, the dry powder device of the present invention is convenient for use, aerodynamic size distributions of the pharmaceutically active ingredient change little with variation of airflow rates and the device shows a high targeting ability to deliver a pharmaceutically active ingredient deep into the lungs.

Brief Description of Drawings

[18] FIG. 1 is an exploded perspective view of a dry powder inhaler device according to one embodiment of the present invention.

[19] FIG. 2 is an exploded perspective view showing a main body and an inhalation portion of the dry powder inhaler device according to one embodiment of the present invention.

[20] FIG. 3 is a perspective view of the dry powder inhaler device according to one embodiment of the present invention.

[21] FIG. 4 is a cross sectional view of the dry powder inhaler device according to one embodiment of the present invention.

[22] FIG. 5 is a top view of the dry powder inhaler device according to one embodiment of the present invention.

[23] FIG. 6 is a bottom view of the dry powder inhaler device according to one embodiment of the present invention.

[24] FIG. 7 is a cross sectional view showing the operation of the dry powder inhaler device according to one embodiment of the present invention.

[25] FIG. 8 is a photograph showing dry powder inhalers with various widths of an entrance of an air passage according to one embodiment of the present invention.

[26] FIG. 9 is a graph showing aerodynamic size distributions of salmeterol as measured in Test Example 1.

[27] FIG. 10 is a graph showing aerodynamic size distributions of fluticasone as measured in Test Example 1.

[28] FIG. 11 is a graph showing aerodynamic size distributions of salmeterol as measured in Test Example 2.

[29] FIG. 12 is a graph showing aerodynamic size distributions of fluticasone as measured in Test Example 2.

Mode for the Invention

[30] Reference now should be made to the drawings, in which the same reference numerals are used throughout the different drawings to designate the same or similar components.

[31] If in the specification, detailed descriptions of well-known functions or configurations may unnecessarily make the gist of the present invention obscure, the detailed descriptions will be omitted.

[32]

[33] For use in the therapy of pulmonary diseases through inhalation, pharmaceutically active ingredients should be finely pulverized. Optimal particle sizes for bronchial inhalation are on the order of 0.1 μm to 10 μm, and preferably on the order of 0.1 μm to 5 μm. When the particle size is less than 0.1 μm, the particles do not deposit into the bronchus, but rather may be expelled out of the body. The U. S. Pharmacopeia 34 <601> 'Aerosols, Nasal sprays, Metered-dose inhalers and Dry powder inhalers' suggests the measurement of aerodynamic size distribution using various apparatuses (Apparatus 1~6). For example, Apparatus 3 (Anderson Cascade Impactor) according to the USP 34 <601> may be employed. Apparatus 3 (Anderson Cascade Impactor) according to the USP 34 <601> is divided into seven stages: from stage 0 to stage 7; and are designed for stage mensuration. Generally, particles collected in stages 1~5 are calculated to have an aerodynamic size distribution of 0.1~5 μm. Accordingly, the quantity of particles collected in stages 1~5 may allow for the inference of the effective dose of a pharmaceutically active ingredient at which the pharmaceutically active ingredient can exert pharmaceutical activity after inhalation into the lung by way of an inhalant. As a rule, the amount of the particles ranging in size from 0.1 to 5 μm is preferably on the order of 10 % to 30 % of the total amount of the particles inhaled by a patient.

[34] As used herein, the term “effective dose” refers to an amount of a pharmaceutically active ingredient at which the pharmaceutically active ingredient exhibits pharmaceutical activity in practice.

[35] In addition, an inhaler device is an important factor in determining the delivery efficiency of the pharmaceutically active ingredient, as well as for safety and convenience of the patient. In spite of commercial availability of many kinds of dry powder inhaler devices, there is still demand for a higher level of delivery efficiency and use convenience.

[36] FIGS. 1 to 6 represent a dry powder inhaler device according to one embodiment of

the present invention in an exploded perspective view, in an exploded perspective view for a main body and an inhalation portion thereof, in a perspective view, in a longitudinal cross sectioned view, in a top view, and in a bottom view, respectively.

[37] With reference to FIGS. 1 to 6, a dry powder inhaler device 1 is introduced according to one embodiment of the present invention, which can be divided into a main body 10 in which a capsule accommodation portion 11 for accommodating a composition-loaded capsule 60 is formed; an inhalation portion 20 to be combined with the main body 10; and a pushbutton assembly 30, installed within the main body 10, capable of moving into and out of the main body 10.

[38] The capsule 60 may be cylindrical so as to readily utilize the composition loaded thereto.

[39] The main body is mainly responsible of the external figure of the inhaler device 1, and has a capsule accommodation portion 11 with an open top in which the capsule 60 is installed. In addition, the main body 10 may have an installation hole 15 formed in a side so as to accommodate the pushbutton assembly 30 therein.

[40] A plurality of installation holes 15 may be provided. For example, in case of a pair of installation holes 15 is formed, they may be formed in opposite sides of the main body 10, facing each other.

[41] The inhalation portion 20 may comprise an inhalation duct 22 communicating with the capsule accommodation portion 11, and a flange 21 extending from the inhalation duct 22. The inhalation duct 22 serves as a pathway to direct the composition from the capsule 60 to the patient upon inhalation while the flange 21 is designed to engage with the main body 10.

[42] Configured to be mounted onto the main body 10, the inhalation portion 20 comprises a peg 24 which extrudes from the bottom of the flange 21 with a cross tooth 23 laterally directing from the end portion of the peg 24.

[43] Corresponding to the peg 24 and the cross tooth 23 of the inhalation portion 20, an engagement hole 12 is formed in the main body 10. The peg 24 is inserted to the engagement hole 12 for the cross tooth 23 to engage with the engagement hole 12.

[44] A slot, although not shown, is formed longitudinally, corresponding to the cross tooth 23, so as to engage with the cross tooth 12.

[45] When the peg 24 is pushed to the bottom of the engagement hole 12 after insertion into the engagement hole 12, the inhalation portion 20 can be rotated on the axis made by the peg 24 and the engagement hole 12 to fit into the main body 10.

[46] The fitting of the inhalation portion 20 into the main body 10 may be accomplished by engagement between a ridge 14 formed within a latching recess 13 of the main body 10, and a hook (not shown) formed in the flange 21 of the inhalation portion 20. The inhaler device 1 is in a close condition when the inhalation portion 20 is fitted into

the main body 10 by latching the ridge 14 onto the hook.

[47] Although the latching mechanism between the main body 10 and the inhalation portion 20 is illustrated with the use of the ridge 14 and the hook in this embodiment, the spirit of the present invention is not limited thereto. For example, a spring-type latching mechanism may be applied.

[48] Turning to the pushbutton assembly 30 which is to be installed in the installation hole 15 of the main body 10, it comprises a needle 33 for perforating the capsule 60, a pushbutton which is movable into and out of the main body 10 and by which the needle 33 is supported, and an elastic member 32 for elastically supporting the pushbutton 31 and the main body 10 therebetween.

[49] Although the elastic member 32 is illustrated as a coiled spring in this embodiment, the spirit of the present invention is not limited thereto.

[50] The needle 33, the pushbutton 31, and the elastic member 32 are disposed on the same axis, and they can move in a horizontal direction. The needle 33 may be fixed inside the pushbutton 31.

[51] In the installation hole 15 of the main body 10, a guide 16 is provided to form a guide hole 16a for guiding the motion of the needle 33.

[52] As the pushbutton 31 works, the needle 33 can thus stably move along the guide hole 16a of the guide 16.

[53] The needle 33 is similar to that for subcutaneous injection, and may be provided with a beveled tip for ease in perforating into the coating and composition of the capsule 60.

[54] Since a needle for subcutaneous injection has low perforation resistance and operates precisely, it, even though large in diameter, can perforate through the capsule 60 in a simple manner without damage to the capsule 60. The use of a small number of, for example, two, needles reduces the contact area between the needles and the capsule, which leads to a minimal damage to the capsule 60 while two perforations with the same cross sectional area are formed.

[55] A pair of pushbutton assemblies 30 may be provided to opposite sides of the main body 10 and may be disposed to face each other.

[56] In the main body 10, an air passage 40 is provided through which external air is introduced into the main body 10.

[57] The air passage 40 may pass through the main body so that the capsule accommodation portion 11 of the main body 10 communicates with the outside of the main body 10.

[58] Accordingly, when a patient inhales, external air is introduced through the air passage 40 into the main body 10 and reaches the capsule accommodation portion 11 where it is mixed with the loaded composition before passage through the inhalation duct 22 of the inhalation portion 20.

[59] In this regard, the inhalation portion 20 may be provided with a grid 50 for filtering impurities.

[60] The grid 50 is disposed between the main body 10 and the inhalation portion 20, for example, at an end portion of the inhalation duct 22.

[61] FIG. 7 is a cross sectional view illustrating the operation of the dry powder inhaler device according to an embodiment of the present invention. With reference to FIG. 7 and other figures, the operation of the dry powder inhaler device is explained.

[62] After the main body is opened by unlocking the inhalation portion 20, the capsule 60 is placed in the capsule accommodation portion 11 of the main body 10. Then, the inhalation portion 20 is rotated to latch onto the main body 10.

[63] When pressed, the pushbutton 31 of the main body 10 is moved inward the main body 10 (as indicated by arrows in FIG. 7) to cause the needle 33 fixed in the pushbutton 31 to perforate the capsule 60, whereby the composition within the capsule 60 is discharged to the capsule accommodation portion 11.

[64] Suction through the inhalation portion 20 causes external air to be introduced into the main body 10 through the air passage 40.

[65] Once introduced into the main body 10, the external air generates an air flow, is mixed with the composition (dry powder) of the capsule accommodation portion 11, and in the main body 10, and flows to the patient through the grid 50 and the inhalation duct 22.

[66] As described above, the suction of the patient is responsible for driving the pharmaceutically active ingredient of the capsule 60 into the airway in the inhaler device 1. In all dry powder inhalers, a pressure drop is generated by air flow upon patient's suction. The pressure drop may act as an important parameter in determining effective doses of inhalants as a function of aerodynamic size distribution, or delivered dose uniformity. In practice, AR (airflow resistance, kPa/Lmin) differs from one device to another. In this regard, complying with the USP chapter <601>, the Dosage Unit Sampling Apparatus (DUSA) for DPIs is capable of sampling at a variety of flow rates from zero up to 100 LPM. The specification suggests performing the test at a flow rate (Q_{out}) for which the pressure drop across the actuator is 4 kPa, using the suction time (T (sec) = 240/ Q_{out}).

[67] To guarantee similar pharmaceutical activity from one patient to another, it is preferred that the aerodynamic size distribution change little with variation in flow rate.

[68] Ranging in a air flow resistance from 0.02 $\sqrt{kPa}$/L/min to 0.03 $\sqrt{kPa}$/L/min, the dry powder inhaler device 1 according to an embodiment of the present invention causes little change in the aerodynamic size distribution of pharmaceutically active ingredients with the variation of flow rates, and can deliver the pharmaceutically active

ingredients deep into the lungs with higher efficiency than conventional inhalers.

[69] In the dry powder inhaler device 1, the airflow resistance is proportional to a root square of the pressure drop (P, kPa) and inversely proportional to the airflow rate (Φ, L/min) (J.P de Koning et al, Effect of an external resistance to airflow on the inspiratory flow curve, International Journal of Pharmaceutics 234 (2002) 257~266).

[70] Therefore, the test for delivered-dose uniformity set forth for the DUSA can be applied to the evaluation of the intrinsic airflow resistance of an inhaler by measuring a change in pressure drop across the inhaler with variance in airflow rate.

[71] Given an airflow resistance of 0.02 $\sqrt{kPa}$/L/min to 0.030 $\sqrt{kPa}$/L/min, the dry powder inhaler device 1 according to an embodiment of the present invention is found to effectively deliver a pharmaceutically active ingredient to Stages 3 to 7 of Apparatus 3 (Anderson Cascade Impactor) according to USP 34 <601>.

[72] Therefore, when having an airflow resistance of 0.02 $\sqrt{kPa}$/L/min to 0.030 $\sqrt{kPa}$ / L/min, the dry powder inhaler device 1 according to the present invention allows for the proper expansion of the lung and thus enables a pharmaceutically active ingredient to be delivered deep into the lungs without deposition on the mouth or the upper respiratory tract.

[73] In the dry powder inhaler 1 according to an embodiment of the present invention, the airflow resistance is determined by the width (w) of an entrance the air passage 40 of the main body 10. Thus, the airflow resistance can be adjusted into a proper value by varying the width of the entrance of the air passage 40.

[74] By way of example, when the entrance of the air passage 40 of the main body 10 has a width of 1.5 mm to 3.5 mm, and preferably 1.5 mm to 3 mm, the airflow resistance falls within the range of 0.02 $\sqrt{kPa}$/L/min to 0.030 $\sqrt{kPa}$/L/min, ensuring an aerodynamic size distribution at which the delivery of a pharmaceutically active ingredient to the lungs can be achieved with maximum efficiency.

[75] Accordingly, the dry powder inhaler device 1 of the present invention helps a pharmaceutically active ingredient of an inhalant arrive at the bronchus and alveoli sufficiently, and is much less prone to changing the aerodynamic size distribution of the pharmaceutically active ingredient with a variation of airflow rates, thus guaranteeing the patient the safe use of the inhalant.

[76]

[77] A better understanding of the effect of the dry powder inhaler device 1 according to the present invention may be obtained through the following Test Examples which are set forth to illustrate, but are not to be construed as limiting the present invention.

[78]

[79] **TEST EXAMPLE 1: Measurement of Airflow Resistance**

[80]

[81] RS01 Model 7 Inhalers (hereinafter referred to as "inhaler devices D") having, as shown in FIG. 8, various widths (w1=1.3 mm, w2=1.8 mm, w3=2.6 mm, and w4=4.0 mm) of an entrance of an air passage 40' were measured for airflow resistance (the width w2 of the entrance of the air passage not shown in FIG. 8). In addition, the inhaler devices D were evaluated for pressure drop (P, kPa) under four airflow rate conditions 28.3L/min, 60L/min, 75L/min, and 90L/min using the delivered dose tester, Apparatus 1 of USP 34 <601>.

[82] From the measurements of pressure drop, the airflow resistance as a function of the width of the entrance of the air passage was calculated using the following equation (J. Aerosol Med. 6 (1993) 99-100).

[83]

[84] $$AirflowResistance(\sqrt{kPa}/L/M)=\frac{\sqrt{PressureDrop(kPa)}}{AirflowRate(L/M)}\left(R=\frac{\sqrt{\chi P}}{Q}\right)$$

[85]

[86] Table 1

[Table 1]

Width of Entrance of Air Passage (mm)		Airflow Rate (L/min)				
		28.3L	60L	75L	90L	Average
1.3mm	Pressure Drop(kPa)	1.15	5.22	6.89	9.45	
	Airflow Resistance ($\sqrt{kPa}$/L/min)	0.036	0.038	0.035	0.034	0.036
1.8mm	Pressure Drop(kPa)	0.78	3.93	4.84	6.61	
	Airflow Resistance ($\sqrt{kPa}$/L/min)	0.031	0.033	0.029	0.029	0.031
2.6mm	Pressure Drop(kPa)	0.41	2.07	3.00	4.14	
	Airflow Resistance ($\sqrt{kPa}$/L/min)	0.023	0.024	0.023	0.023	0.023
4.0mm	Pressure Drop(kPa)	0.28	1.6	1.94	2.62	
	Airflow Resistance ($\sqrt{kPa}$/L/min)	0.019	0.021	0.019	0.018	0.019

[87]

[88] Table 1 summarizes airflow resistances depending on the width of the entrance of the air passage. As is apparent from data of Table 1, the air resistances vary with the widths (w1~w4) of the entrance of the air passage even in the same inhaler device D.

[89]

[90] **TEST EXAMPLE 2: Measurement of Aerodynamic Size Distribution I**

[91]

[92] In a mixer, indicated amounts of salmeterol xinafoate and fluticasone propionate of Table 2 were admixed with 2 mg of lactose, and then blended with the remainder (18 mg) of lactose, together with balls, for 20 min. The resulting blend was left for 12 hours in the mixer to remove static electricity therefrom (stabilization process) before it was loaded to transparent capsule No. 3 using a capsule filler.

[93]

[94] Table 2

[Table 2]

Ingredient	Amount (mg)
Salmeterol xinafoate	0.0725 (0.05 as salmeterol itself)
Fluticasone propionate	0.2500
Lactose	20.0000
Sum	20.3225

[95]

[96] The composition of Table 2 was subjected to a test for aerodynamic size distribution. Inhaler devices D with widths of the entrance of the air passage 40' ranging from 1.3 mm to 4.0 mm (w1, w2, w3, w4) were analyzed for particle size distribution by measuring the contents of the pharmaceutically active ingredients in Stages 1 to 5 at airflow rates of 28.3L/min, 60L/min, and 75L/min using USP 34 <601> Apparatus 3(Anderson Cascade Impactor) under the following condition. The results are depicted in FIGS. 9 and 10.

[97]

[98] <Analysis condition of salmeterol and fluticasone>

[99] Column: a stainless tube 15 cm long with an inner diameter of about 4.6 mm, filled with octadecyl-silylated silica gel with a size of 5 μm for liquid chromatography.

[100] Mobile phase: a mixture of methanol: acetonitrile: water (50:16:34, v/v/v), added with 0.6 % (w/v) ammonium acetate

[101] Detector: UV absorption spectrophotometer (wavelength 228 nm)

[102] Temp.: 40 ℃

[103] Airflow rate: 1.0 mL/min

[104] Injection load: 100 μL

[105]

[106] As can be seen in FIGS. 9 and 10, the contents of the pharmaceutically active ingredients in Stages 1 to 5 were observed to be uniform over all of the airflow rates when the entrance of the air passage 40 ranged in width from 1.8 mm to 2.6 mm (w2, w3) (salmeterol: around 10 μg, fluticasone: around 60 μg). In contrast, a width of 1.3

mm (w1) or 4.0 mm (w4) of the entrance of the air passage 40' at which the airflow resistance is not between 0.02 $\sqrt{kPa}$/L/min and 0.030 $\sqrt{kPa}$/L/min caused a large change in effective dose with a variation of airflow rates, and resulted in a smaller effective dose than did the widths corresponding to an airflow resistance of from 0.02 $\sqrt{kPa}$/L/min to 0.030 $\sqrt{kPa}$/L/min.

[107] Thus, when it is configured to range in airflow resistance from 0.02 $\sqrt{kPa}$/L/min to 0.030 $\sqrt{kPa}$/L/min, the inhaler device allows for only a slight change in aerodynamic size distribution with a variation of suction speeds (airflow rates), with the concomitant delivery of maximum effective doses to the lungs.

[108]

[109] **TEST EXAMPLE 3: Measurement of Aerodynamic Size Distribution II**

[110]

[111] Using the composition of Table 2, a test for aerodynamic size distribution was performed. In the inhaler device D with a width of 2.6 mm (w3) of the entrance of the air passage 40', the pharmaceutically active ingredients were analyzed for particle size distributions in Stages 0 to 7 at an airflow rate of 60 L/min using USP 34 <601> Apparatus 3(Anderson Cascade Impactor) under the condition of Test Example 2. The results are depicted in FIGS. 11 and 12. For comparison, Seretide Diskus 250 (GSK), a commercially available inhalant containing salmeterol and fluticasone, was tested under the same condition.

[112] As can be seen in FIGS. 11 and 12, a dry powder inhaler device 1 which is designed to have an airflow resistance of 0.02 $\sqrt{kPa}$/L/min to 0.030 $\sqrt{kPa}$/L/min exhibits a higher aerodynamic size distribution after Stage 4 than does the comparative Seretide Diskus.

[113] Hence, the dry powder inhaler device 1 with an airflow resistance ranging from 0.02 $\sqrt{kPa}$/L/min to 0.030 $\sqrt{kPa}$/L/min in accordance with the present invention can direct the pharmaceutically active ingredient deep into the lungs, improving the pharmaceutical effect.

[114] Taken together, the data obtained above indicate that the dry powder inhaler device 1 designed to have an airflow resistance of 0.02 $\sqrt{kPa}$/L/min to 0.030 $\sqrt{kPa}$/L/min in accordance with the present invention can sufficiently introduce a pharmaceutically active ingredient to the target, that is, the lungs, and generate little change in the aerodynamic size distribution of the pharmaceutically active ingredient with a variation of airflow rates, thus guaranteeing safety in use for the patient.

[115]

[116] Although the preferred embodiments of the present invention have been disclosed for illustrative purposes, those skilled in the art will appreciate that various modifications, additions and substitutions are possible, without departing from the scope and spirit of

the invention as disclosed in the accompanying claims.

Claims

[Claim 1] A dry powder inhaler device, comprising:
a main body in which a capsule accommodation portion for accommodating a composition-loaded capsule is formed;
an air passage, formed at the main body, for introducing external air into the main body therethrough by patient's suction; and
an inhalation portion, combined with the main body, for guiding the external air introduced into the main body, together with the composition, to the patient,
wherein said dry powder inhaler device is designed to have an airflow resistance of 0.02 $\sqrt{kPa}$/L/min to 0.03 $\sqrt{kPa}$/L/min within the main body.

[Claim 2] The dry powder inhaler device of claim 1, wherein the air passage passes through the main body so that the capsule accommodation portion communicates with an outside of the main body.

[Claim 3] The dry powder inhaler device of claim 2, wherein the airflow resistance can be adjusted by adjusting a width of an entrance of the air passage.

[Claim 4] The dry powder inhaler device of claim 3, wherein the width of the entrance of the air passage ranges from 1.5 mm to 3 mm.

[Claim 5] The dry powder inhaler device of claim 1, further comprising at least one pushbutton assembly, disposed at one or more sides of the main body, which is structured to move into and out of the main body to exert an external force on the capsule, whereby the composition is discharged out of the capsule.

[Claim 6] The dry powder inhaler device of claim 5, wherein the pushbutton assembly comprises:
a needle for perforating the capsule;
a pushbutton which is movable into and out of the main body and by which the needle is supported; and
an elastic member for elastically supporting the pushbutton and the main body therebetween.

[Claim 7] The dry powder inhaler device of claim 1, further comprising a grid, disposed between the main body and the inhalation portion, for filtering impurities.

[Claim 8] The dry powder inhaler device of claim 1, wherein the inhalation portion comprises:

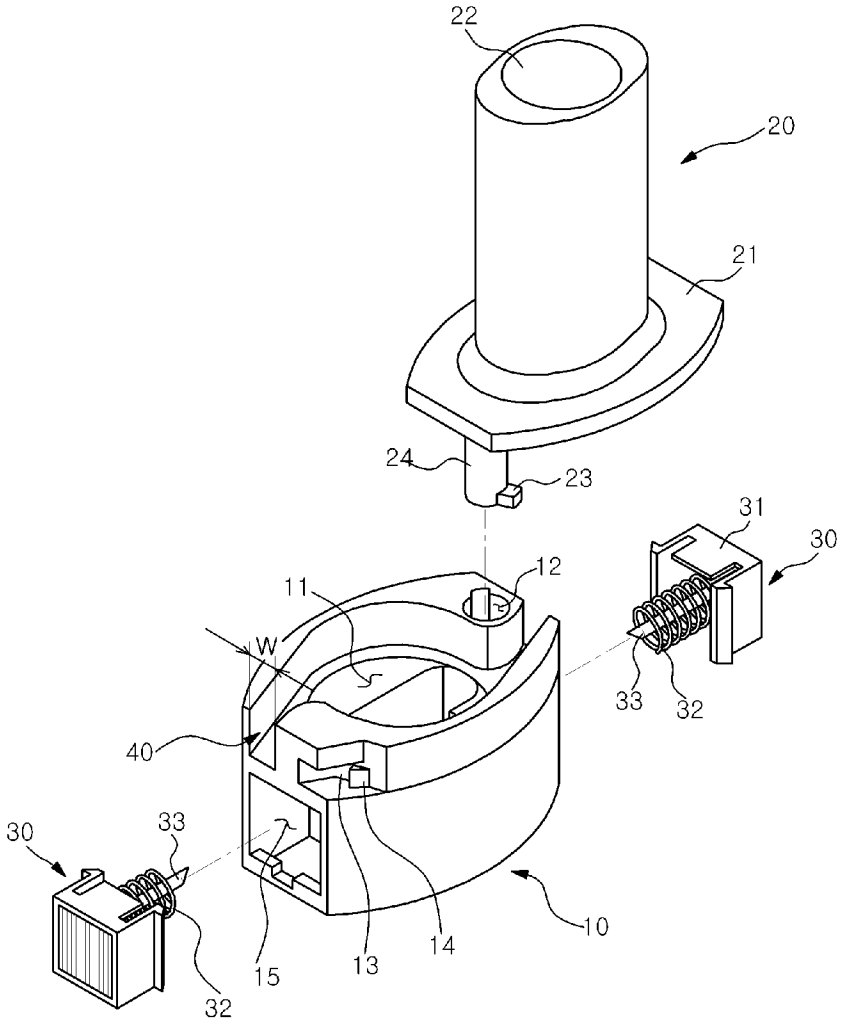
an inhalation duct communicating with the capsule accommodation portion; and

a flange, extended from the inhalation duct, for combining the inhalation portion with the main body.

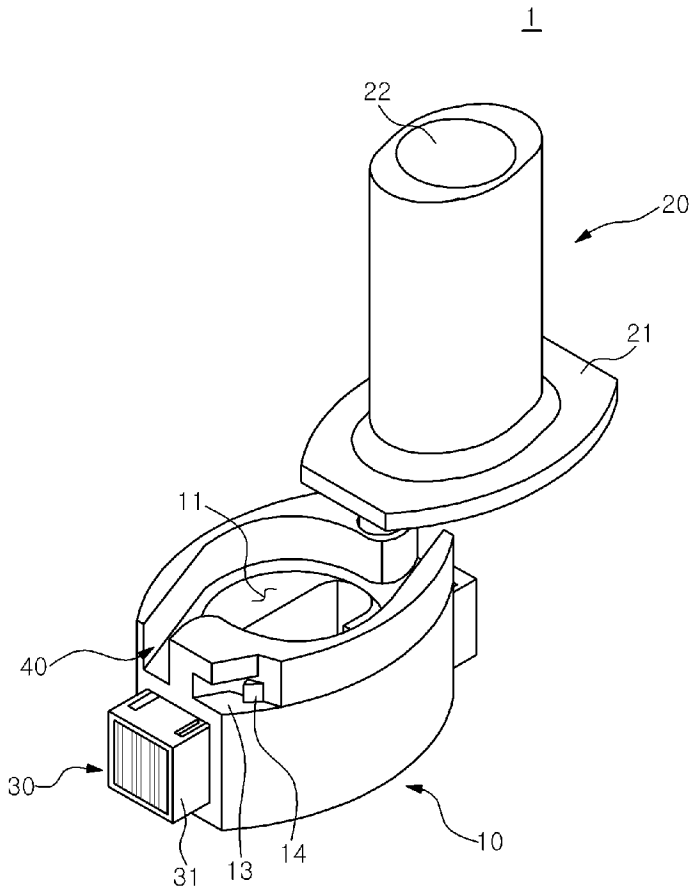
[Claim 9] The dry powder inhaler device of claim 1, wherein the inhalation portion comprises a peg which extrudes from the inhalation portion with a cross tooth laterally directing from an end portion of the peg, and the main body has an engagement hole corresponding to a figure of the peg and the cross tooth, wherein when the cross tooth is engaged with the engagement hole by inserting the peg into the engagement hole, the inhalation portion can be rotated on the axis made by the peg and the engagement hole to close or open the capsule accommodation portion of the main body.

[Claim 10] The dry powder inhaler device of claim 9, wherein when the inhalation portion closes the capsule accommodation portion, the inhalation portion is latched onto the main body by engagement between a ridge formed within a latching recess of the main body, and a hook formed in the inhalation portion.

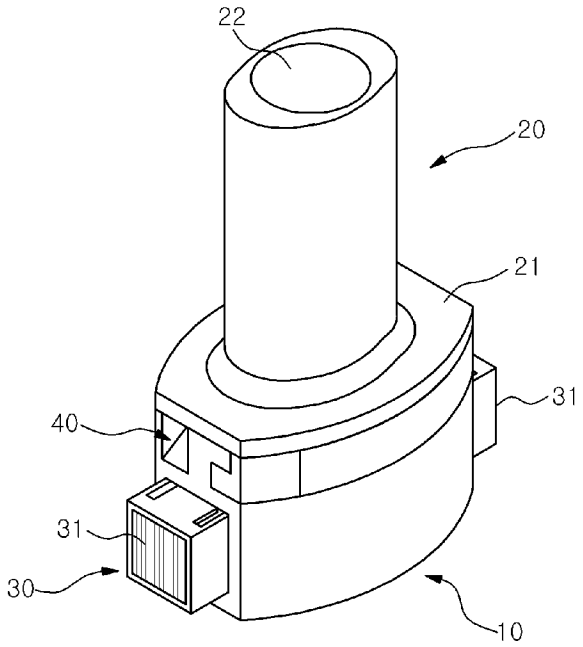
[Fig. 1]



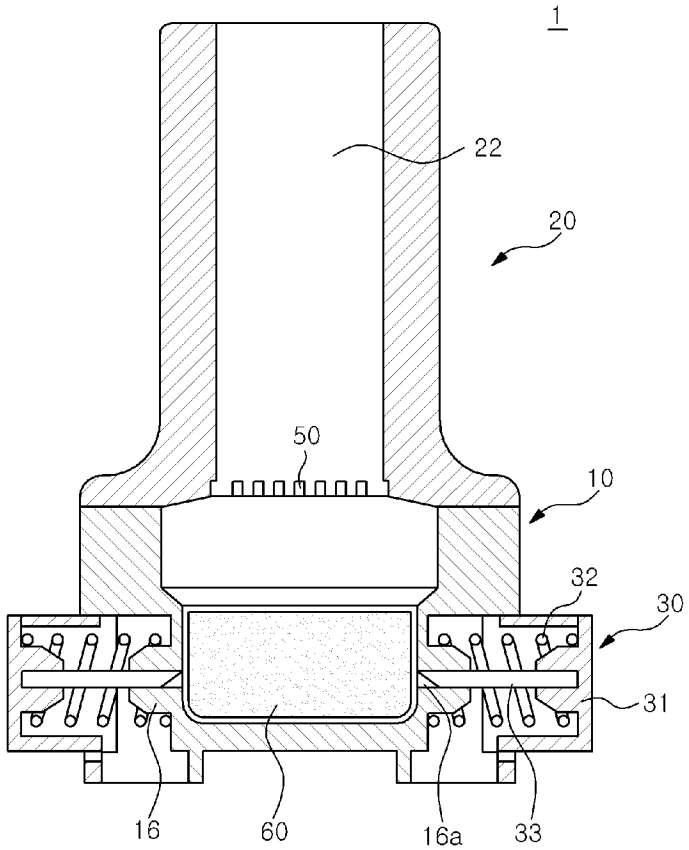
[Fig. 2]



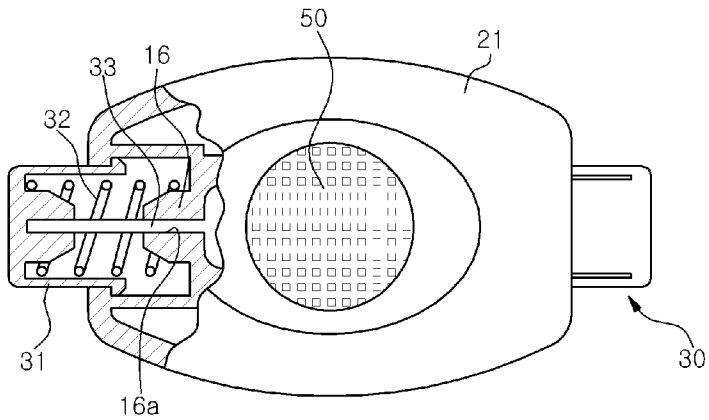
[Fig. 3]



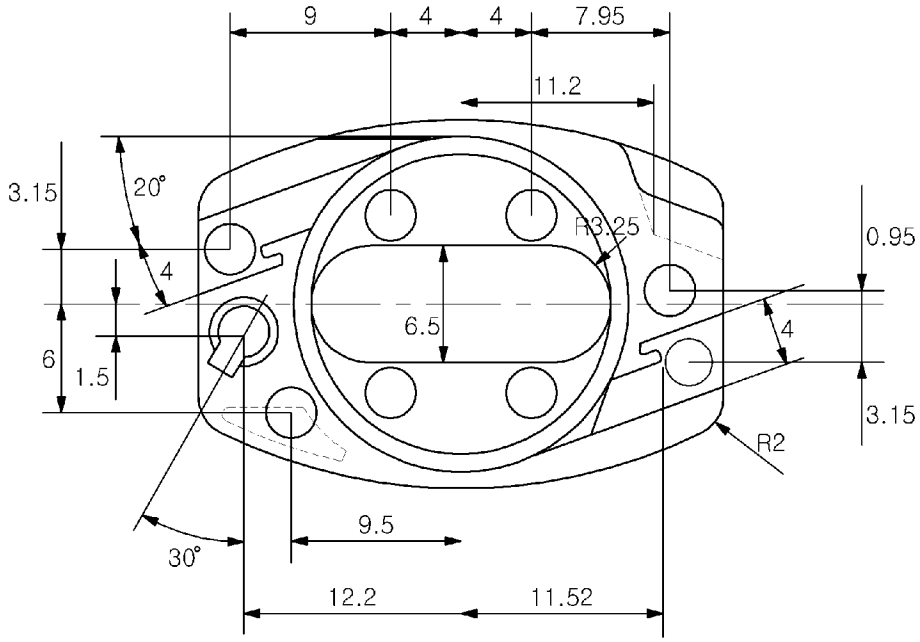
[Fig. 4]



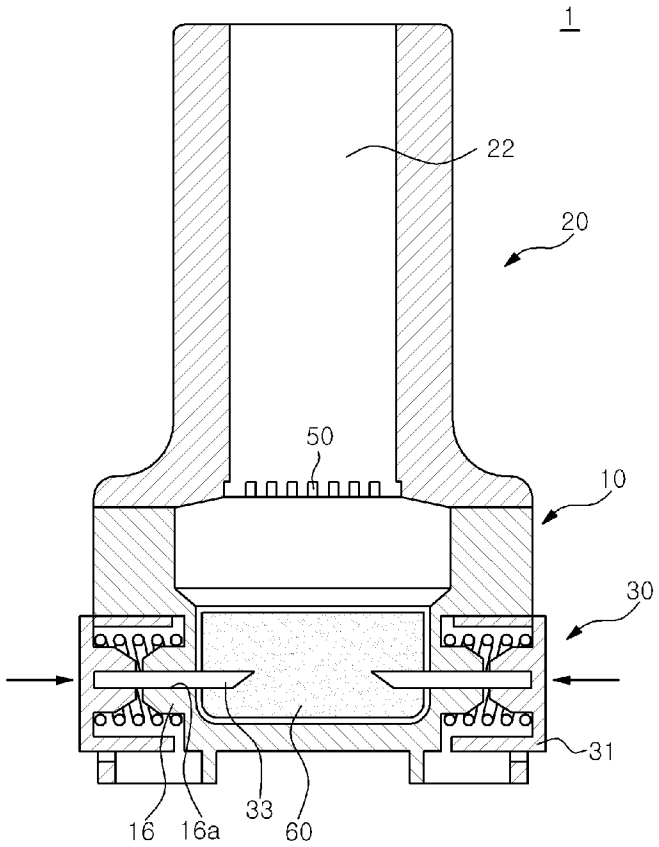
[Fig. 5]



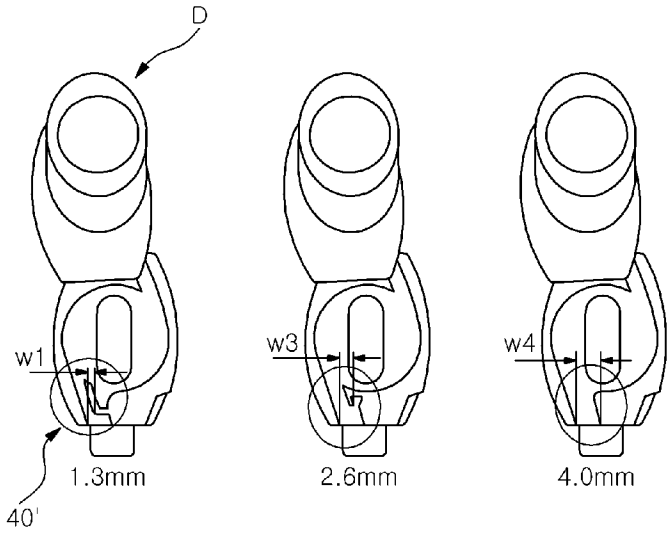
[Fig. 6]


9
4
4
7.95
11.2
3.15
20°
4
6
1.5
6.5
R3.25
0.95
4
3.15
R2
9.5
30°
12.2
11.52

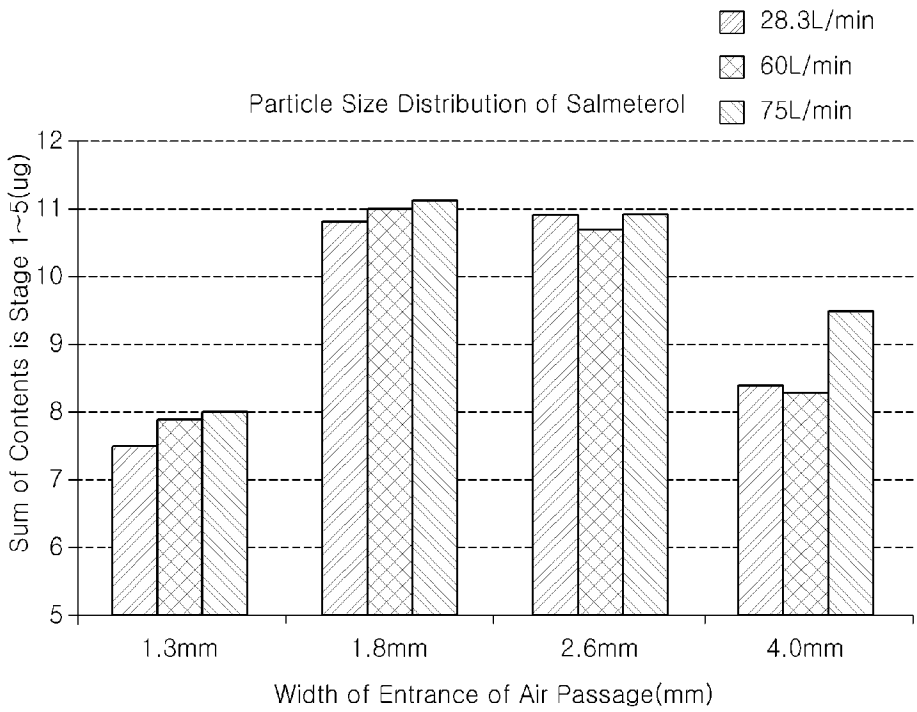
[Fig. 7]


1
22
20
50
10
30
31
16
16a
33
60

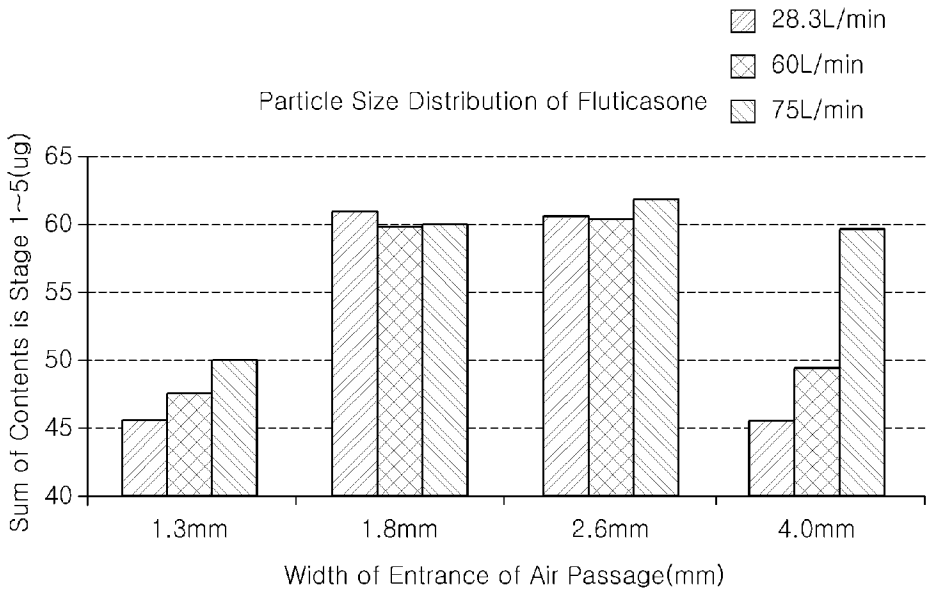
[Fig. 8]


D
w1
w3
w4
1.3mm
2.6mm
4.0mm
40'

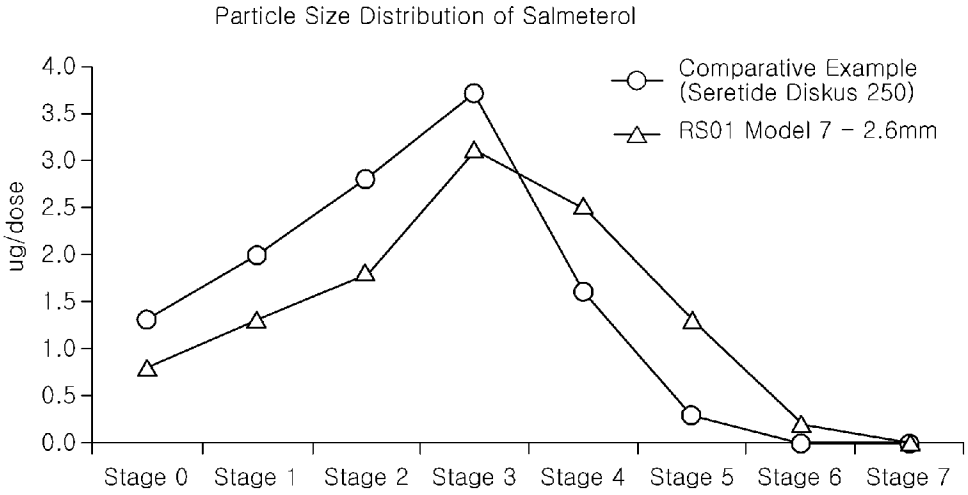
[Fig. 9]


28.3L/min
60L/min
75L/min
Particle Size Distribution of Salmeterol
Sum of Contents is Stage 1~5(ug)
12
11
10
9
8
7
6
5
1.3mm
1.8mm
2.6mm
4.0mm
Width of Entrance of Air Passage(mm)

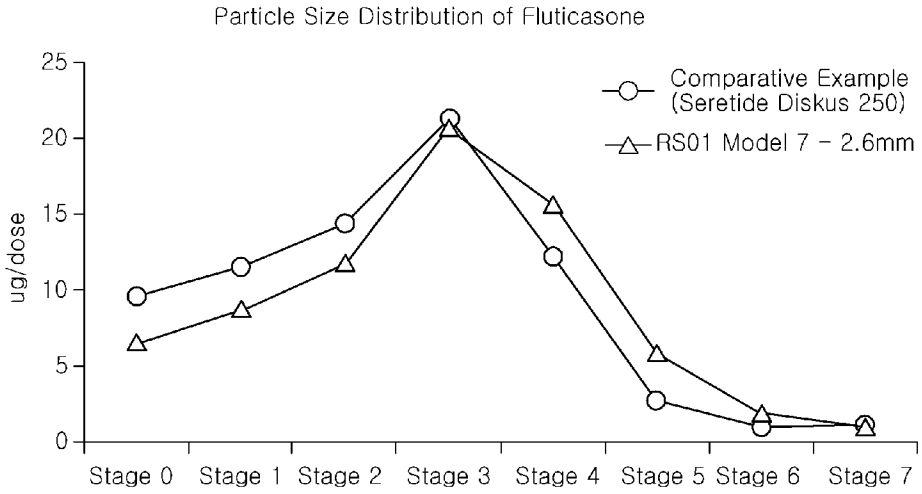
[Fig. 10]



[Fig. 11]



[Fig. 12]



PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference PIB307124HMI	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
International application No. **PCT/KR2013/008985**	International filing date *(day/month/year)* **08 October 2013 (08.10.2013)**	(Earliest) Priority Date *(day/month/year)* 11 October 2012 (11.10.2012)
Applicant **HANMI PHARM.CO., LTD.**		

This International search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of **4** sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language**, the international search was carried out on the basis of :
      ☒ the international application in the language in which it was filed
      ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b))
   b. ☐ This international search report has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43.6*bis*(a)).
   c. ☐ With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.
2. ☐ **Certain claims were found unsearchable** (See Box No. II)
3. ☐ **Unity of invention is lacking** (See Box No. III)
4. With regard to the **title,**
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established by this Authority to read as follows:
5. With regard to the **abstract,**
   ☒ the text is approved as submitted by the applicant.
   ☐ the text has been established, according to Rule 38.2, by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. With regard to the drawings,
   a. the figure of the **drawings** to be published with the abstract is Figure No. **1**
      ☒ as suggested by the applicant.
      ☐ as selected by this Authority, because the applicant failed to suggest a figure.
      ☐ as selected by this Authority, because this figure better characterizes the invention.
   b. ☐ none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/KR2013/008985

A. CLASSIFICATION OF SUBJECT MATTER

A61M 15/06(2006.01)i, B65D 83/06(2006.01)i

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M 15/06; A61M 11/00; A61M 13/00; A61M 15/00; B65D 83/06

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
Korean utility models and applications for utility models
Japanese utility models and applications for utility models

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
eKOMPASS(KIPO internal) & Keywords: inhale, inhalation, channel, dry powder, capsule

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2011-020554 A1 (GMBH, GAMPTEC et al.) 24 February 2011 See abstract, claims 1,14-19, columns 14,19, figs.1,3b,4	1-8
A		9,10
A	KR 10-2004-0108704 A (BOEHRINGER INGELHEIM PHARMA GMBH & CO. KG) 24 December 2004 See abstract, claims 6-8, page 4, fig.1	1-10
A	JP 2009-148586 A (QUADRANT TECHNOLOGIES.CO., LTD.) 09 July 2009 See abstract, claims 1-5, figs.1,2	1-10
A	WO 2011-110970 A1 (RANBAXY LABORATORIES CO., LTD.) 15 September 2011 See abstract, claims 1-5, figs.1-2	1-10

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* Special categories of cited documents:
"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier application or patent but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed
"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents,such combination being obvious to a person skilled in the art
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
29 January 2014 (29.01.2014)	**03 February 2014 (03.02.2014)**

Name and mailing address of the ISA/KR
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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.
PCT/KR2013/008985

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