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A Pressure Equalising Device for a Double Container

The invention relates to a pressure equalising device for a double container which comprises a stiff outer container and a collapsible inner container. The inner container contains a liquid.

The invention aims to provide a device which is suitable for pressure equalisation between the ambient air and the gas space between the inner container and outer container, which is economical to produce and which is protected from obstruction.

It is known for fluids which contain a medicament, for example, to be stored until use in a flexible inner container disposed in a stiff outer container. When liquid is taken from the inner container by means of a metering pump the inner container collapses. If the outer container does not include an opening, a reduced pressure is produced in the closed intermediate space between the two containers. When using a metering pump which can generate only a low suction pressure, it becomes more difficult to draw off liquid as soon as the reduced pressure between the two containers has become of approximately the same magnitude as the suction pressure. It is then necessary to bring about a pressure equalisation effect in the intermediate space between the two containers.

DE 41 39 555 describes a container comprising a stiff outer container and an easily deformable inner bag. That container is produced by a co-extrusion blow moulding process from two thermoplastic materials which do not form a join to each other. The outer container has a closed bottom and contains at least one opening for pressure equalisation between the ambient atmosphere and the space between the outer container and the inner bag. In its shoulder portion the outer container has at least one unwelded seam between two mutually oppositely disposed outer container wall portions which are not welded to each other. Preferably, two unwelded seams are provided in the shoulder region of the outer container. The inner bag is sealingly closed in that region by welded seams. Air can pass into the intermediate space between the outer container and the inner bag through the unwelded seam portions in the shoulder region of the outer container. The edges which are not welded together at the open seam in the shoulder region of the outer container tend to come to bear



against each other in the presence of reduced pressure. For that reason, it is further proposed that preferably a plurality of holes be provided in the upper region of the wall of the outer container as venting openings, the holes being produced by ultrasound or mechanically by perforating the outer container, for example. All openings in the wall of the outer container in the shoulder region and the upper wall region are covered over by means of the housing of the pump which can be fitted onto the container.

The double containers in accordance with the state of the art contain open seams or holes in the outer container. Without exception, the outer container comprises a thermoplastic material.

If the flexible inner container is not completely diffusion-tight and the liquid in the inner container is volatile or contains volatile components, liquid is lost in the inner container due to diffusion, or the composition of the liquid changes in a manner which is possibly unacceptable. That effect is promoted, if, after the pressure equalisation has ended, no more air flows into the intermediate space between the outer container and the inner container for a long time, and if the cross-section of the pressure equalisation openings in the outer container are as in known double containers.

Therefore, the problem is set of providing a device for a double container which is suitable for pressure equalisation between the ambient air and the gas space between the inner container and the outer container, even when the inner container contains a liquid which is volatile or which contains a volatile component, in relation to which the inner container is limitedly diffusion-tight. Even when the filled double container is stored for many years and used for the prescribed number of months, the quantity of liquid in the inner container, or the concentration of liquid components should only change to an extent which is considerably less than when one of the known double containers is used.

In accordance with the invention, that object is attained by a pressure equalising device for a double container which consists of an outer container and an inner container and the inner container contains, at least partially volatile, fluid, and the double container is disposed in an ambient environment, wherein

- The inner container is diffusion-tight to a limited extent vis-à-vis the at least partially volatile fluid, and is collapsible, and the outer container is diffusion-tight and rigid.
- The outer container is sealingly connected to the inner container.
- A gas-filled intermediate space is present between the two containers.
- At least one passage communicates the gas-filled intermediate space between the outer container and the inner container with the ambient environment of the double container.
- The at least one passage has a cross-sectional area with an equivalent diameter of between 10 and 500 μm .
- The length of the at least one passage is between five thousand times and one tenth of the equivalent diameter of the at least one passage.

The equivalent diameter of the at least one passage is the diameter of a circle, the surface area of which is equal to the cross-sectional surface area of the at least one passage. The at least one passage can preferably be from one hundred times to one tenth, particularly preferably from ten times to once, as long as the equivalent diameter of the at least one passage.

The passage is preferably of a cross-section which is approximately as wide as it is high, that is to say preferably a round or approximately square cross-section or a triangular cross-section. The passage cross-section can also be of a rectangular, trapezoidal, semi-round, slot-shaped or irregular configuration. The ratio of the lengths of the sides of a slot-shaped passage can be up to 50 to 1. A plurality of passages may be arranged regularly, e.g. on the intersections of a grid, or irregularly, e.g. in statistically distributed configuration. The cross-sectional area of the passage is less than 1 mm^2 and can extend into the region of some thousand square micrometers.

The passage can be straight or curved or can be in the form of a meander, a spiral or a helix. The passage can be provided, preferably in the form of a bore, in the wall of the outer container. In addition, the passage can be disposed in an insert which preferably comprises plastic material and which is fitted sealingly to the wall of the outer container, preferably in an inwardly inverted recess in the bottom of the outer container. In that case, the end of the passage which is towards the intermediate space communicates with an opening in the wall of the outer container. That opening is of a larger cross-section than the passage.

At the one end of the passage, preferably at the end towards the ambient atmosphere, it is possible to arrange a gas-permeable filter, e.g. a fibre fleece or a body of open-pore sintered material, to act as a dust-protection means.

The end of the passage which is towards the ambient atmosphere can be closed, during the period of storage of the double container filled with a liquid, by means of a sealing foil which is completely or partially torn off, or pierced, prior to liquid being drawn off from the inner container for the first time.

The wall of the at least one passage can be smooth or rough.

The at least one passage can be produced in the form of a microbore, e.g. by means of a laser beam, in a plate. A passage in the form of a meander or spiral can be produced, e.g. by selective etching of a silicon surface; a passage of this kind can be of a triangular or trapezoidal cross-section. It is also possible to produce a passage of triangular cross-section and of almost any desired shape by embossing a (metal-) surface. A helical passage can be produced on the peripheral surface of a cylinder which fits in a tube. In addition, a passage of this kind can be arranged on the peripheral surface of a hollow cylinder in which a cylindrical body fits. Passages of virtually any desired shape can be produced by lithography and moulding from plastic material or metal.

The half-lives and the one tenth-lives of pressure equalisation in the case of a pressure difference of 20 hPa (20 mbar) between the ambient atmosphere and the gas space with a volume of 3 millilitres are set out by way of example in the following Table for passages of circular cross-section, of different lengths and of different diameters:

Passage length mm	Passage Diameter μm	Half-Life Hours	One Tenth-Life Hours
0.2	80	1.8	5.8
0.2	70	3.3	10-6
0.2	60	6.4	21.0
0.2	50	13.5	
0.2	50	13.5	
1	75	13.5	
10	133	13.5	
100	236	13.5	

Instead of the one passage, it is possible to provide a plurality of passages of this kind, or it is possible to provide a plate comprising porous material with open pores, e.g. comprising an open-pore sintered material. The pores have a mean pore diameter of between 0.1 μm and 150 μm . The pore volume is from 1% to 40% by volume of the sintered body. The sintered body can consist of plastics material, such as polyethylene, polypropylene, polyvinylidene fluoride, or glass, quartz, ceramic or metal. The plate thickness can be from 1 mm to 5 mm. The preferably round plate can preferably be sealingly fitted into a recess in the bottom of the outer container, e.g. by being glued or pressed therein.

In addition, it is possible to use a permeable diaphragm which contains a plurality of passages of this kind, in the form of a foil, a cloth or a fleece or non-woven fabric; they can comprise a thermoplastic material, such as polytetrafluoroethylene or polyetheretherketone, or an elastomeric plastic material, such as silicone or latex. Permeable diaphragms in the form of a cloth or fleece, or non-woven cloth, can comprise natural fibres, mineral fibres, glass fibres, carbon fibres, metal fibres or plastic fibres. It is also possible to use a permeable diaphragm in the form of a metal such as gold, silicon, nickel or stainless steel, or of glass or ceramic.

The passages in permeable diaphragms of this kind can be arranged irregularly and can be produced by ion bombardment or by plasma etching, for example. The passages can also be arranged regularly and can be produced by lithography and moulding or by laser boring, for example: in that case, the many passages inside the permeable diaphragm can be within

narrow tolerances according to the shape and size of the passage cross-section and according to passage length.

The diffusion-tight outer container preferably comprises a stiff material, e.g. metal. An outer container of this kind facilitates storage and handling of the double container and protects the inner container from external mechanical effects.

The pressure equalising device according to the invention is used, for example, in a double container which is used to accommodate a medical liquid which may, for example, contain a medicament dissolved in a solvent. Suitable solvents are, for example, water, ethanol or mixtures thereof. Examples of medicaments are Berotec (Fenoterol hydrobromide; 1-(3,5-dihydroxy-phenyl)-2-[(1-(4-hydroxy-benzyl)-ethyl]-amino]-ethanol-hydrobromide), Atrovent (Ipratropium bromide), Berodual (a combination of Fenoterol hydrobromide and Ipratropium bromide), Salbutamol (or Albuterol), Combivent, Oxivent (Oxitropium bromide), Ba 679 (Tiotropium bromide), BEA 2108 (di-(2-thienyl)glycolic acid tropenol ester), Flunisolid, Budesonid, and others.

The pressure equalising device according to the invention has the following advantages:

- it does not contain any movable parts and is a static device;
- the gas permeability is adjustable, even when a permeable diaphragm or a sintered plate is used;
- with any pressure difference, it permits pressure equalisation which begins straight away;
- a pressure difference is compensated gradually. The time constant, and thus duration, of the pressure equalisation effect can be adapted during prescriptive use to the progress in terms of time of the metered drawing off of liquid from the inner container;
- it can be used for diffusion-tight outer containers of any material. The outer container can consist of a stiff material – such as metal or plastic – or a flexible material;
- it does not permit any accidental intervention in the gas space between the outer container and inner container, and it protects the collapsible inner container;
- the pressure difference is practically zero after the pressure-equalisation time,
- it produces a defined communication between the gas space and the ambient air;
- it is gas-permeable when the sealing foil is removed, and permits gas to pass in both

directions;

- it does not require any intervention from the outside and no outside force and is continuously operative;
- a volatile substance which has diffused from the liquid present in the inner container, through the wall of the inner container, into the intermediate space between the inner container and outer container escapes from the intermediate space predominantly by diffusion through the at least one passage. This means that even over a long period of use of the liquid in the inner container only a very small proportion of a volatile substance is lost from the liquid in the inner container. This loss is significantly less than with known double containers.
- the double container containing a liquid in the inner container can be stored for many months without a noticeable loss of substance, even with the limited diffusion sealing integrity in respect of the inner container, and is usable for several months;
- it can be produced economically in large numbers.

The pressure equalisation device according to the invention is used, for example, with a double container which may contain the liquid to be atomised in the atomiser described in WO – 97/12687.

The device according to the invention will be described in greater detail by way of example with the aid of the drawings.

Figure 1a is a view in section through the double container before liquid is drawn off for the first time. The outer container (1) contains the collapsible inner container (2) which is filled with a liquid (3). The draw-off connection (4) projects into the liquid (3). The inner container is sealingly connected by its end (not shown) to the outer container. The gas space (5) is disposed between the two containers. Arranged in the bottom (6) of the outer container is the straight passage (7) which communicates the gas space (5) with the ambient atmosphere outside the double container. That passage is covered over by the sealing foil (8).

Figure 1b shows a section through the double container, after part of the liquid has been drawn off from the inner container. The sealing foil (8) is shown in a condition of being partially torn away, and the inner container is shown as being partially collapsed.

Figure 2 shows a section through a further embodiment of the double container prior to liquid being drawn off from the inner container for the first time. At its end towards the ambient atmosphere, the straight passage (7) is sealingly closed by means of a pressed-in plug (9). This plug is removed by hand by means of the loop (10) before liquid is drawn off from the inner container for the first time.

Figure 3a shows a passage (11) in spiral form with somewhat more than three turns in the outward side of the bottom (6) of the outer container (1). Figure 3b shows a section through this embodiment. The one end of the passage opens into the recess (12), whilst the other end opens into the opening (13). The spiral passage is closed by means of the sealing foil (8) which is pierced by means of the needle (14) before liquid is drawn off for the first time.

Figure 4 shows another embodiment in section through the double container. The bottom (6) of the outer container contains a recess in which the insert (15) is disposed which is sealed off from the wall of the recess by means of the annular seal (17). The insert (15) contains the straight passage (7), one end of which opens into the opening (18) in the bottom of the recess. The filter (16) is disposed in front of the other end of the passage (7).

Figure 5 shows another embodiment in section, wherein the insert (19) is disposed in an inwardly projecting recess in the bottom (6) of the outer container. The insert (19) is fixed in the recess by the snap-action connection (20), and is sealed off from the recess by means of the sealing ring (21). The straight passage (23) is disposed outside the central point of the insert (19). The one end thereof opens into the opening (25) in the bottom of the recess, while the other end thereof opens into an aperture in the insert (19) in which a filter (24) is disposed. The insert (19) contains a further aperture (26). The channel (22) connects the aperture (26) to the aperture for the filter (24). The insert (19) is covered over by means of the sealing foil (8) which is pierced by means of the needle (14) before liquid (3) is drawn off from the inner container (2) for the first time. When the insert (19) is pressed into the recess in the bottom (6) of the container, care is to be taken to ensure that the insert is in the correct position so that the opening (25) is in front of the passage (23).

Figure 6 shows a view in section of an embodiment wherein the insert (27) is also disposed in an inwardly projecting recess in the bottom (6) of the container. The insert (27) is fixed in the recess by means of the snap-action connection (20) and is sealed off from the recess by means

of the sealing ring (21). The straight passage (23) opens into the peripheral groove (28a; 28b) in the insert (27). The peripheral groove can vary in depth. In Figure 6, at the location (28a) in the region of the passage (23) it is shallower than in its remaining part (28b). The opening (25) in the bottom of the recess opens in any azimuthal position of the insert (27) in the peripheral groove (28).

Figure 7 is a view in section of another embodiment. A plate (29) of sintered material is pressed into an inwardly displaced recess in the bottom (6) of the outer container. The recess in the bottom contains the opening (25). During storage time, the bottom of the outer container is covered over by the sealing foil (8) which is pierced or torn off before liquid is drawn off from the inner container for the first time.

Claims

1. A pressure equalising device for a double container which consists of an outer container and an inner container, and the inner container contains a, at least partially volatile, fluid, and the double container is disposed in an ambient environment, wherein

- the inner container is diffusion-tight to a limited extent vis-a-vis the, at least partially volatile, fluid, and is collapsible, and the outer container is diffusion-tight and rigid,
- the outer container is sealingly connected to the inner container,
- a gas-filled intermediate space is present between the two containers,
- at least one passage communicates the gas-filled intermediate space between the outer container and the inner container with the environment of the double container,
- the at least one passage has a cross-sectional area with an equivalent diameter of between 10 μm and 500 μm , and
- the length of the at least one passage is between five thousand times and one tenth of the equivalent diameter of the at least one passage.

2. A pressure equalising device according to claim 1, characterised by

- a passage, the length of which is preferably between one hundred times and one tenth, and particularly preferably between ten times and once, of the equivalent diameter of the at least one passage.

3. A pressure equalising device according to claims 1 or 2, characterised by

- a passage of round, approximately square, triangular, or trapezoidal cross-section.

4. A pressure equalising device according to any one of claims 1 to 3, characterised by

- a passage which is straight, or
- a passage which is shaped in the form of a meander or a spiral or a helix.

5. A pressure equalising device according to any one of claims 1 to 4, characterised by

- a passage which is arranged in the wall of the outer container,
- or a passage which is arranged in an insert which preferably comprises plastic material disposed at the wall of the outer container, preferably in a recess projecting into the outer container, and which communicates with an opening in the wall of the outer container.

6. A pressure equalising device according to any one of claims 1 to 5, characterised by

- a passage with a cross-sectional area of less than 1 square millimeter.

7. A pressure equalising device according to any one of claims 1 to 6, characterised by

- a passage, at one end, preferably at the end facing the ambient atmosphere, of which is arranged a gas-permeable filter.

8. A pressure equalising device according to any one of claims 1 to 7, characterised by

- a passage, the end of which facing the ambient atmosphere is closed by means of a sealing foil.

9. A pressure equalising device according to claim 1, characterised by

- a plurality of passages which communicate the gaseous space between the outer container and the inner container with the ambient atmosphere of the double container, wherein the passages are present in the form of pores in a plate comprising an open-pore sintered material, which has a mean pore diameter of between 0.1 micrometers and 150 micrometers and a pore volume of between 1% and 40% of the volume of the sintered body.

10. A pressure equalising device according to claim 1, characterised by

- a plurality of passages which are present in a permeable diaphragm in the form of a foil, a non-woven cloth or a fleece.

11. A pressure equalising device according to claim 10, characterised by
 - a plurality of passages which are present in a permeable diaphragm comprising a thermoplastic material, such as polytetrafluorethylene or polyetheretherketone,
 - or a plurality of passages which are present in a permeable diaphragm comprising an elastomer, such as silicone or latex.
12. A pressure equalising device according to claim 10, characterised by
 - a plurality of passage which are arranged in a permeable diaphragm in the form of a foil of metal, such as gold, silicon, nickel or stainless steel, or of glass or ceramic, and which are arranged in an irregular or regular manner.
13. A pressure equalising device according to claim 9, characterised by
 - a plurality of passages which are present in the form of pores in a plate comprising an open-pore sintered material, preferably of polyethylene, polypropylene, polyvinylidene fluoride, or of glass, quartz, ceramic or metal.
14. A pressure equalising device according to claim 1, characterised by
 - an outer container comprising a stiff or rigid material, preferably a metal.