(12) STANDARD PATENT (11) Application No. **AU 2015221812 B2**
(19) AUSTRALIAN PATENT OFFICE

(54) Title
Inhaler

(51) International Patent Classification(s)
A61M 15/00 (2006.01)

(21) Application No: **2015221812** (22) Date of Filing: **2015.02.23**

(87) WIPO No: **WO15/128789**

(30) Priority Data

(31) Number	(32) Date	(33) Country
663/MUM/2014	**2014.02.25**	**IN**

(43) Publication Date: **2015.09.03**
(44) Accepted Journal Date: **2019.12.19**

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(56) Related Art
WO 2012/047182 A2
US 2006/0237016 A1

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
3 September 2015 (03.09.2015)

WIPO | PCT

(10) International Publication Number
WO 2015/128789 A1

(51) International Patent Classification:
A61M 15/00 (2006.01)

(21) International Application Number:
PCT/IB2015/051350

(22) International Filing Date:
23 February 2015 (23.02.2015)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
663/MUM/2014 25 February 2014 (25.02.2014) IN

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(81) Designated States *(unless otherwise indicated, for every kind of national protection available)*: AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States *(unless otherwise indicated, for every kind of regional protection available)*: ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

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(54) Title: INHALER

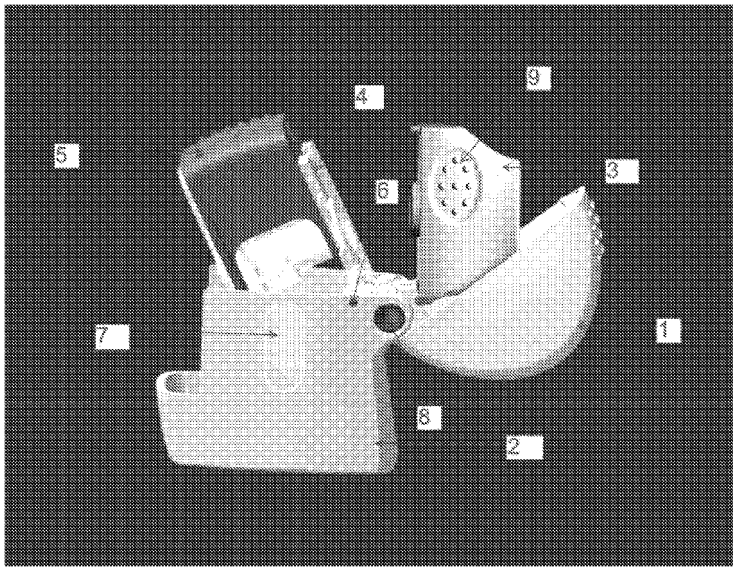

Figure 1

(57) Abstract: An inhaler device comprising: a housing (2), a base plate (4) covering the housing (2), a medicament holder (10) integrated with the base plate (4), a mouthpiece (3) sitting over the base plate (4), a lid (1) which covers the mouthpiece (3), at least one piercing element (11), an actuating member (5), a spring (12), and is characterized in that the inhaler device is a two hinge system (6,8) wherein the base plate (4) is joined to hinge (6); the mouthpiece (3) and the lid (1) are joined to the hinge (8).

WO 2015/128789 A1

Declarations under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

— *as to the applicant's entitlement to claim the priority of the earlier application (Rule 4.17(iii))*

Published:

— *with international search report (Art. 21(3))*

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Technical Field

The present invention relates to an inhalation device for inhalation of powdered pharmaceutical compositions contained in capsules which are inserted in a medicament holder of the inhalation device.

Background Art

Inhalation devices provide for the treatment and management of respiratory disorders. Today dry powder inhalation devices play a role in the field of targeted drug delivery to the affected airways of lungs. Dry powder inhalers (DPIs) have been available since 1967 and Aventis was first to develop DPI by name SPINHALER for the delivery of Sodium Cromoglycate. Since then, many improvements in the design and use of inhalation devices were observed.

In general the powdered inhalation devices are used for inhaling either single or multi-dose of powdered medicament from capsules. The devices are configured to have medicament holders which hold the capsules containing the powdered medicament. A piercing mechanism provided with the device pierces the capsule and enables the medicament to get dispersed into the air sucked by the user during the process of inhalation. The emptied capsule remains in the device which is then discarded prior to the next use of the device.

US 3,807,400 discloses some improvements in the inhaling devices with whirling chamber, devices that may be considered in their essential operation per se known and are intended to disperse the contents of a capsule filled with a powder medicinal composition. The device according provides a mouth piece that is a telescopic structure and two piercing devices that are placed into a rotatable member according to a diametral opposed position and are actuated by the member, the telescoping structure when extended forming the whirling chamber, the mantel of the latter mentioned member being formed with a cam able to give a number of piercing operations to both piercing devices.

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US 8,006,695 describes an inhaler device for inhalation of a medicament from a pierceable capsule comprises a housing for receiving a medicament capsule; closure means for closing the housing, said closure means being moveable relative to the housing; piercing means suitable for piercing a medicament capsule; wherein movement of the closure means relative to the housing causes movement of the piercing means. US 8,006,695 also discloses a holder for a medicament capsule which holder comprises a chamber suitable for receiving a medicament capsule; and means for generating turbulence in a fluid flow through the chamber such that, in use, the turbulent fluid flow causes vibration of a capsule received by the chamber so as to assist in releasing medicament contained within the capsule.

US 7,694,676 describes an inhaler for inhaling powdered pharmaceutical compositions from capsules includes: a lower part; a plate which can be latched to the lower part and with which the lower part can be closed off; a capsule holder for receiving the capsules, this holder being adapted to be lowered into the lower part; a mouthpiece latchable to the plate; a lid which covers the mouthpiece in a closed position and latches it by means of a closure element, the lower part, the plate, the mouthpiece and the lid being hinged together by means of a single joint.

US 8,022,082 discloses an inhaler comprising: a housing containing two windows, a deck in which there are air inlet ports and which is provided with a screen secured by a screen housing, an inhalation chamber connected to the deck on which there is a push button provided with two sharpened pins and movable counter to a spring, a mouthpiece which is connected to the housing, the deck, and a cover via a spindle to enable it to be flipped open or shut, and three holes with diameters below 1 mm in the central region around the capsule chamber and underneath the screen housing and screen.

US 7,252,087 discloses an inhaler utilizing a multi-functional actuating member. Multi-functional actuating member as disclosed in US ‘087 in a first functional position allows a

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closure element to be disengaged from a lower part of the housing, and in a second functional position allows a mouthpiece to be pivoted away from the lower part of the housing.

US 7,284,553 discloses a powder inhaler operating on the Bernoulli principle. It discloses an inhaler with a capsule chamber including raised elements on either the inner surface of the capsule chamber or on the outer surface of the capsule.

It is to be understood that, if any prior art is referred to herein, such reference does not constitute an admission that the prior art forms a part of the common general knowledge in the art, in Australia or any other country.

Summary

The present invention is directed to inhaling devices with a two-hinge system intended to disperse the contents of the powdered pharmaceutical composition.

According to an aspect, there is provided an inhaler device comprising: a housing, a base plate covering the housing, a medicament holder integrated with the base plate, a mouthpiece sitting over the base plate, a lid which covers the mouthpiece, at least one piercing element, an actuating member, a spring configured to link the actuating member to the medicament holder, and wherein the inhaler device is a two hinge system, said hinges being included in the housing, wherein the base plate is joined to hinge; the mouthpiece and the lid are joined to another hinge, wherein the base plate is hinged separately from the mouthpiece and lid.

In some forms, the inhaler disclosed herein is used for powdered inhalant delivery based on the factors that influence treatment compliance such as drug to be delivered, ease of handling and patient's preference.

In the normal use of the Dry Powder Inhaler; patient opens the lid, then the mouth piece and inserts the capsule containing powdered pharmaceutical composition. Patient then presses the

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actuating member that leads to piercing of the capsule containing powdered pharmaceutical composition. The at least one piercing element attached to the actuating member pierce the capsule from one side allowing the powdered pharmaceutical composition contained in the capsule to come out when the patient inhales from the mouthpiece.

The 'two-hinge' design in the inhaler employs two separate hinges. One hinge may be for the lid and the mouth piece and second may be for the base plate. The patient is required to open the base plate only as and when required. Use of second and distinct hinge prevents the accidental opening of the base plate, thereby avoiding the contamination of the medicament. Also, the non-protruding actuating member makes handling and storing of the device very convenient.

Further, the shape of the inhaler which is round across the top and on one side is configured at an angle in such a way that patient is able to have an appropriate grip on the device and finds it very convenient to actuate the device without losing control over the holding of the device

In some embodiments, an inhaler device includes two hinge systems, wherein the mouthpiece and the lid is joined to a single hinge.

In some embodiments, an inhaler utilizing base plate is devoid of any holes.

In some embodiments, an inhaler wherein the gripping aid is disposed distal to the actuating member.

In some embodiments, the at least one piercing element are attached from inside of the actuating member.

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In some embodiments, the spring is configured to link the actuating member. In some embodiments, wherein in order to assist piercing, the actuating member when pressed causes the spring element to get compressed which enables the piercing elements to move linearly.

In some embodiments, the device further comprises a gripping aid on the mouthpiece which offers a grip to open the mouthpiece.

In some embodiments, the device further comprises an inspection window to see across the inhaler device.

In some embodiments, the gripping aid is disposed distal to the actuating member.

In some embodiments, the medicament holder is mounted on the underside of the base plate.

In some embodiments, the base plate is devoid of any holes.

In some embodiments, the medicament holder is designed to contain a capsule with powdered pharmaceutical composition.

In some embodiments, the powdered pharmaceutical composition is suitable for the treatment of asthma or chronic obstructive pulmonary disease by inhalation.

In some embodiments, the powdered pharmaceutical composition contained within the capsule is a dry powder medicament.

Brief description of the accompanying drawings

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

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Figure 1 illustrates a side perspective view of an embodiment of an inhaler in accordance with the present invention wherein the housing (2) which accommodates the base plate (4) and is covered by the latter, the mouthpiece (3) with gripping aid (9). The base plate (4) is joined to the hinge (6) and the mouthpiece (3) and the lid (1) is hinged together distinctly from the base plate to hinge (8). The gripping aid (9) is disposed distal to the actuating member (5).

Figure 2 illustrates a top perspective view of an embodiment of a medicament holder (10) mounted on the underside of an embodiment of a base plate (4).

Figure 3 illustrates a closed view of an embodiment of a mouthpiece (3) sitting over the base plate (4) that is integrated with the medicament holder (10). The two hinges (6, 8) are distinctly marked.

Figure 4 illustrates a radial partial sectional view of the inhaler depicting the lid (1), mouthpiece (3), piercing elements (11), actuating member (5), spring (12), medicament holder (10), inspection windows (7), and the mouthpiece and lid attached to hinge (8).

Figure 5 illustrates a side perspective of the inhaler in a closed position.

Figure 6 illustrates a top view of the inhaler base plate (4) devoid of any holes.

Figure 7 illustrates a side view of the inhaler with an embodiment of a distinct two hinge system (6, 8).

Figure 8 illustrates the graph for square root of the pressure drop versus the flow rate in the present inhaler depicting relatively high resistance to air flow.

Detailed Description

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The following presents a simplified summary of the disclosure in order to provide a basic understanding of some aspects of the disclosure. This summary is not an extensive overview of the present disclosure. It is not intended to identify the key/critical elements of the invention or to delineate the scope of the disclosure. Its sole purpose is to present some concept of the disclosure in a simplified form as a prelude to a more detailed description of the disclosure presented later.

Disclosed is an inhaler for inhaling powdered pharmaceutical compositions from capsules which are inserted in a medication holder provided in the inhaler before use. After the capsule has been inserted in the medication holder of the device, the patient can press an actuating member which can be moved from a resting position, thereby cooperating with at least one piercing element which can enter into the medication holder. The capsule is pierced by the minimum of one piercing element and the pharmaceutical composition is released.

Other aspects, advantages, and salient features of the disclosure will become apparent to those skilled in the art from the following detailed description, which, taken in conjunction with the annexed drawings, discloses exemplary embodiments of the disclosure.

The inhaler according to the present disclosure as shown in the figures 1, 2, 3 and 4 essentially comprises of a housing (2) which accommodates the base plate (4) and is covered by the latter, the mouthpiece (3) with gripping aid (9); the said base plate (4) is joined to the hinge (6) and the mouthpiece (3) and the lid (1) is hinged together distinctly from the base plate to hinge (8); The gripping aid (9) is disposed distal to the actuating member (5).Inspectional window (7) further allows to inspect the internal elements of the device. A medicament holder (10) is mounted on the underside of the base plate (4). One or more piercing elements (11) for piercing the capsules are attached from inside of the actuating member (5) and a spring (12) is also configured to link the actuating member; characterized in that the actuator when pressed from outside, the spring element (12) gets compressed and

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enables the piercing elements (11) to move linearly and pierce the capsule such that the medicament inside the capsule is released and the spring element retracts thereafter.

The terms and words used in the following description and claims are not limited to the bibliographical meanings, but, are merely used to enable a clear and consistent understanding of the disclosure.

Lid (1) offers protection to the device components by preventing entry of dust or any other extraneous particles.

Mouthpiece (3) is the component through which the patient inhales the powdered pharmaceutical composition.

Base plate (4) ensures that the medicament holder (10) is held securely and always remains aligned to the mouth piece (3) for a smooth flow of the medicament.

Actuating member (5) is responsible for locking & unlocking of the lid (1) and holds the piercing elements (11) in an appropriate position. When the actuating member (5) is moved forward, it ensures appropriate piercing of the capsule in such a way that the powdered pharmaceutical composition is available for inhalation by the patient.

Hinge (6) is responsible for holding the base plate (4) in an appropriate position in such a way that the medicament holder (10) is always aligned to the mouth piece (3).

Inspection window (7) provides a view of the medicament holder (10) and allows the patient to confirm the presence of capsule in the medicament holder (10).

Hinge (8) is responsible for appropriate movement of the lid (1) and mouth piece (3).

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Gripping aid (9) on the mouth piece offers a grip for the patient to open the mouth piece so that the capsule containing the powdered pharmaceutical composition could be placed in the medicament holder (10).

In an embodiment of present disclosure, the inhaler is operated in the following manner.

a) The lid (1) is opened by pressing the actuating member (5)
b) The lid (1) is pulled upwards and away from the base to expose the mouthpiece (3)
c) The mouthpiece (3) is opened by pulling the gripping aid (9) located on both sides of the mouthpiece (3).
d) The capsule is placed in the medicament holder (10) of the inhaler of the present invention
e) The mouthpiece (3) is closed firmly. The lid (1) is kept open.
f) The inhaler of the present invention is held in such a position that the mouthpiece (3) is pointed upwards
g) The actuating member (5) is pressed to move the piercing element (11) to pierce the capsules.
h) The powdered pharmaceutical composition is inhaled from the capsule.

The device may be made from any suitable material. In some embodiments, the device is made of plastic, for example ABS (acrylonitrile butadiene styrene), PC (polycarbonate), PA (polyacetal) or PS (polystyrene), or mixtures thereof, or of an antistatic material such as delrin or stainless steel

The inhaler according to the disclosure allows the pharmaceutical composition to be delivered more reliably compared to the devices known from the prior art.

Some advantages of the present inhaler are as follows.

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1. The patient is required to open the base plate only as and when required. Use of second and distinct hinge prevents the accidental opening of the base plate, thereby avoiding the contamination of the medicament.
2. Also, the non-protruding actuating member makes handling of the device and storing of the device, very convenient.
3. Further, the shape of the inhaler which is round across the top and on one side, is configured at an angle in such a way that patient is able to have an appropriate grip on the device and finds it very convenient to actuate the device without losing control over the holding of the device

An inhaler device with a two-hinge system utilizing a base plate devoid of any holes was measured to have a flow resistance of about 0.07 /L min^{-1}, resulting in a flow rate of about 40 L min^{-1} with a pressure drop of about 4 kPa across the inhaler.

The flow resistance can be calculated using the formulae: $R = P^{0.5} / Q$

where Q is the flow rate (L/min), P is the pressure drop (kPa) across the inhaler and R is the flow resistance [$kPa^{0.5}$/ (L/min)].

In the system, the inhalation pressure drops of between 2 kpa and 6 kpa produced resultant flow rates of about between 25 and 55 liters per minute.

The present disclosure relates to the use of an inhaler device as described above for the administration of powdered pharmaceutical composition that is suitable for the treatment of asthma or chronic obstructive pulmonary disease by inhalation.

The pressure drop versus flow rate curve depends upon the construction of the inhaler.

The inhaler in accordance with the present disclosure was tested to measure its resistance to flow which is an important characteristic of inhalers.

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According to the Bernoulli principle, when the square root of the pressure drop is plotted versus the flow rate, the resistance of the inhaler is the slope of the linear portion of the curve. An exemplary graph can be seen in Fig 8 for an inhaler device in accordance with the present invention. The graph depicted in Fig 8 indicates relatively high resistance to air flow, the curve increasing rapidly with the flow rate.

The inhaler according to the present disclosure may include design features provided by the recognition that different powdered drugs have different characteristics. Thus, for increased delivery efficiency, the flow parameters of the inhaler should advantageously be adjusted for the specific drug being delivered. These adjustments can be made by adjusting the air flow. The air flow can be controlled by drilling additional air supply hole or by increasing and decreasing the size of the opening of the air supply hole.

In some embodiments, the powdered pharmaceutical composition contained within the capsule is a dry powder medicament. The term capsule is intended to be understood broadly and includes any suitable receptacle for powdered pharmaceutical compositions. The capsule may be formed from any suitable material, including gelatin, HPMC, or plastic.

In an embodiment, the disclosure provides pharmaceutical composition which includes powdered pharmaceuticals can be administered by inhalation. Particularly preferred in this context are pharmaceutical compositions selected from among the anticholinergics, beta-2-agonists, steroids, PDE IV-inhibitors, LTD4-antagonists and EGFR-kinase inhibitors.

Anticholinergics for use may be selected from among TIOTROPIUM bromide, oxitropium bromide, flutropium bromide, ipratropium bromide, glycopyrronium salts, trospium chloride, tolterodine, tropenol 2,2-diphenylpropionate methobromide, scopine 2,2-diphenylpropionate methobromide, scopine 2-fluoro-2,2-diphenylacetate methobromide, tropenol 2-fluoro-2,2-diphenylacetate methobromide, tropenol 3,3',4,4'-tetrafluorobenzilate methobromide, scopine

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3,3',4,4'-tetrafluorobenzilate methobromide, tropenol 4,4'-difluorobenzilate methobromide, scopine 4,4'-difluorobenzilate methobromide, tropenol 3,3'-difluorobenzilate methobromide, scopine 3,3'-difluorobenzilate methobromide, tropenol 9-hydroxy-fluorene-9-carboxylate methobromide, tropenol 9-fluoro-fluorene-9-carboxylate methobromide, scopine 9-hydroxy-fluorene-9-carboxylate methobromide, scopine 9-fluoro-fluorene-9-carboxylate methobromide, tropenol 9-methyl-fluorene-9-carboxylate methobromide, scopine 9-methyl-fluorene-9-carboxylate methobromide, cyclopropyltropine benzilate methobromide, 2,2-diphenylpropionate cyclopropyltropine methobromide, cyclopropyltropine 9-hydroxy-xanthene-9-carboxylate methobromide, cyclopropyltropine 9-methyl-fluorene-9-carboxylate methobromide, cyclopropyltropine 9-methyl-xanthene-9-carboxylate methobromide, cyclopropyltropine 9-hydroxy-fluorene-9-carboxylate methobromide, methyl 4,4'-difluorobenzilate cyclopropyltropine methobromide, tropenol 9-hydroxy-xanthene-9-carboxylate methobromide, scopine 9-hydroxy-xanthene-9-carboxylate methobromide, tropenol 9-methyl-xanthene-9-carboxylate methobromide, scopine 9-methyl-xanthene-9-carboxylate methobromide, tropenol 9-ethyl-xanthene-9-carboxylate methobromide, tropenol 9-difluoromethyl-xanthene-9-carboxylate methobromide and scopine 9-hydroxymethyl-xanthene-9-carboxylate methobromide, optionally in the form of the racemates, enantiomers or diastereomers thereof and optionally in the form of the solvates and/or hydrates thereof.

Beta-2-agonists used may be selected from among albuterol, bambuterol, bitolterol, broxaterol, carbuterol, clenbuterol, fenoterol, formoterol, hexoprenaline, ibuterol, isoetharine, isoprenaline, levosalbutamol, mabuterol, meluadrine, metaproterenol, orciprenaline, pirbuterol, procaterol, reproterol, rimiterol, ritodrine, salmeterol, salmefamol, soterenot, sulphonterol, tiaramide, terbutaline, tolubuterol, CHF-1035, HOKU-81, KUL-1248, 3-(4-{6-[2-hydroxy-2-(4-hydroxy-3-hydroxymethyl-phenyl)-ethylamino]-hexyl- oxy}-butyl)-benzenesulphonamide, 5-[2-(5,6-diethyl-indan-2-ylamino)-1-hydroxy-ethyl]-8-hydroxy-1H-quinolin- -2-one, 4-hydroxy-7-[2-{[2-{[3-(2-phenylethoxy)propyl]sulphonyl}ethyl]-amino}ethyl]-2(3H)-benzothiazolone, 1-(2-fluoro-4-hydroxyphenyl)-2-[4-(1-benzimidazolyl)-2-methyl-2-butylamin- o]ethanol, 1-[3-(4-methoxybenzyl-amino)-4-hydroxyphenyl]-2-[4-(1-

benzimida- zolyl)-2-methyl-2-butylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-[3-(4-N,N-dimethylaminoph- enyl)-2-methyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-[3-(4-methoxyphenyl)-2-me- thyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-[3-(4-n-butyloxyphenyl)-2- -methyl-2-propylamino]ethanol, 1-[2H-5-hydroxy-3-oxo-4H-1,4-benzoxazin-8-yl]-2-{4-[3-(4-methoxyphenyl)-1- ,2,4-triazol-3-yl]-2-methyl-2-butylamino}ethanol, 5-hydroxy-8-(1-hydroxy-2-isopropylaminobutyl)-2H-1,4-benzoxazin-3-(4H)-on- e, 1-(4-amino-3-chloro-5-trifluoromethylphenyl)-2-tert.-butylamino)ethanol and 1-(4-ethoxycarbonylamino-3-cyano-5-fluorophenyl)-2-(tert.-butylamino)- ethanol, optionally in the form of the racemates, enantiomers or diastereomers thereof and optionally in the form of ihrer pharmacologically acceptable acid addition salts, solvates and/or hydrates thereof.

The steroids used may be selected from among prednisolone, prednisone, butixocortpropionate, RPR-106541, flunisolide, beclomethasone, triamcinolone, budesonide, fluticasone, mometasone, ciclesonide, rofleponide, ST-126, dexamethasone, (S)-fluoromethyl6.quadrature.,9.quadrature.-difluoro-17.quadrature.-[(2-f- uranylcarbonyl)oxy]-11.quadrature.-hydroxy-16.quadrature.-methyl-3-oxo-and- rosta-1,4-diene-17.quadrature.-carbothionate, (S)-(2-oxo-tetrahydro-furan-3S-yl) 6.quadrature.,9.quadrature.-difluoro-11.quadrature.-hydroxy-16.quadrature- .-methyl-3-oxo-17.quadrature.-propionyloxy-androsta-1,4-diene-17.quadratur- e.-carbothionate and etiprednol-dichloroacetate (BNP-166), optionally in the form of the racemates, enantiomers or diastereomers thereof and optionally in the form of the salts and derivatives thereof, the solvates and/or hydrates thereof.

PDE IV inhibitors used may be selected from among enprofyllin, theophyllin, roflumilast, ariflo (cilomilast), CP-325,366, BY343, D-4396 (Sch-351591), AWD-12-281 (GW-842470), N-(3,5-dichloro-1-oxo-pyridin-4-yl)-4-difluoromethoxy-3-cyclopropylmethox- ybenzamide, NCS-613, pumafentine, (-)p-[(4aR*,10bS*)-9-ethoxy-1,2,3,4,4a,10b-hexahydro-8-methoxy-2-methylbe- nzo[s][1,6]naphthyridin-6-yl]-N,N-diisopropylbenzamide, (R)-(+)-1-(4-bromobenzyl)-4-[(3-cyclopentyloxy)-4-methoxyphenyl]-2-pyrrol- idone, 3-(cyclopentyloxy-

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4-methoxyphenyl)-1-(4-N'-[N-2-cyano-S-methyl-isot- hioureido]benzyl)-2-pyrrolidone, cis[4-cyano-4-(3-cyclopentyloxy-4-methoxyphenyl)cyclohexane-1-carboxylic acid], 2-carbomethoxy-4-cyano-4-(3-cyclopropylmethoxy-4-difluoromethoxyph- enyl)cyclohexan-1-one, cis[4-cyano-4-(3-cyclopropylmethoxy-4-difluoromethoxyphenyl)cyclohexan-1-- ol], (R)-(+)-ethyl[4-(3-cyclopentyloxy-4-methoxyphenyl)pyrrolidin-2-yliden- e]acetate, (S)-(-)-ethyl[4-(3-cyclopentyloxy-4-methoxyphenyl)pyrrolidin-2-- ylidene]acetate, CDP840, Bay-198004, D-4418, PD-168787, T-440, T-2585, arofyllin, atizoram, V-11294A, CI-1018, CDC-801, CDC-3052, D-22888, YM-58997, Z-15370, 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(2-thienyl)-9H-pyrazolo[3,4-c]-1,2,4-- triazolo[4,3-a]pyridine and 9-cyclopentyl-5,6-dihydro-7-ethyl-3-(tert-butyl)-9H-pyrazolo[3,4-c]-1,2,4- -triazolo[4,3-a]pyridine, optionally in the form of the racemates, enantiomers or diastereomers thereof and optionally in the form of the pharmacologically acceptable acid addition salts thereof, solvates and/or hydrates thereof.

LTD4-antagonists used may be selected from among montelukast, 1-(((R)-(3-(2-(6,7-difluoro-2-quinolinyl)ethenyl)phenyl)-3-(2-(2-hydroxy-- 2-propyl)phenyl)thio)methylcyclopropane-acetic acid, 1-(((1(R)-3(3-(2-(2,3-dichlorothieno[3,2-b]pyridin-5-yl)-(E)-ethenyl)phen- yl)-3-(2-(1-hydroxy-1-methylethyl)phenyl)propyl)thio)methyl)cyclopropanace- tic acid, pranlukast, zafirlukast, [2-[[2-(4-tert-butyl-2-thiazolyl)-5-benzofuranyl]oxymethyl]phenyl]acetic acid, MCC-847 (ZD-3523), MN-001, MEN-91507 (LM-1507), VUF-5078, VUF-K-8707 and L-733321, optionally in the form of the racemates, enantiomers or diastereomers thereof, optionally in the form of the pharmacologically acceptable acid addition salts thereof as well as optionally in the form of the salts and derivatives thereof, the solvates and/or hydrates thereof.

EGFR-kinase inhibitors used may be selected from among cetuximab, trastuzumab, ABX-EGF, Mab ICR-62, 4-[(3-chloro-4-fluorophenyl)amino]-6-{[4-(morpholin-4-yl)-1-oxo-2-buten-1- -yl]amino}-7-cyclopropylmethoxy-quinazoline, 4-[(R)-(1-phenyl-ethyl)amino]-6-{[4-(morpholin-4-yl)-1-oxo-2-buten-1-yl]-- amino}-7-cyclopentyloxy-quinazoline, 4-[(3-

chloro-4-fluoro-phenyl)amino]-6-{[4-((R)-6-methyl-2-oxo-morpholin-4- -yl)-1-oxo-2-buten-1-yl]amino}-7-[(S)-(tetrahydrofuran-3-yl)oxy]-quinazoli- ne, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[2-((S)-6-methyl-2-oxo-morpholin- -4-yl)-ethoxy]-7-methoxy-quinazoline, 4-[(3-chloro-4-fluorophenyl)amino]-6-({4-[N-(2-methoxy-ethyl)-N-methyl-am- ino]-1-oxo-2-buten-1-yl}amino)-7-cyclopropylmethoxy-quinazoline, 4-[(R)-(1-phenyl-ethyl)amino]-6-({4-[N-(tetrahydropyran-4-yl)-N-methyl-am- ino]-1-oxo-2-buten-1-yl}amino)-7-cyclopropylmethoxy-quinazoline, 4-[(3-chloro-4-fluorophenyl)amino]-6-({4-[N-(2-methoxy-ethyl)-N-methyl-am- ino]-1-oxo-2-buten-1-yl}amino)-7-cyclopentyloxy-quinazoline, 4-[(3-chloro-4-fluorophenyl)amino]-6-{[4-(N,N-dimethylamino)-1-oxo-2-bute- n-1-yl]amino}-7-[(R)-(tetrahydrofuran-2-yl)methoxy]-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6,7-bis-(2-methoxy-ethoxy)-quinazoline, 4-[(R)-(1-phenyl-ethyl)amino]-6-(4-hydroxy-phenyl)-7H-pyrrolo[2,3-d]pyrim- idine, 3-cyano-4-[(3-chloro-4-fluorophenyl)amino]-6-{[4-(N,N-dimethylamino-)-1-oxo-2-buten-1-yl]amino}-7-ethoxy-quinoline, 4-[(R)-(1-phenyl-ethyl)amino]-6-{[4-((R)-6-methyl-2-oxo-morpholin-4-yl)-1- -oxo-2-buten-1-yl]amino}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluorophenyl)amino]-6-{[4-(morpholin-4-yl)-1-oxo-2-buten-1- -yl]amino}-7-[(tetrahydrofuran-2-yl)methoxy]-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-{[4-(5,5-dimethyl-2-oxo-morpholin-4-yl)-1-o- xo-2-buten-1-yl]amino}-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{2-[4-(2-oxo-morpholin-4-yl)-piperi-din-1-yl]-ethoxy}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-amino-cyclohexan-1-yloxy)-- 7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-methanesulphonylamino-cycl- ohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(tetrahydropyran-3-yloxy)-7-methoxy- -quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{1-[(morpholin-4-yl)carbonyl]-piper- idin-4-yloxy}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(piperidin-3-yloxy)-7-methoxy-quina- zoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[1-(2-acetylamino-ethyl)-piperidin-4-yloxy]-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(tetrahydropyran-4-yloxy)-7-ethoxy-- quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{trans-4-[(morpholin-4-yl)carbonyla- mino]-cyclohexan-1-yloxy}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{1-[(piperidin-1-yl)carbonyl]-piper- idin-4-yloxy}-7-

methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(cis-4-{N--[(morpholin-4-yl)carbony- l]-N-methyl-amino}-cyclohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-ethansulphonylamino-cycloh- exan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(1-methanesulphonyl-piperidin-4-yloxy)-7-(2-methoxy-ethoxy)-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[1-(2-methoxy-acetyl)-piperidin-4-y- loxy]-7-(2-methoxy-ethoxy)-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-(tetrahydropyran-4-yloxy]-7-methoxy-quinazo- line, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(cis-4-{N-[(piperidin-1-yl)car- bonyl]-N-methyl-amino}-cyclohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{cis-4-[(morpholin-4-yl)carbonylami- no]-cyclohexan-1-yloxy}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{1-[2-(2-oxopyrrolidin-1-yl)ethyl]-- piperidin-4-yloxy}-7-methoxy-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-(1-acetyl-piperidin-4-yloxy)-7-methoxy-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-(1-methyl-piperidin-4-yloxy)-7-meth- oxy-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-(1-methanesulphonyl-piperidin-4-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(1-methyl-piperidin-4-yloxy)-7(2-me- thoxy-ethoxy)-quinazoline, 4-[(3-ethynyl-phenyl)amino]-6-{1-[(morpholin-4-yl)carbonyl]-piperidin-4-y- loxy}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{1-[(N-methyl-N-2-methoxyethyl-amin- o)carbonyl]-piperidin-4-yloxy}-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(1-ethyl-piperidin-4-yloxy)-7-metho- xy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[cis-4-(N-methanesulphonyl-N-methyl- -amino)-cyclohexan-1-yloxy]-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[cis-4-(N-acetyl-N-methyl-amino)-cy- clohexan-1-yloxy]-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-methylamino-cyclohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[trans-4-(N-methanesulphonyl-N-meth- yl-amino)-cyclohexan-1-yloxy]-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-dimethylamino-cyclohexan-1- -yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(trans-4-{N-[(morpholin-4-yl)carbonyl]-N-methyl-amino}-cyclohexan-1-yloxy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-[2-(2,2-dimethyl-6-oxo-morpholin-4-- yl)-ethoxy]-7-[(S)-(tetrahydrofuran-

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2-yl)methoxy]-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(1-methanesulphonyl-piperidin-4-ylo- xy)-7-methoxy-quinazoline, 4-[(3-chloro-4-fluoro-phenyl)amino]-6-(1-cyano-piperidin-4-yloxy)-7-metho- xy-quinazoline, and 4-[(3-chloro-4-fluoro-phenyl)amino]-6-{1-[(2-methoxyethyl)carbonyl]-piper- idin-4-yloxy}-7-methoxy-quinazoline, optionally in the form of the racemates, enantiomers or diastereomers thereof, optionally in the form of the pharmacologically acceptable acid addition salts thereof, the solvates and/or hydrates thereof.

Examples of acid addition salts with pharmacologically acceptable acids which the compounds may be capable of forming include salts selected from among the hydrochloride, hydrobromide, hydroiodide, hydrosulphate, hydrophosphate, hydromethanesulphonate, hydronitrate, hydromaleate, hydroacetate, hydrobenzoate, hydrocitrate, hydrofumarate, hydrotartrate, hydrooxalate, hydrosuccinate, hydrobenzoate and hydro-p-toluenesulphonate, preferably hydrochloride, hydrobromide, hydrosulphate, hydrophosphate, hydrofumarate and hydromethanesulphonate.

The powdered pharmaceutical compositions may contain the above-mentioned active substances as well as the salts, esters thereof, or combinations of these active substances, salts and esters.

Although the invention herein has been described with reference to particular embodiments, it is to be understood that these embodiments are merely illustrative of the principles and applications of the present invention. It is therefore to be understood that numerous modifications may be made to the illustrative embodiments and that other arrangements may be devised without departing from the spirit and scope of the present invention.

In the claims which follow and in the preceding description of the invention, except where the context requires otherwise due to express language or necessary implication, the word “comprise” or variations such as “comprises” or “comprising” is used in an inclusive sense,

i.e. to specify the presence of the stated features but not to preclude the presence or addition of further features in various embodiments of the invention.

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CLAIMS

1. An inhaler device comprising:
- a housing,
-a base plate covering the housing,
- a medicament holder integrated with the base plate,
- a mouthpiece sitting over the base plate,
- a lid which covers the mouthpiece,
- at least one piercing element,
- an actuating member,
- a spring configured to link the actuating member to medicament holder,
wherein the inhaler device is a two-hinge system, said hinges being included in the housing, wherein
- the base plate is joined to hinge;
- the mouthpiece and the lid are joined to another hinge,
wherein
- the base plate is hinged separately from the mouthpiece and lid.

2. An inhaler device according to claim 1, wherein the at least one piercing element is attached from inside of the actuating member.

3. An inhaler device according to either claim 1 or claim 2, wherein in order to assist piercing, the actuating member when pressed causes the spring element to get compressed which enables the at least one piercing element to move linearly.

4. An inhaler device according to any one of the preceding claims, wherein the device further comprises a gripping aid on the mouthpiece which offers a grip to open the mouthpiece.

5. An inhaler device according to any one of the preceding claims, wherein the device further comprises an inspection window to see across the inhaler device.

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6. An inhaler device according to claim 4, wherein the gripping aid is disposed distal to the actuating member.

7. An inhaler device according to any one of the preceding claims, wherein the medicament holder is mounted on the underside of the base plate.

8. An inhaler device according to any one of the preceding claims, wherein the base plate is devoid of any holes.

9. An inhaler device according to any one of the preceding claims, wherein the medicament holder is designed to contain a capsule with powdered pharmaceutical composition.

10. An inhaler device according to claim 9, wherein the powdered pharmaceutical composition is suitable for the treatment of asthma or chronic obstructive pulmonary disease by inhalation.

11. An inhaler device according to claim 9, wherein the powdered pharmaceutical composition contained within the capsule is a dry powder medicament.

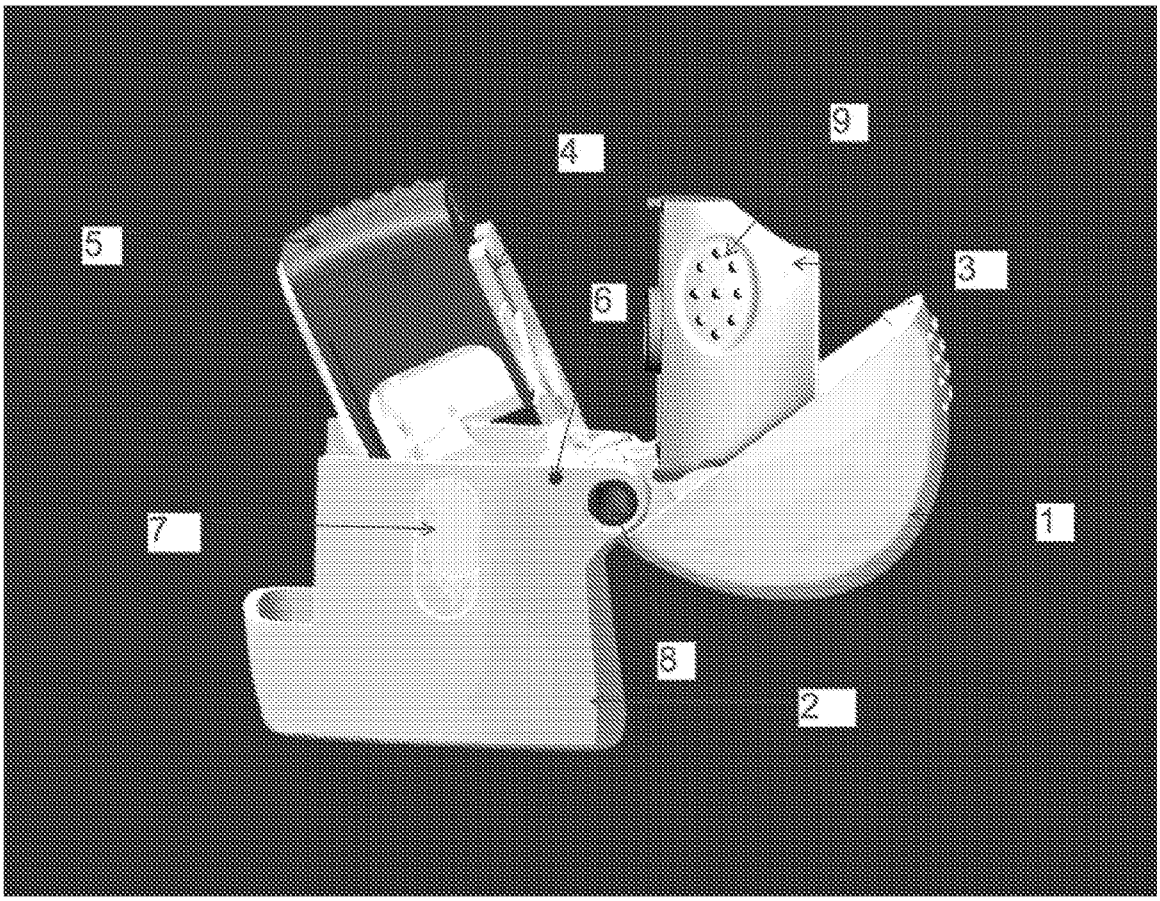

Figure 1

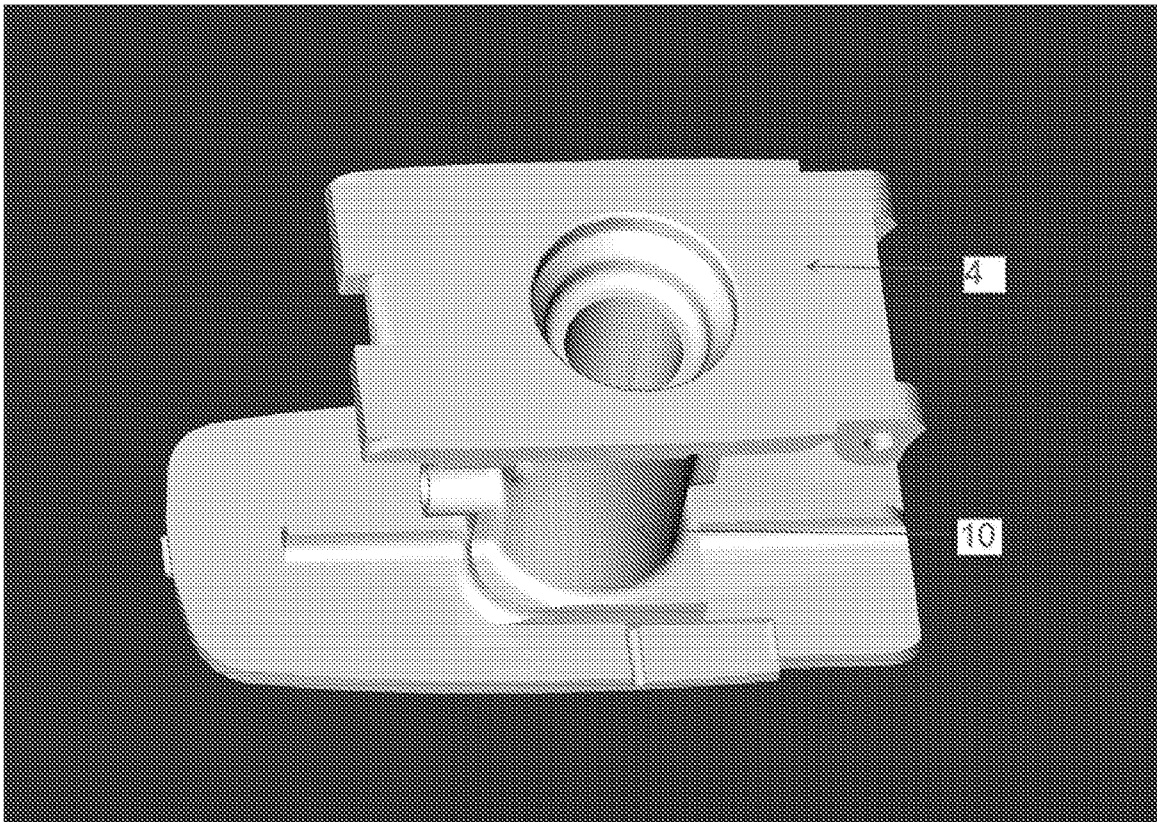

Figure 2

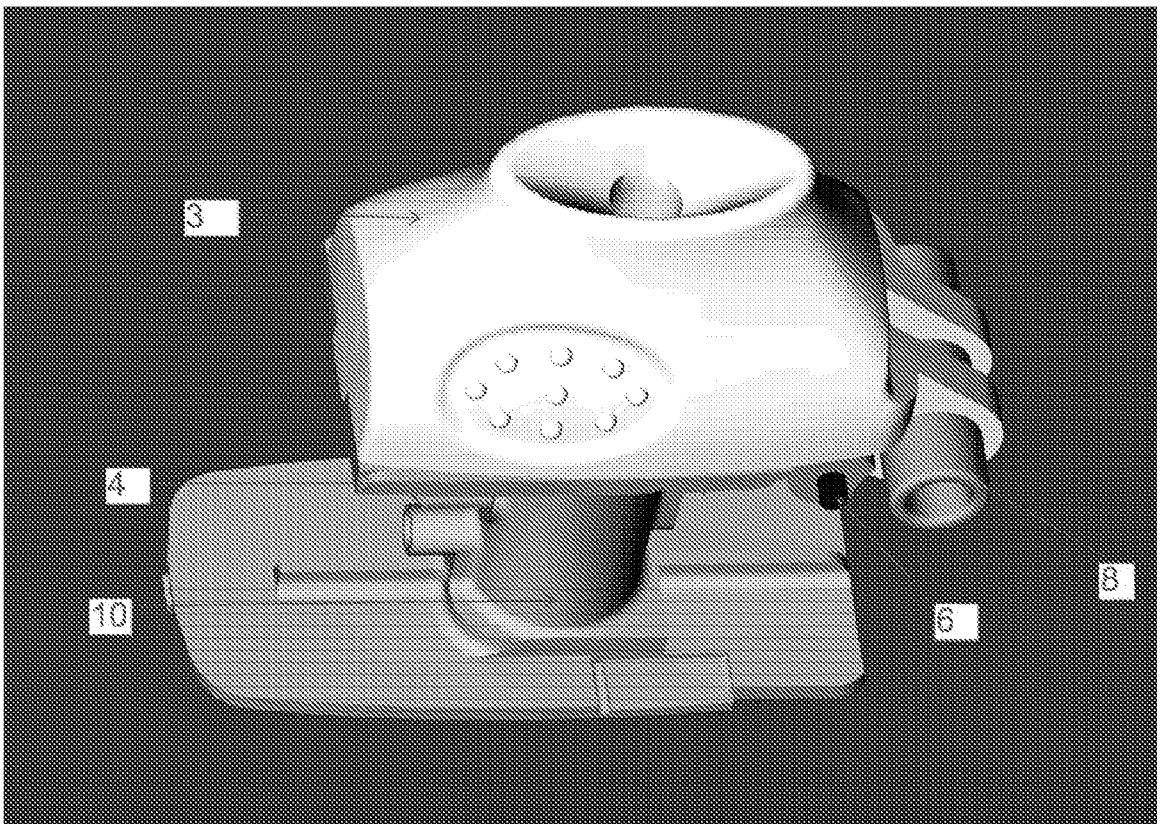

Figure 3

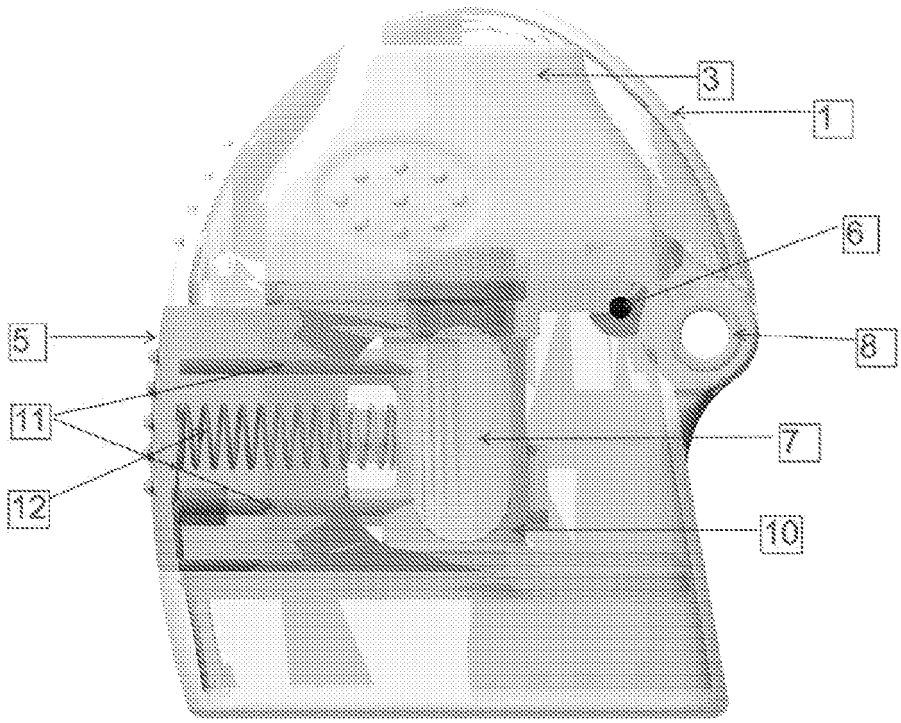

Figure 4

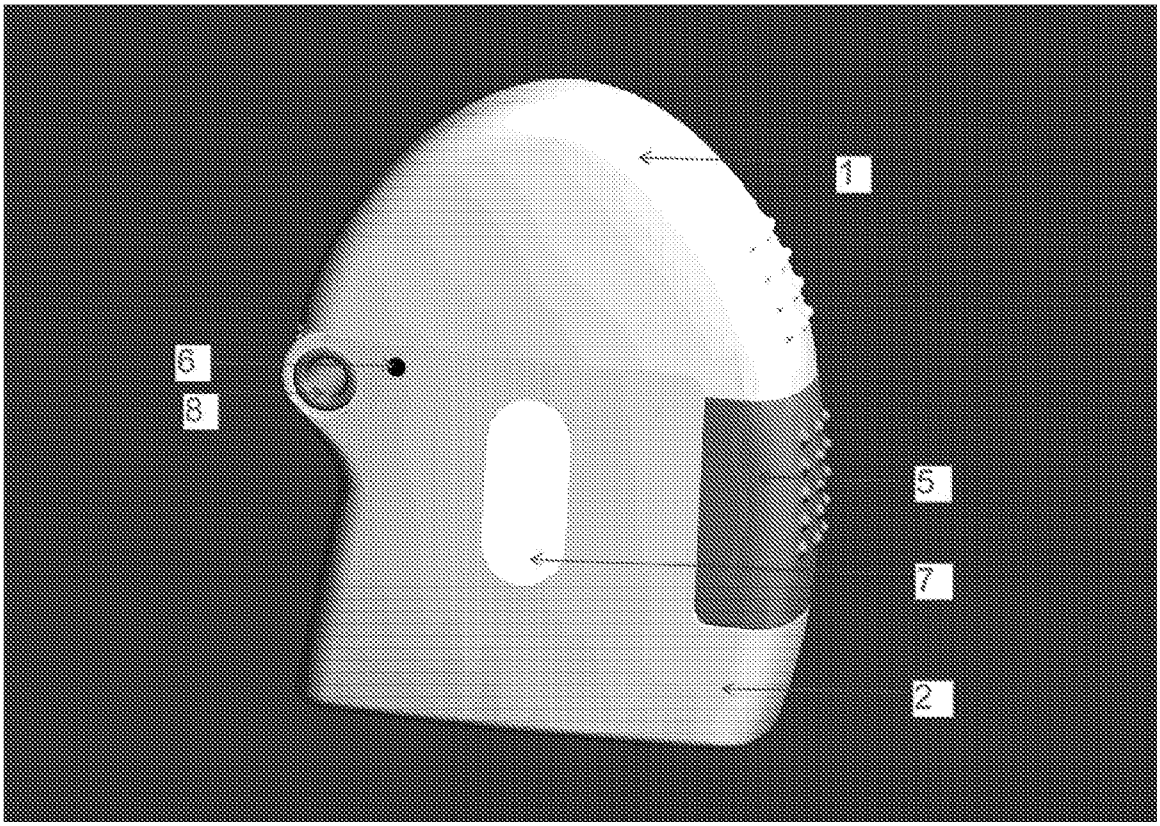

Figure 5

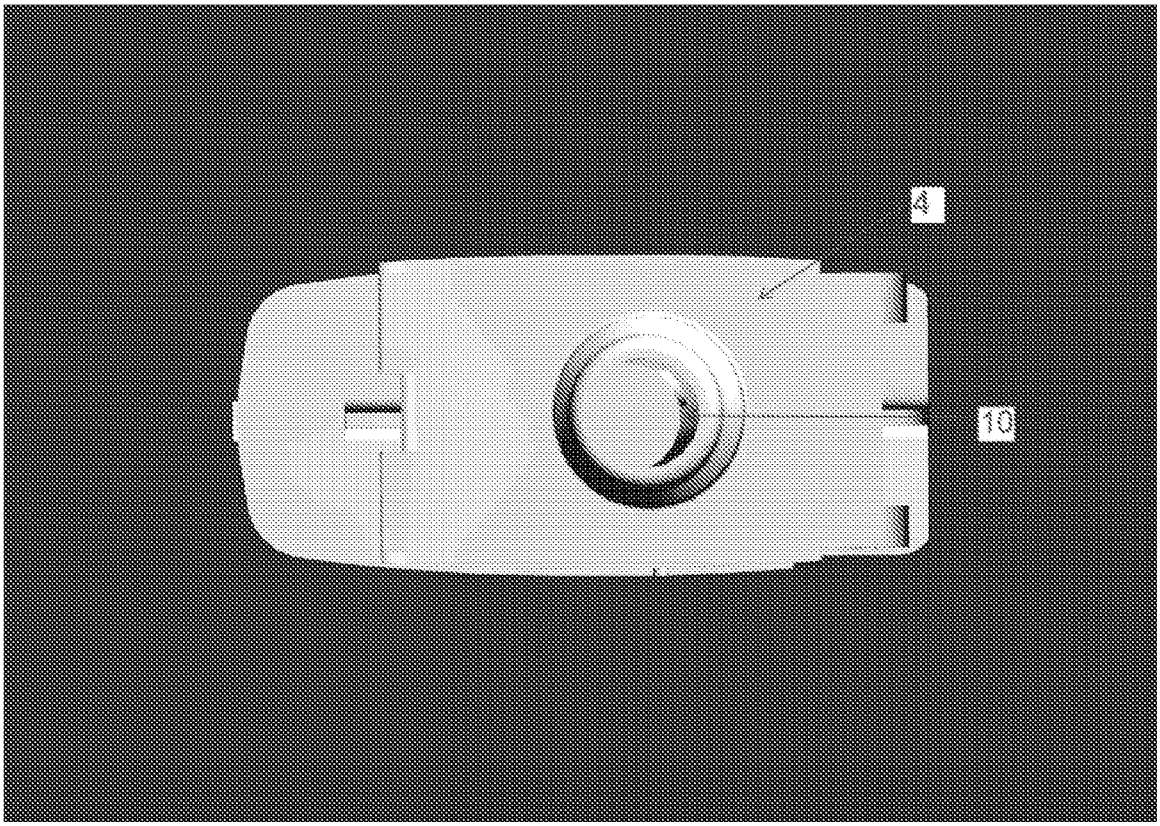

Figure 6

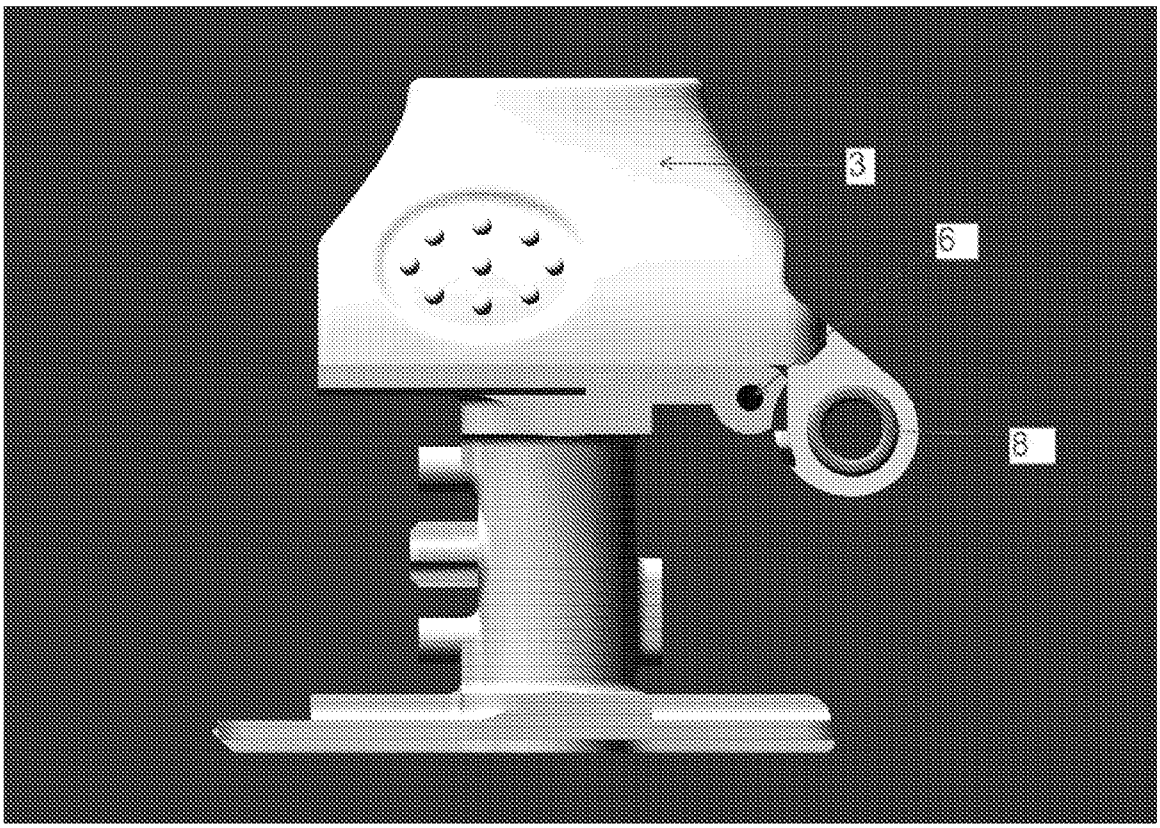

Figure 7

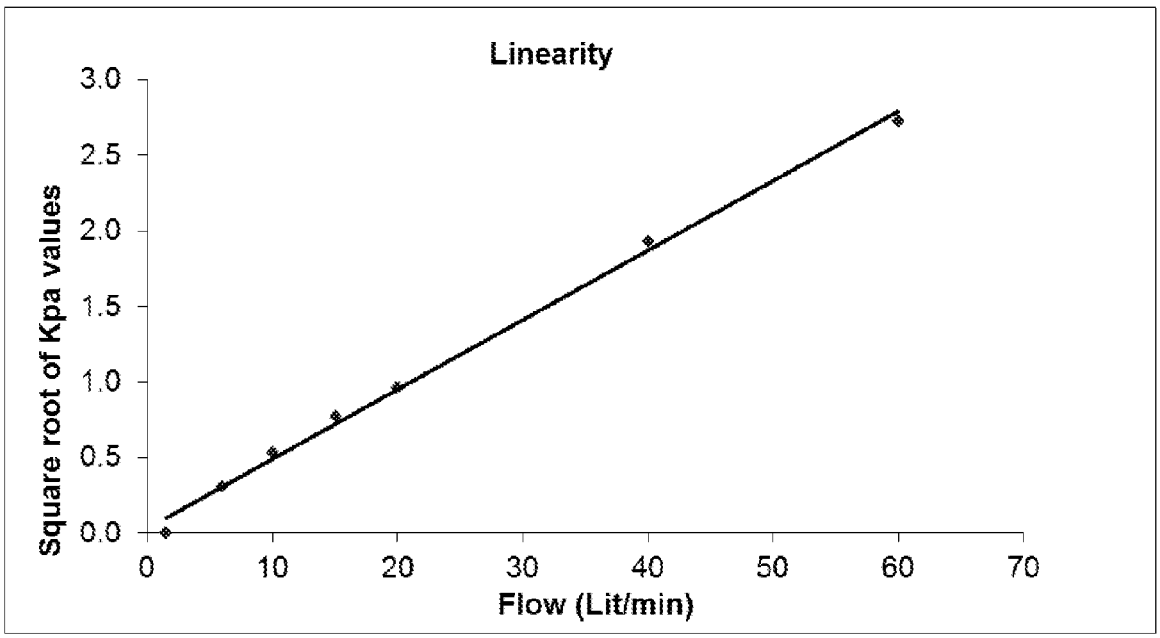
Linearity
Square root of Kpa values
3.0
2.5
2.0
1.5
1.0
0.5
0.0
0
10
20
30
40
50
60
70
Flow (Lit/min)

Figure 8