

INHALER DEVICE FOR INHALABLE LIQUIDS

FIELD

[0001] The present invention relates to an inhaler device for inhalable liquids, in particular for the administration of inhalable volatile liquids such as halogenated volatile liquids, to a patient.

BACKGROUND

[0002] The storage and administration of inhalable liquids to patients that comprise active agents, or that are themselves the active agent, commonly presents challenges. Active agents such as therapeutic agents or pharmaceutical agents, are often formulated for: oral delivery in the form of tablets and capsules, nasal delivery in the form of sprays, and liquid formulations for intravenous delivery depending on a number of factors.

[0003] Where it is advantageous to administer active agents to a patient's lungs, for example to treat or alleviate respiratory diseases, the active agent may be administered by oral inhalation, alone or in combination with the intranasal inhalation. Suitable inhaler devices may include, for example, metered dose inhalers and dry powder inhalers. These types of inhalation devices typically require pressurised means to deliver the active agent to the desired site of action in the lungs. In addition, liquids that contain active agents or that are themselves the active agent usually require transformation into an inhalable, respirational form at the point of administration to be suitable for delivery.

[0004] Transforming a liquid into an inhalable form, such as by nebulisation or aerosolizing into respirational sized droplets or heating to form a vapour, requires delivery devices to include moving, mechanical, heating and/or electrical means which adds to the complexity of the design, manufacturing and end user costs, the operability and/or patient use.

[0005] The use of volatile liquids as active agents or comprising active agents is known. One such example is halogenated volatile liquids. Halogenated volatile liquids have been described as useful for inducing and/or maintaining anaesthesia (including amnesia, muscle paralysis, and/or sedation) and/or analgesia and may therefore be useful as anaesthetics and/or analgesics. The anaesthetic properties of fluorinated compounds have been known since at least 1946 (Robbins, B.H. J Pharmacol Exp Ther (1946) 86: 197-204). This was followed by the introduction of fluoroxene, halothane and methoxyflurane into clinical use in the 1950s and the subsequent development of enflurane, isoflurane, sevoflurane and desflurane which are in clinical use in some countries today (Terrell, R.C. Anesthesiology (2008) 108 (3): 531-3).

[0006] Halogenated volatile liquids, when used for general anaesthesia, may be delivered under positive pressure to a patient via a delivery system that includes a vaporizer and a flow of

breathable carrier gas. More recently, halogenated volatile liquids have been formulated for use in local or regional anaesthesia and delivery via non-inhalation routes. Examples include: formulation as: microdroplets for intradermal or intravenous injection (e.g. US 4725442; C/143964);

compositions suitable for formulation as a solution, suspension, cream, paste, oil, lotion, gel, foam, hydrogel, ointment, liposome, emulsion, liquid crystal emulsion and nanoemulsions for topical, intrathecal, epidural, transdermal, topical, oral, intra-articular, mucosal, buccal, rectal, vaginal, intramuscular, intravesical and subcutaneous delivery (e.g. WO 2008/070490, WO 2009/094460, WO 2010/129686); and stable and injectable liquid formulations (WO 2013/016511).

[0007] The main considerations for the safe storage and handling of volatile liquids commonly include vapour pressure build up, the robustness of the container, and the integrity of the container seal(s). The chemical nature of the volatile liquid may also be important if the active agent is capable of permeating, solubilizing or otherwise reacting with the container material(s) upon storage. A number of storage containers for halogenated volatile liquids have been described including:

rigid polymeric containers of various shapes and sizes to replace glass vials, such as: capped bottles, large tanks, and shipping containers (e.g. WO 1999/034762, WO2012/116187);

rigid polymeric bottles fitted with a gasketless valve assembly and pliable containers with a threaded spout for fluid connection to deliver liquid anaesthetics to an anaesthetic machine or vaporizer (e.g. WO 2010/135436, WO 2013/106608, WO 2013/149263, WO 2015/034978);

a container with a capped membrane for delivering a stored liquid anaesthetic to a vaporizer via a slotted tube (WO 2009/117529);

and rigid polymeric and aluminium containers optionally coated with materials to impart or enhance vapour barrier characteristics or container inertness (e.g. WO2002/022195, WO 2003/032890, WO 2010/129796).

[0008] Despite the various advances in formulating volatile liquids in non-inhalable forms, such as the halogenated volatile liquids, as well as containers to store them, there still remains a need for inhalable forms of volatile liquids and devices to store and/or administer them to patients.

[0009] Attempts to design new inhalers for inhalable medicines in general are ongoing. For example, WO2008/040062 describes a diverse number of inhaler device concepts that depend on complex constructions and moving parts for storing and/or delivering inhalable liquids and powdered solids into a patient's mouth or nose. The various devices described are adapted to

hold one or two medicament containers in the form of pressurised canisters, ampoules, vials and plungers. The devices are described as being activated by sliding an outer wall of the device in relation to an inner wall of the device to deliver the liquid medication from a medication container. In a number of embodiments, the device includes a moveable mouthpiece which deploys in order to open the air pathway. The device is also described as including one or more one-way valves to provide a unidirectional air flow for one or both inhaled air and exhaled air (a series of one-way valves to direct the flow of inhaled and exhaled air has also been generally described in WO 2007/033400 which is an incorporation by reference of a device previously described in WO 1997/003711).

[0010] When required for use, the devices of WO 2008/040062 are claimed as being capable of releasing the medication by punching means namely two punches to perforate the two respective frangible ends of a medication container, although various other means are generally described including: pressurised means (e.g. by a pressurised canister); frangible means (e.g. by rupturing an ampoule with a striker or by punching a frangible membrane or seal of a vial with punch means); crushable means (e.g. by crushing a vial with a plunger); dislodging means (e.g. by dislodging an unscrewed cap from a vial); and plunging means (e.g. by plunging the medication from the plunger barrel).

[0011] However, inhalable liquids such as halogenated volatile liquids require an effective air chamber into which the vapour may evaporate and allow an effective airflow through the air/vapour chamber for delivery to a patient. Accordingly, embodiments such as those described in, for example, Figures 48A, 48B, 48C, 49A, 49B, 50A, 50B, 51 A, 51 B, 56A, 56B, 57, 58A, 58B, 58C and 58D of WO2008/040062, would not be expected to work in practice as the evaporative means (i.e. wick) is prevented from being effectively exposed to effective airflow by the walls of the liquid storage container itself.

[0012] Inhaler devices that are useful for administering inhalable liquids may be generally considered to operate by either passive or active means in order to deliver the active agent(s) to a patient. Inhaler devices with active means may include pressurized, moving, mechanical, heating and/or electrical means to, for example, nebulise, vaporize and/or generally deliver the active agent(s). In contrast, inhaler devices with passive means rely solely on the vaporisation or evaporation of the active agent(s) at ambient conditions and respiration of the patient to deliver the active agent(s).

[0013] The Analgizer™ inhaler device (Abbott Laboratories Corporation) is an example of a device that operates by passive means to deliver an inhalable liquid. According to the USPTO TESS database, the Analgizer™ was a registered, now lapsed, trademark in respect of an

inhaler for the supervised self-administration of inhalation anaesthesia and was first used in 1968. The Analgizer™ was a very simple device that consisted of a white cylindrical polyethylene open-ended tube having a mouthpiece and an absorbent wick of polypropylene which was tightly rolled into a 'Swiss-roll' shape, i.e. cross-sectional view. The inhalation anaesthetic, methoxyflurane (15ml), was poured into the open-ended base of the inhaler and onto the tightly wound wick immediately prior to use. A patient was then able to self-administer the liquid anaesthetic by inhaling through the mouthpiece.

[0014] The Green Whistle™ inhaler device (Medical Developments International Limited) was subsequently developed during the 1990s and has since been used in Australia for the delivery of methoxyflurane as an analgesic (1.5mL or 3mL, storage brown glass vial container with screw cap). Although similar in respect of its simplicity of design to the Analgizer™, the Green Whistle™ device introduced certain functional improvements such as the inclusion of a one-way valve at the base end to prevent drug vapour loss from the device upon patient exhalation and an activated carbon ('AC') chamber designed to be externally fit into a dilution hole in the mouth piece to filter exhaled drug vapours. Additional design modifications to the base end included the introduction of cap lugs to assist removal of the cap from the glass vial used to store the drug dose to be delivered, a dome to facilitate the spread of the poured liquid onto the 'S-shaped' wick (cross-sectional view) or, in the alternative to a dome, an inlet nipple to allow for the attachment of a breathable gas line to direct the gas through the device. The Green Whistle™ device is designed for single patient use.

[0015] Methoxyflurane (Penthrox®/™, Medical Developments International Limited) offers a non-narcotic, i.e. non-opioid analgesic alternative to common analgesics such as morphine and fentanyl. Methoxyflurane also presents an alternative to analgesics which are administered in oral tablet form or intravenously to a patient and may therefore be particularly useful when rapid pain relief is required in clinical, surgical (e.g. pre- and post- operative) and/or emergency settings (e.g. emergency department and triage management as well as by first-responders such as paramedics and search and rescue teams). However, the Green Whistle™ device is currently the only device that is commercially available to administer methoxyflurane. According to the device's instructions for use, the administrator is required to hold the methoxyflurane bottle upright to use the base of the inhaler to loosen the bottle cap and then to remove the cap by hand before tilting the inhaler to a 45 angle and pouring the contents of the bottle into the base while rotating the device. An AC-chamber may be optionally fitted externally to the device either beforehand or afterwards. While the device is effective, the number of steps and separate components may present handling difficulties for the administrator or self-administrator, for example, in high-stress and/or emergency settings.

[0016] The embodiments of the present invention seek to address one or more of the disadvantages identified above, and/or to at least provide the public with a useful alternative.

[0017] The reference in this specification to any prior publication or information derived from it, or to any matter which is known is not and should not be taken as an acknowledgement or admission or any form of suggestion that prior publication, or information derived from it, or known matter, forms part of the common general knowledge in the field of endeavour to which this specification relates.

SUMMARY

[0018] According to a first aspect of the invention, there is provided an inhaler device for delivering an inhalable liquid to a patient, the inhaler device comprising:

- a mouthpiece; an air inlet;

- a liquid container for hermetically storing inhalable liquid; a wicking material for supporting inhalable liquid;

- a piercing member configured to pierce the liquid container;

- a first one-way valve configured to enable gas to flow into the mouthpiece during inhalation, and prevent gas from flowing in the opposite direction during exhalation;

wherein

- the mouthpiece, first one-way valve, wicking material, and air inlet are fluidly connected to provide an inhalation chamber; and

- the inhaler device is configured such that:

- the liquid container may be provided in a first position in which the piercing member does not engage the liquid container and inhalable liquid remains hermetically stored within the liquid container;

- the liquid container may be displaced from the first position to a second position such that the piercing member pierces the storage container to release inhalable liquid onto the wicking material, whereby during inhalation air entering the air inlet flows through the inhalation chamber to deliver inhalable liquid vapour from the wicking material to the patient via the mouthpiece.

[0019] In an embodiment according to the first aspect, the inhaler device further comprises: a return air chamber in fluid communication with a second one-way valve, such that during inhalation the first one-way valve is open and the second one way valve is closed, and during exhalation the first one way valve is closed and the second one-way valve is open to enable exhaled gas to flow from the mouthpiece through the return air chamber.

[0020] In an embodiment according to the first aspect, the return air chamber comprises

filtering material configured to filter volatile liquid vapour from the exhaled breath of a patient upon exhalation.

[0021] In an embodiment according to the first aspect, the filtering material comprises activated carbon, optionally activated charcoal pellets.

[0022] In an embodiment according to the first aspect, the liquid container contains a halogenated volatile liquid.

[0023] In an embodiment according to the first aspect, the halogenated volatile liquid is selected from the group consisting of halothane (2-bromo-2-chloro-1,1,1-trifluoroethane), sevoflurane (fluoromethyl-2,2,2-trifluoro-1-(trifluoromethyl)ethyl ether), desflurane (2-difluoromethyl-1,1,2,2,2-tetrafluoroethylether), isoflurane (1-chloro-2,2,2-trifluoroethyldifluoromethyl ether), enflurane (2-chloro-1,1,2-trifluoroethyldifluoromethyl ether) and methoxyflurane (2,2-dichloro-1,1-difluoroethylmethyl ether).

[0024] In an embodiment according to the first aspect, the halogenated volatile liquid is methoxyflurane.

[0025] In an embodiment according to the first aspect, the piercing member comprises at least one channel such that, when the liquid container is in the second position, inhalable liquid from the storage container may pass through the at least one channel and onto the wicking material.

[0026] In an embodiment according to the first aspect, the wicking material is spaced from the piercing member to allow passage of air through the at least one channel into the liquid container, thereby preventing or reducing an air-lock from restricting release of inhalable liquid from the liquid container.

[0027] In an embodiment according to the first aspect, the inhaler device comprises spacer tabs configured to space the wicking material from the piercing member.

[0028] In an embodiment according to the first aspect, the wicking material and/or the piercing member remains stationary within the inhaler device while the liquid container is displaced from the first position to the second position.

[0029] In an embodiment according to the first aspect, the liquid container comprises only a single region configured to be pieced.

[0030] In an embodiment according to the first aspect, the inhaler device is configured to

enable air to pass by or around the liquid container, optionally the inhaler device is configured prevent air from passing through the liquid container.

[0031] In an embodiment according to the first aspect, the inhaler device comprises a diluter hole positioned to enable a portion of inhalation air to bypass the wicking material before passing into the mouthpiece.

[0032] In an embodiment according to the first aspect, the diluter hole is positioned and configured to enable the patient to restrict or block the diluter hole with a finger.

[0033] In an embodiment according to the first aspect, the mouthpiece comprises a filter configured to reduce or prevent inhalation of liquid droplets by the patient.

[0034] In an embodiment according to the first aspect, the filter is formed of a polymeric non-woven material.

[0035] In an embodiment according to the first aspect, the inhaler device is configured to enable replacement of the liquid container and/or the wicking material.

[0036] In an embodiment according to the first aspect, the wicking material is configured to enable inhalation air to pass through and along multiple surfaces of the wicking material, optionally the wicking material is configured to enable inhalation air to pass through and along a first surface and a reverse surface of the wicking material.

Definitions

[0037] Throughout this specification and the claims which follow, unless the context requires otherwise:

terms such as 'side', 'end', 'top', 'bottom', 'above', 'below', and the like are only used to describe elements as they relate to one another, but are in no way meant to recite specific orientations of the device, to indicate or imply necessary or required orientations of the device, or to specify how the invention described herein will be used, mounted, displayed, or positioned in use;

'active agents' refers to therapeutic agents and non-therapeutic agents and compounds, formulations and compositions comprising them, and 'active agent' has a corresponding meaning;

'air' or 'gas' may be used interchangeably;

'alleviate', 'alleviation' and variations thereof refers to relieving, lessening, reducing, ameliorating or an improvement in the symptom(s) and/or underlying cause(s) of a condition

and/or disease in a patient;

'comprise' and variations thereof such as 'comprises' and 'comprising', will be understood to imply the inclusion of a stated integer or step or group of integers or steps but not to the exclusion of any other integer or step or group of integers or steps;

'delivery dose' refers to the dose of inhalable liquid or active agent for administration to a patient;

'filter', 'filtering' and variations thereof refers to the ability of a substance to absorb, adsorb, capture, trap, scavenge, scrub or partially or entirely remove the inhalable volatile liquid vapour from the exhaled breath of a patient upon exhalation;

'halogenated volatile liquids' refers to volatile liquids which (i) comprise at least one halogen atom selected from the group consisting of a chlorine (Cl), bromine (Br), fluorine (F) and iodine (I) atoms, or (ii) comprise an active agent which comprises at least one halogen atom selected from the group consisting of a chlorine (Cl), bromine (Br), fluorine (F) and iodine (I) atoms. In some embodiments, halogenated, particularly fluorinated, hydrocarbons and halogenated, particularly fluorinated, ethers may be preferred. In some embodiments, halogenated ethers may be particularly preferred and include but are not limited to, halothane (2-bromo-2-chloro-1,1,1-trifluoroethane), sevoflurane (fluoromethyl-2,2,2-trifluoro-1-(trifluoromethyl)ethyl ether), desflurane (2-difluoromethyl-1,2,2,2-tetrafluoroethyl ether), isoflurane (1-chloro-2,2,2-trifluoroethyl difluoromethyl ether), enflurane (2-chloro-1,1,2-trifluoroethyl difluoromethyl ether) and methoxyflurane (2,2-dichloro-1,1-difluoroethyl methyl ether);

'inhalable liquid' refers to liquids that comprise active agents or that are themselves the active agent and that are readily inhalable or capable of being or adapted to be inhaled by a patient. In some embodiments, inhalable volatile liquids, particularly halogenated volatile liquids are preferred;

'inhalation', 'Inhalable' and variations thereof refers to the intake of, for example but not limited to air, breathable gases, inhalable liquids, by a patient and includes both oral and nasal inhalation. In some embodiments, oral inhalation is particularly preferred;

'and/or' means 'and' and 'or' where the context allows for both;

'patient' refers to both human and veterinary patients. In some embodiments, human patients may be particularly preferred. Reference to a patient will therefore be understood to mean the person or animal to whom the inhalable liquid is administered to and in the case of human patients, will be understood to include administration by self-administration;

'pharmaceutical agent' refers to a drug, or a compound, formulation or composition that comprises a drug, for the treatment of symptom(s) and/or underlying cause(s) of a condition and/or disease in a patient. The term pharmaceutical agent may be used interchangeably with therapeutic agent or active agent;

'respiratory', 'respirational' and variations thereof refers to the act of respiring, breathing, inhaling and exhaling, such as for example but not limited to air, breathable gases, inhalable liquids and active ingredients, by a patient;

'room temperature' refers to ambient temperatures which may be, for example, between 10°C to 40°C but more typically between 15°C to 30°C;

'therapeutic agent' refers to an active agent, or a compound, formulation or composition (including biological compounds, formulations and compositions) that comprises an active agent, that is capable of treating a patient or offers a therapeutic or medical benefit to a patient or that has or that requires regulatory and/or marketing approval for therapeutic use in a patient. Therapeutic agents include pharmaceutical agents. In contrast, a 'Non-therapeutic agent' will be understood to mean an active agent which may not have or require regulatory and/or marketing approval for a therapeutic use such as, for example, smokeless tobacco products and electronic cigarettes, or does not have a recognised or identified therapeutic use but may be used by a patient for a non-therapeutic reason such as general health, wellbeing or physiological benefit such as, for example, nutraceutical products.

'treat', 'treatment' and variations thereof refers to the alleviation, modulation, regulation or halting of the symptom(s) and/or underlying cause(s) of a condition and/or disease in a patient. In some embodiments treatment may include preventative or prophylactic treatment; and

'volatile liquids' refers to substances that predominantly exist in a liquid form but readily form vapours, evaporate or vaporize such that they partially exist in a vapour form under ambient conditions for example, at room temperature and at normal atmospheric pressures.

BRIEF DESCRIPTION OF THE FIGURES

[0038] FIGURES 1A and 1B show an external view of an inhaler device having a fluid container in a first position and a second position respectively according to an embodiment of the invention.

[0039] FIGURES 2A and 2B show a cross-sectional cut-away view of the device of Figure 1A along line A-A with the fluid container in the first position.

[0040] FIGURE 3 shows a cross-sectional cut-away view of the device of Figure 1B along line B-B with a fluid container in the second position.

[0041] FIGURES 4 shows a disassembled view of the inhaler device of Figure 1A.

[0042] FIGURE 5 shows a cross section of the inhaler device in Figure 1B with the fluid container in a second position, indicating airflows within the device in use.

[0043] FIGURE 6 shows an isometric and cross-sectional view of an end cap of the inhaler device of Figure 1A.

[0044] FIGURES 7A and 7B show an isometric view of an end cap and receptacle of the inhaler device of Figure 1A.

[0045] FIGURE 8 shows isometric and cross-sectional views of a holder for an inhaler device as shown in Figure 1A.

[0046] FIGURES 8A, 8B and 8C show different embodiments of an opener in accordance with the present invention.

[0047] FIGURES 8D and 8E show the receptacle in the first position in accordance with the inhaler device of Figure 1 and the second position in accordance with the inhaler device of Figure 1B respectively.

[0048] FIGURE 8F shows a further embodiment of an opener in accordance with the present invention.

[0049] FIGURES 8G and 8H show a further embodiment of an opener in accordance with the present invention.

[0050] FIGURES 9A and 9B show different views of a wicking material in accordance with the inhaler device of Figure 1A.

[0051] Figure 10 shows different views of sections of the body of the inhaler device of Figure 1B.

[0052] FIGURES 11A, 11B and 11C show different embodiments of cartridges and closure mechanisms in accordance with the present invention.

[0053] FIGURE 12 shows an isometric view of a valve arrangement of the inhaler device of Figure 1A.

[0054] FIGURE 13 shows a cross sectional view of the opener of Figures 8G and 8H.

[0055] FIGURE 14 shows a further embodiment of the inhaler device.

LIST OF COMPONENTS

10 – inhaler device
11 – hand strap
12 – mouthpiece
14 – body

16 – receptacle
18 – liquid

20 – cartridge

22 – opener
23 – projection
24 – chamber
26 – fluid pathway
28 – window

30 – wicking material
31 – voids
32 – holder
34 – valve assembly **34a** – valve support **34b** - valve plate
36 – receiver

38 – dock

40 – air inlet

42 – apertures

44 – diluter hole
50 – exhalation chamber **52** – adsorbent material **54** - exit ports
56 – end cap

58 – chamber body **60** – filter assembly **64** – filter
70 - slotted guides
72 – recessed portion
74 – central raised portion
76 – recessed portion
80 – spacer tabs
100 – canula
101 – piercing member
102 – bore
104 – cannula

105 – piercing member
106 – bore
108 – cannula
110 – bore
120 – vial
122 – closure
130 – vial
132 – screw-type closure
133 – aperture
134 – membrane
140 – closure
142 – plug
150 – tab
152 – ridge
158 – piercing member
160 – hollow shaft
162 – flow member
164 – ventilation path
166 – channels
180 – diluter hole
182 – mouthpiece

DETAILED DESCRIPTION

[0056] In broad terms, the present invention relates to a new inhaler device for the administration of inhalable liquids to a patient, such as halogenated volatile liquids, particularly methoxyflurane for use as an analgesic. The present invention is now further exemplified with reference to embodiments as set out below and in the drawings.

Embodiments

[0057] Embodiments of the invention will now be described with reference to the non-limiting examples.

[0058] In accordance with a first embodiment, Figures 1A and 1B shows an inhaler device

having a hand strap **11**, mouthpiece **12**, a body **14**, a receptacle **16** and end cap **56** in a first position and a second position respectively. In the first position shown in Figure 1A, the receptacle **16** projects from the body **14** of inhaler device **10**, and may be covered by an end cap **56**. In Figure 1B, the receptacle **16** has been moved to a second position where the receptacle **16** has moved into body **14** of inhaler device **10** as described below.

[0059] Further detail of the inhaler device **10** is shown in Figure 2A and 2B, where receptacle **16** is shown in the first arrangement, housing a cartridge **20** partially within the body **14** of the inhaler device **10**. The cartridge **20** may hold a fluid, for example a liquid **18**, such as a volatile liquid, such as methoxyflurane. Also within body **14** is an opener **22** connected to a chamber **24** by fluid pathway **26**. Chamber **24** may include a wicking material **30**.

[0060] In Figures 1A and 2B, the cartridge **20** is located within the receptacle **16**, such that air may flow around the cartridge **20**, through receptacle **16** and into chamber **24**. Examples of air flow are as shown in Figure 5. In other embodiments (not shown) the receptacle **16** and cartridge **20** may be integral with each other, for example moulded from a single piece. In other embodiments (not shown) the air flow to the chamber **24** may be around the receptacle **16**, through the cartridge **20** or separate to the receptacle **16** and cartridge **20** entirely.

[0061] As shown in Figure 4, the cartridge **20** may be loaded into the receptacle **16** during assembly or manufacture of the finished inhaler **10**. The cartridge **20** may be a vial, such as a glass walled 5ml vial having a screw on lid. The lid may have a pierceable portion, such as a butyl rubber section with a low permeability polymer coating such as a PTFE coating to assist in sealing in volatile liquids such as methoxyflurane. Figure 2 shows the receptacle **16** and cartridge **20** in the first position, where the opener **22** has not engaged the cartridge **20**. Figures 1B, 3 and 5 show the receptacle **16** and a cartridge **20** in a second position where the opener **22** has engaged the cartridge **20** to release liquid **18**.

[0062] The embodiments shown and described herein are adapted to dispense liquid that is capable of vaporising at room temperatures in sufficient amounts to be medically effective and not require storage pressure to assist in dispensing the liquid to the patient.

[0063] Receptacle **16** may include a window **28** allowing visual inspection of the contents of the cartridge **20**. If cartridge **20** is transparent, such as a glass or plastic vial, the level of liquid remaining in cartridge **20** will be visible, to determine the level of liquid in the cartridge **20** prior to opening to determine whether all the liquid **18** has been dispensed from the cartridge **20**.

[0064] In Figure 4 cartridge **20** fits into receptacle **16** during assembly. Receptacle **16** holding cartridge **20** is loaded into a holder **32**. Holder **32** incorporates a number of elements, including a

receiver **36** for wicking material **30**, and a dock **38** for receptacle **16**. The dock **38** allows the receptacle **16** to move from the first position to the second position by engaging with the receptacle **16** as described below.

[0065] Wicking material **30** may be provided according to various, different configurations. In the embodiment shown in Figure 9, wicking material **30** is shown as a single piece in an S-shape, such that wicking material **30** is generally located along the walls of receiver **36**, and across the centre of receiver **36**. Within the receiver **36**, wicking material **30** has voids **31** that allow the free passage of air, which picks up vapour from liquid **18** evaporating on the wicking material **30**, where it exits the receiver **36**, which in use is located in chamber **38** within body **10** as shown in Figures 3 and 5.

[0066] According to the present embodiment the wicking material **30** is securely held in the receiver **36** of holder **32** to ensure that the orientation and arrangement of the wicking material **30** is consistent and stable. Wicking material **30** may be made of a variety of materials such as a polypropylene felt or sintered polypropylene, to provide appropriate wicking with the liquids such as methoxyflurane. When assembled, the inhaler devices may be packed and stored for some time before use and the wicking material may not have significant strength. Further, inhaler device **10**, may be used in a variety of locations, and be subject to rough handling prior to use. It is envisaged that the inhaler device **10** may be used in a variety of environments, including in moving ambulances, in military operations, or situations in the field outside a hospital environment. As such, locating device as described below may be employed to retain the wicking material in its preferred location.

[0067] Figure 10 shows different views of the body **14** of the inhaler device **10**. Specifically, the end of the body **14** proximal the mouthpiece **12**. Tab **150** inside the body **14** assists in locating the wicking material **30**, at opposite ends of the body **14** to the tabs **80**, which also assist in locating the wicking material **30**. Optionally, a ridge **152** may run along all or part of the inside of the body **14** in chamber **24** to prevent movement, such as rotation, of the wicking material within the chamber **24**.

[0068] According to certain embodiments of the inhaler device **10**, air flow through the wicking material **30** and any gaps or voids **31** after dispensation of liquid **18** onto wicking material **30** is consistent to provide a repeatable air/vapour ratio. Unlike purely liquid analgesics, the operation of analgesics such as methoxyflurane is dependent on the ratio of vapour of active pharmaceutical ingredient to air. If too little vapour is inhaled, the therapeutic effect may not be sufficient. The importance of the user being able to control or adjust the concentration or delivery of the active pharmaceutical ingredient is discussed below.

[0069] The receptacle **16** is moveable from a first position shown in Figures 1A and 2, to a second position shown in Figures 1B and 3 to release liquid **18**. The cartridge **20** is locked into position with and moves when the receptacle **16** is moved, and opener **22** moves to pierce or penetrate a pierceable portion of the cartridge **20** as shown in Figures 3 and 5. Different embodiments of cartridges and pierceable portions are shown in Figures 11A, 11B and 11C and described below. If the inhaler device **10** is held substantially vertically or at an incline with the mouthpiece **12** held lowermost, liquid **18** within the cartridge **20** will then move from the cartridge **20** through a pierced aperture in a closure **132** shown in Figure 11B through fluidpathway **26** and into chamber **24** where it will be absorbed by wicking material **30**. According to the embodiment shown, the wicking material **30** is of such a volume that not all the spaces within it are filled with fluid, some air remains as described above.

[0070] Different configurations of cartridge are shown in Figures 10A, 10B and 10C. A vial **120** is shown in Figure 11A having a closure **122** that may be attached via heat or ultrasonic welding. The closure **122** may be a piece of plastics material chosen to weld easily to the vial **120**, be pierceable and be impermeable to the liquid **18**.

[0071] Cartridge **20** shown in Figure 11B has a screw type closure **132**, for example made of a stiff plastics material. The top of the closure **132** may contain an aperture **133**, and a membrane **134** may be placed within the closure to fit between the closure **132** and cartridge **20** when the closure is applied. The closure **132** may be screwed to the top of the cartridge **20**, holding the membrane **134** tightly against the cartridge **20** to prevent leakage during storage prior to use. The membrane **134** may be pierceable via a canula style piercing member as shown as opener **22** in Figure 2B and 3.

[0072] An additional embodiment is shown in Figure 11C where a cartridge such as a vial **130** (only the top of which is shown) has a crimp style closure **140** having a plug **142** fitting under the closure **140** and accessible through aperture **144**. During assembly, the vial **130** is filled with liquid, and the closure **140** containing plug **142** is fitted to the vial **130** where the edges of the closure **140** are crimped around edges of the vial **130**. The plug **142** is held tightly between the closure **140** and vial **130** to provide a seal. The plug **142** is made from a pierceable material such as butyl rubber, and may incorporate an additional impermeable membrane (not shown) if required. In each case described and shown in Figures 10A, 10B and 10C, a closure method is described that is pierceable and retains liquid during storage.

[0073] In use, a patient may place their mouth over the mouthpiece **12** and inhale air, drawing it through the inhaler device as shown in Figure 5. Air enters air inlet **40** through, for example apertures **42**, then around cartridge **20** and into chamber **24** where it interacts with fluid **18** in

wicking material **30**. Wicking material **30** supports the liquid **18** and provides a large surface area interface between liquid **18** and air, such that air flowing through the wicking material **30** picks up vapour from the fluid **18**. When fluid **18** is a volatile fluid such as methoxyflurane, the vapour level can be high enough to produce a therapeutic response in the person inhaling the air through the inhaler device **10**. In order to allow the patient to vary the concentration of the air/vapour mix, a diluter hole **44** is provided in the body **10**, which provides air containing no vapour direct to the mouthpiece. A patient can fully or partially block the diluter hole **44**, such as with their finger, to adjust the concentration of vapour in the air exiting the mouthpiece **12** into the patient. Uncovering diluter hole **44** dilutes the vapour in the air by allowing air that has not passed through the receiver **36** to enter the inhaler device **10** before inhalation by a patient.

[0074] In another embodiment of the inhaler device **10** shown in figure 13, the diluter hole **180** is placed at the end of the device adjacent mouthpiece **182**. This embodiment allows easier placement of a one-way valve (not shown) such as a reed valve, to prevent exhaled air from leaving the device except through the chamber **50**.

[0075] Exhaled air from a patient will contain some remaining vapour which was not absorbed by the patient. The patient may exhale air back into the mouthpiece, whereupon the valve assembly **34** (new Figure 4 will require simple description of parts) directs the air containing remaining vapour, into exhalation chamber **50** as shown in Figures 3 and 5. Chamber **50** may contain an adsorbent material **52** such as an activated charcoal to adsorb vapour remaining in exhaled air. Exhaled air exits the inhaler device from exit port **54**. A parts view of Chamber **50** is shown in Figure 4, wherein a chamber body **58** is used to house adsorbent material **52** such as activated charcoal pellets and ensure no leakage of air into the body **10**. Chamber **50** allows the retaining adsorbent material separate to other parts of the inhaler device **10** during assembly.

[0076] In some embodiments (not shown) the chamber **50** is not required and the patient may breathe out normally not into the device. Valve assembly **34** would still prevent air flow from returning back through the chamber **24**.

[0077] In one embodiment shown in Figure 6, an end cap **56** is provided to engage with and cover the end of receptacle **16** when the receptacle **16** is in a first position as shown in Figure 1. In one form the end cap **56** engages with the receptacle by, for example, interference projections **57** to positively engage the receptacle **16** and prevent it from moving to the second position shown in Figures 3 and 5 until end cap **56** is removed.

[0078] In use the end cap **56** must be removed, to expose the receptacle **16**, whereupon a patient may then move the receptacle to the second position, and in the process, the opener **22**

engages with closure (number and pictures) to pierce the closure and release liquid **18** as herein described. This has significant advantage over prior art methods that had a separate vial, for example when trying to open the liquid container and pour it onto the wicking material in a moving vehicle such as an ambulance.

[0079] Optionally, as shown in Figure 4, a filter assembly **60** is shown including filter holders **62** either side of filter **64**. The filter assembly **60** is located on the mouthpiece side of valve assembly **34**. This prevents foreign material from entering the inhaler device **10** and potentially interfering with the valve assembly **34**. Filter assembly **60** also prevents material that may be held within the inhaler device **10**, being inhaled by a patient. The filter **64** may be a non-woven material or other suitable material. It may also prevent droplets of liquid **18** from entering the mouth or airways of a patient, rather than as a vapour mixed with air. Such materials as polypropylene may be used.

[0080] Figure 8 shows multiple views of an embodiment of holder **32**. Holder **32** includes opener **22**, receiver **36** for receiving receptacle **16** (not shown) dock **38** for receiving wicking material **30** (not shown) and slotted guides **70**. Slotted guides **70** have two recessed portions **72** which define the first and second position of the receptacle **16**. The central raised portion **74** between the two recessed portions **76** as shown in Figure 8E provides a positive resistance to the receptacle moving to the second position without a minimum force being exerted. Further, once in the second position, the central raised portion prevents the receptacle sliding away from the opener, and possibly preventing full discharge of the liquid into the wicking material **30**.

[0081] Also shown in Figure 8 are spacer tabs **80** within the receiver **36** of holder **32**. Spacer tabs **80** ensure that an air gap exists between the wicking material **30** and the fluid pathway **26**. This assists in ensuring liquid **18** spread around wicking material **30**, the cartridge **20** is appropriately vented to prevent an air lock preventing liquid draining from the cartridge, and that air can flow freely over wicking material **30** and through receiver **36**. This provides better drainage of the cartridge **20** and provides a more consistent air to vapour mix from initial opening of the receptacle **16** until most of the liquid has vapourised into the air flow through the inhaler device **10**. Spacer tabs **80** also ensure that the wicking material **30** is held securely in place.

[0082] Opener **22** is shown as one embodiment of a piercing member in Figure 2B and Figure 3 with additional embodiments shown in Figures 8A, 8B and 8C. In Figure 8 the opener **22** is shown with an aperture **22A** and a projection **23**. Projection **23** is designed to pierce pierceable members of cartridges such as those shown in Figures 10A, 10B and 10C.

[0083] In Figure 8A, a canula **100** is shown having a piercing member **101** and bores **102**.

Although two are shown distal from the end of piercing member **101**, multiple bores **102** maybe used.

[0084] In Figure 8B, piercing member **105** is offset from the centreline of cannula **104** and bore **106** exits from the side of the cannula **104**.

[0085] In Figure 8C, cannula **108** has a single large bore **110**. In the embodiments shown, the arrangements of the bore in relation to the cannula are adapted to reduce the chance of the pierceable member blocking the bore and preventing liquid from draining from the cartridge. In some cases, it has been found that draining of liquid from cartridges can be incomplete or blocked if the bore of the piercing member is blocked. Opener **22** has an aperture to increase the size of the opening, and the other embodiments place the bore or bores in locations that have reduced risk of blockage. The choice of embodiment is dependent on the type of closure used on the cartridge.

[0086] In figure 8F, a further embodiment of an opener **66** is shown. Opener **66** has two piercing members **67** surrounding a fluid channel **68** which connects to fluid pathway **26** (not shown). A Slot **69** is located between piercing members **67**. In use, when the cartridge **20** such as that shown in figure 11B, is moved from a first position to a second position, the piercing members **67** pierce membrane **134** such that the piercing members **67** move into the cartridge **20** but that the membrane **134** does not extend past the slot **69**. The piercing members are designed to cut a round section from membrane **134**. The slot **69** allows a fluid pathway around the round section, should it get caught between the piercing members **67** and otherwise block fluid channel **68**.

[0087] In Figures 8G and 8H, a piercing member **158** is shown having a hollow shaft **160** supported in a flow member **162**. The hollow shaft may be made from metal and be in the form of a blunt needle having a ventilation path **164**, adapted to pierce for example the plug **142** of vial **130**. The flow member **162** may be constructed from a plastics material and have a number of flow channels **166** to allow flow of liquid from the vial **130** to the wicking material. Figure 13 shows the piercing member piercing the plug **142** wherein air may flow into the vial **130** to assist in release of liquid (in this case MeOF, or Methoxyflurane) through the flow channels **166**. This is advantageous where the liquid is stored in vials that are not pressurized, and therefore liquid may not flow easily if there is not an air channel.

[0088] An embodiment of the one-way valve **34** is shown in Figure 12 consisting of a support **34a** and flexible valve plate **34b**. Flexible valve plate **34b** has a lobe covering the air pathway to the chamber **24** housing the wicking material **30** and another lobe covering the return air pathway

to exhalation chamber **50**. Differences in air pressure each side of the lobes will cause deflection and allow air to flow thus creating a one-way valve for each chamber **24** and **50** respectively. Support **34a** is located on the opposite side of the valve plate **34b** to form the seal when air is inhaled. This embodiment provides a simple but effective seal using two easily assembled parts.

[0089] The wicking material **30** may be made from any material that is suitable for absorbing the inhalable liquid and passively releasing it as a vapour. Wicking properties will generally be understood to include the ability of a material to facilitate or enhance the rate of evaporation or vaporisation of a liquid from its surface by distributing the liquid, whether by drawing, spreading, pulling or otherwise, throughout the material from its initial point of contact and/or as it evaporates from an exposed surface area of the material. The wicking material should incorporate a large surface area to volume ratio to assist in ensuring good vaporisation of the liquid into the surrounding air. In one embodiment the wicking material is a wicking felt or a porous polymeric material. In a preferred embodiment the wicking material is a polypropylene wicking felt. In another embodiment, a sintered polypropylene material may be used.

[0090] The inhaler device described in various embodiments herein has a benefit that the ratio of active pharmaceutical ingredient may be varied by the patient/user by a number of means. Firstly, the user may control the concentration of active pharmaceutical ingredient by covering the diluter hole **44** or **180** in Figure 14 to increase the concentration (reducing additional airflow bypassing the wicking material **30**) or by leaving the diluter hole fully or partially open, to allow air to mix with the air and vapour flowing through the receiver **36** and wicking material **30**.

[0091] Additionally, the user does not need to only breath in air from the inhaler device **10**. The user may inhale through the inhaler device **10** one or more times to obtain relief, then when breath normally. Active pharmaceutical ingredients such as Methoxyflurane will provide analgesia for many minutes after inhalation, so if a user is in pain, the inhaler device **10** is designed to be held and controlled by them, to manage their own pain. This also allows the user to communicate during the process of taking the analgesic, in such circumstances where medical professionals may be assessing the injuries of the user or other information.

[0092] It will be understood to persons skilled in the art of the invention that modifications may be made without departing from the spirit and scope of the invention. The embodiments or examples as described herein are therefore to be considered as illustrative and not restrictive.