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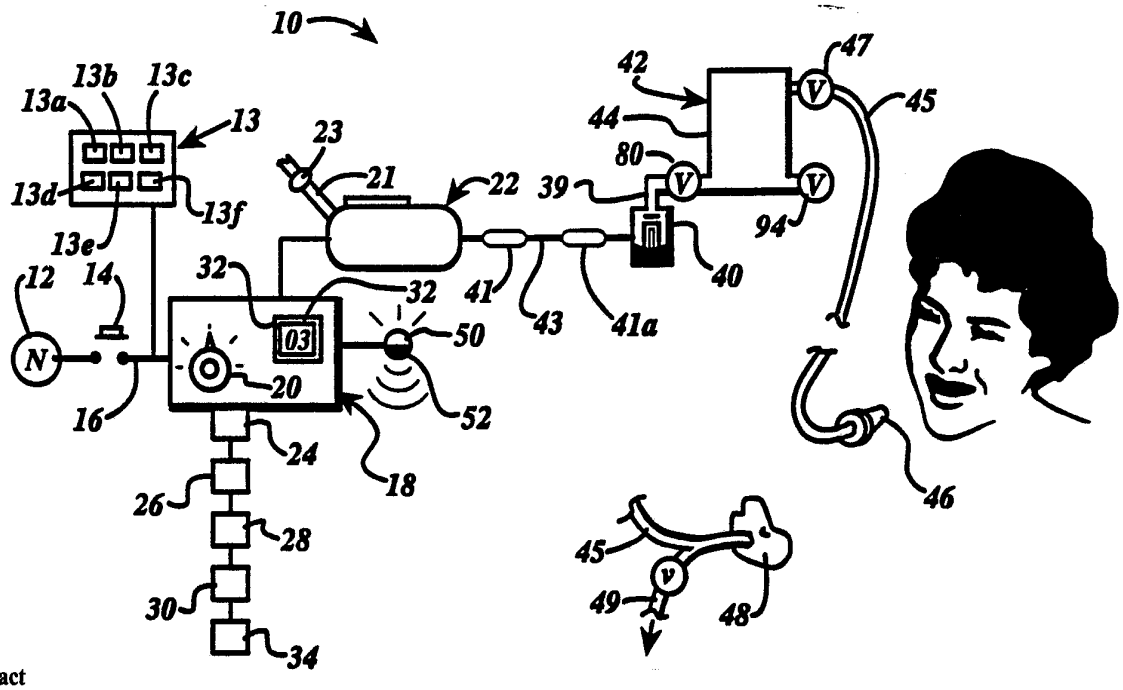

(57) Abstract

A device for accurately delivering aerosolized doses of a medicament disperses a measured amount of drug (40) in a measured volume of carrier gas (22) and transfers the resulting aerosol to a chamber (42) prior to inhalation by a patient. The chamber (42) is filled efficiently with the aerosol, and inhalation by the patient draws the aerosol dose into the lungs. This is followed by the inhalation of atmospheric air (96) that will push the initial dose well into the lung interior. The apparatus optimally includes a dose regulator (13a), a counter (13c), a clock (13e), a dose memory (30) and a signal (32) to indicate when a dose is ready by inhalation. Optimal chamber designs are disclosed.

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METHOD AND DEVICE FOR DELIVERING AEROSOLIZED MEDICAMENTS

The present invention is a continuation-in-part of application Serial No. 07/724,915, filed on July 2, 1991, the full disclosure of which is incorporated herein by reference.

BACKGROUND OF THE INVENTION

1. Field of the Invention

This invention relates to a structure and method of administering precisely measured doses of a therapeutic by inhalation.

An accurate mechanism for delivering precise doses of aerosol drugs into the interior of human lungs has been an objective of many workers in the art. One of the most popular aerosol delivery devices is the propellent-driven metered dose inhaler (MDI), which releases a metered dose of medicine upon each actuation. Although these devices may be useful for many medicines, only a small variable percentage of the medicine is delivered to the lungs. The high linear speed with which the dosage leaves the device, coupled with incomplete evaporation of the propellants, causes much of the medicine to impact and stick to the back of the throat. This impacting and sticking creates a local concentration of drugs much of which is eventually swallowed. In the trade, this impact area is called a "hot spot" and can cause local immuno-suppression and the development of fungal infections with bronchosteriods. With broncodilators, for instance, the swallowed dose can contribute to unwanted systemic side effects such as tremor and tachycardia.

MDI's also require a degree of coordination between activation and inhalation. Many patients are incapable of this task, especially infants, small children and the elderly. In an effort to overcome some of the above limitations of MDI's, others have interposed "spacers" between the conventional MDI and the patient. The primary function of these spacers is to provide extra volume to allow time for increased propellent droplet evaporation prior to inhalation and to reduce the velocity and impact of the medicine at the back of the throat.

Although spacers do compensate for some of the inadequacies in the conventional MDI, it has been found that much of the medicine that may have ordinarily been deposited on the throat remains in the spacer and the total dose deposited in the lungs is small. It has been found that only approximately 8% of the medicine reaches the interior of the lung with conventional MDI's. Approximately 13% of the medicine reaches the lung when it is equipped with a spacer.

Other workers in the art have attempted to provide a metered dose of a medicant by using dry powder inhalers (DPI). Such devices normally rely on a burst of inspired air that is drawn through the unit. However, these units are disadvantaged in that the force of inspiration varies considerably from person to person. Some patients are unable to generate sufficient flow to activate the unit. DPI's have many of the disadvantages of MDI's in that a large percentage of the medicant is deposited in the throat because of incomplete particle dispersion and the impact at the rear of the throat. Although pocket size MDI's and DPI's are very convenient they have disadvantages some of which are cited above.

Other workers in the art have refined aqueous nebulization delivery systems. Although such systems require a continuous gas compressor, making them less portable than the MDI's and the DPI's, many nebulizers provide a low velocity aerosol which can be slowly and deeply inhaled into the lungs. Precision of dosage delivery, however, remains a serious problem and it is difficult to determine how much medicament the patient has received. Most nebulizers operate continuously during inhalation and exhalation. Dosage is dependent on the number and duration of each breath. In addition to breath frequency and duration, the flow rate, i.e., the strength of the breath that is taken from a nebulizer can effect the particle size of the dose inhaled. The patient's inhalation acts as a vacuum pump that reduces the pressure in the nebulizer. A strong breath can draw larger unwanted particles of medicant out of the nebulizer. A weak breath, on the other hand, will draw insufficient medicant from the nebulizer.

Electro-mechanical ventilators and devices have also been used in recent years to deliver inhalable materials to a patient. These devices permit mixing of a nebulized medicant into breathing circuit air only during pre-set periods of a breathing cycle. An example of this type of machine is the system taught by Edgar et al., in their U.S. Patent No. 4,677,975, issued in July of 1987 where a nebulizer is connected to a chamber which in turn is connected to a mouthpiece, an exhaust valve, and an inlet valve. A breath detector and timer are used to deliver nebulized materials to the patient during a portion of the breathing cycle. However, in Edgar and others of this type, the patient's intake strength can effect the nebulizer operation with many of the consequences heretofore mentioned. Moreover, the amount of nebulized material delivered in each breath can vary significantly, contributing to inaccurate total dosages. In a modification of Edgar et al. (Elliott, et al. (1987) Australian Paediatr. J. 23:293-297), filling of the chamber with aerosol is timed to occur during the exhalation phase of the breathing cycle so that the patient is not inhaling through the device during nebulization. This design, however, requires that the patient maintain a constantly rhythmic breathing pattern into and out of the device, which is inconvenient and can contaminate the device with oval microbes. Moreover, no provision is made on the devices to efficiently capture the aerosol in the chamber so that as many as 80 breaths or more must be taken to obtain a dose of medication.

The delivery of therapeutic proteins and polypeptides by inhalation presents additional problems. Many protein drugs are produced recombinantly and can thus be very expensive. It is therefore important that loss of a protein drug within the delivery device be reduced or preferably eliminated. That is, substantially all drug initially charged within the device should be aerosolized and delivered to the patient without loss within the device or released externally of the device. The protein drugs should further be delivered to the patient under conditions which permit their maximum utilization. In particular, protein drugs should be completely dispersed into

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