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COMPONENTS FOR INHALATION DEVICES

Technical field of the invention

The present invention relates to components for devices for inhaling medicament, especially those components which can affect airborne particles or come into contact with medicament.

Background

Inhalation devices include dry powder inhalers, intended to dispense medicament which is in the form of a dry powder, and pressurised metered dose inhalers, which generally contain a medicament dissolved or suspended in a liquefied propellant gas, optionally together with surfactants and other excipients. The mechanism for dispensing the medicament varies between inhalers, but in general the medicament must exit the body of the inhaler and pass through a channel to a mouthpiece from where it exits. The mouthpiece may connect with a spacer, that is, a dispersion chamber designed to facilitate inhalation.

A metered dose inhaler releases a metered dose of medicine upon each actuation, and for maximum benefit with direct inhalation a degree of co-ordination between activation and inhalation is required. Powder inhalers are activated by the air flow generated at inhalation and for maximum benefit a certain air flow is required. With a spacer, the medicament is dispensed into the spacer chamber from where it can be inhaled simply by breathing normally. The residence time of the medicament in the spacer can be from a few seconds to several minutes, for example.

An example of a dry powder inhaler is the Turbuhaler ® inhaler. Examples of spacer devices include the Nebuhaler ® and Nebuchamber ® spacers.

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In the course of inhalation, medicament will come into contact with various parts of the inhalation apparatus, including for example the body, channel and mouthpiece of the inhaler, and the spacer. Such components are generally (but not essentially) made of a polymeric material, for example polypropylene or polyethylene, which is moulded into the required shape.

Not all of a nominal dose of medicament from an inhaler will reach its intended target, which may be, for example, the lungs. The medicament which does not reach the target, e.g., the lungs, is lost, for example in the apparatus, mouth and respiratory tract. Clearly, the amount of wastage should be as little as possible.

WO 91/19524 describes an inhaler for inhaling pulverulent medicament from within a capsule, including a capsule chamber which may be formed of components made of a polymer with low surface resistivity in order to minimise the extent to which released powdered medicament can agglomerate on the surface of the air passage through the inhaler. The surface resistivity desired is preferably less than 10^{12} Ohms or more preferably less than 10^{8} Ohms. The polymer may incorporate carbon or steel filler, for example in the form of fibres, or non-fibrous chemical additives. As examples of the polymer are mentioned a polyether block amide product with chemical additives and a range of polypropylenes with chemical additives. The inhaler also comprises a mouthpiece, which may be integral with the chamber, preferably having at least its inner wall formed from such a polymer of low surface resistivity.

WO 95/20414 describes a spacer for children, primarily intended to be used in conjunction with a metered dose inhaler. The spacer is made from stainless steel, which has a surface resistivity such that electrostatic attraction between the respirable particles and spacer walls is minimised. The surface resistivity is lower than 10^{9} Ohm, preferably lower than 10^{6} Ohm and most preferably lower than 1.

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The present invention is concerned with polymeric materials in components for inhalation devices. We have found that the amount of medicament which is retained in a device comprising components made of polymeric material can be significantly reduced by incorporating carbon black or another appropriate material into the polymer. Components according to the invention have anti-static properties which minimise the amount of medicament retained on the component walls.

Carbon blacks are obtainable for example from Degussa AG, Frankfurt, Germany. They are chemically and physically well-defined products, which are manufactured by incomplete combustion of oils or gases, and are composed of more than 96% finely dispersed carbon with small amounts of oxygen, hydrogen, nitrogen and sulphur. They may be produced for example as dispersions, pastes, chips or pellets. Today the most important method for the manufacture of carbon blacks is the so-called "furnace black" process. This process can produce a large variety of carbon blacks, for example with particular particle sizes and specific surface areas. It also permits the control of particle aggregation, i.e., the carbon black structure. Carbon blacks consist of chained branched aggregates of approximately spherical "primary" particles. Extensive branching, or interlinking, produces carbon black having a "high structure", while less extensive interlinking produces a "low structure" carbon black. One method for the determination of structure is the "DBP absorption" test, which is described in ISO 4656 and ASTM D-2414. In this method, dibutylphthalate (DBP) is added dropwise to a certain amount of carbon black that has been placed in a calibrated kneading machine and the torque exerted by the kneading machine is measured. A change in the torque indicates that all of the voids between the carbon black aggregates have been filled with DBP and the surface has been wetted. The consumption of DBP thus allows determination of the degree of aggregation of the carbon black. In general, the higher the DBP absorption in ml/100g (the "DBP number"), the higher the carbon black structure. Carbon blacks with a low structure have a DBP number of less than 70 ml/100 g of carbon black; those with a medium structure have DBP numbers of between 70 and 100 ml/100 g, and those with a high structure have a DBP number of above 110 ml/100 g of

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carbon black. The so-called "extra conductive" carbon blacks typically have DBP numbers in excess of 300 ml/100 g of carbon black.

The primary use of carbon blacks is in the reinforcement of rubber, for pigmentation, UV stabilisation and as conductive blacks.

The invention

In one aspect of the present invention there is provided a component for use in an inhalation apparatus, said component being made of or coated with a polymeric material, characterised in that the polymeric material is loaded with carbon black in an amount sufficient to impart to the polymeric material a specific volume resistivity of less than 10^9 Ohmcm.

In another aspect, the present invention provides a polymeric component for use in an inhalation apparatus, said component having a specific volume resistivity of less than 10^9 Ohmcm.

In another aspect, the present invention provides an inhalation apparatus comprising a component according to the invention.

Preferably the specific volume resistivity is less than about 10^6 Ohmcm, more preferably less than about 10^4 Ohmcm. In an especially preferred embodiment, the present invention provides a component for use in an inhalation apparatus, said component being made of or coated with a polymeric material, characterised in that the polymeric material is loaded with carbon black in an amount sufficient to impart to the polymeric material a specific volume resistivity of less than about 10^2 Ohmcm.

Specific volume resistivity may be measured using commercially available apparatuses for measuring conductivity.

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The use a of carbon black dispersion is particularly advantageous as good dispersion of the carbon black in the polymer can be achieved. Preferably, the carbon black-loaded polymeric material comprises a homogeneous mixture of the carbon black and the polymer.

The very low specific volume resistivity values which may be achieved in accordance with the present invention are particularly valuable when the inhaler component is a spacer device. In a spacer device, a comparatively long medicament residence time is necessary, and the longer the residence time, the more opportunity there is for the medicament to "attach" to the spacer walls.

However the component of an inhalation apparatus according to the present invention may alternatively be another component, for example the body of an inhaler device, the channel, or the mouthpiece, for example. The term "apparatus" includes all components and devices which together or separately may be used in the course of inhalation.

The amount of carbon black to be employed may vary according to the quality of the carbon black employed. Low and medium structured carbon blacks may be included in amounts of up to 40% of the carbon black loaded polymeric material, whereas highly conductive, or highly structured, carbon blacks preferably constitute for example up to 25%, or up to 20%, or up to 15%, or up to 12%, or around 10%, or around 9%, or around 8%, or around 7%, or around 6%, or around 5%, or around 4%, of the carbon-black loaded polymeric material. For a highly conductive carbon black, a content of between about 3% and about 15%, preferably between 6% and 10% and especially between 8% and 10%, for example around 9%, is currently thought to give optimum surface volume resistivity values.

Preferably, the carbon black for use in the present invention has a DBP number of at least 50 ml/100 g. More preferably the carbon black is highly structured or is an extra conductive carbon black, and has a DBP value of at least 110 ml/100 g.

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Suitable carbon blacks are commercially available, for example from Degussa AG, or from Cabot Plastics, Belgium. Examples of Degussa carbon blacks are the range of carbon blacks known as Printex® , for example "Printex L", "Printex L 6", and the extra conductive "Printex XE2".

The polymeric material can be any which can be moulded into the desired shape. For example the polymeric material may be a polypropylene, a polyethylene, a polyester, a polycarbonate, a polystyrene, a polyoxyethylene, a fluoropolymer, or a copolymer. Suitable polymers may be obtained for example from Hoechst AG, Frankfurt, Germany. As specific examples of polymers may be mentioned the polyethylenes Hostalen®, Hostalen GUR®; the polypropylenes Hostalen PP® and Hostacen®; as well as Topas®, Hostaform®, Kemetal®, Celanex®, Vandar®, Impet®, Celstram®, Fortron®, Vectra® and Hostaflon®, all available from Hoechst AG.

Preferably, the polymeric material is a polypropylene or a polyethylene.

The carbon black loaded polymer, and the homogeneous mixture, may be manufactured by conventional methods, for example by extrusion of the polymer together with the carbon black. The mixing parameters, flow conditions and cooling down conditions may be optimised easily by methods well known to a person skilled in the art, according to the particular polymer and carbon black used.

Carbon black loaded polymeric materials are also commercially available, for example from Premix Oy of Rajamäki, Finland.

The components according to the present invention may be made by conventional moulding techniques, for example by injection moulding or by blow moulding. The moulding parameters may be optimised easily by a person skilled in the art, according to the particular materials used. The preferred method of manufacture is injection moulding. Typical injection moulding parameters might be for example a cylinder nozzle temperature of 200-

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250°C, a mould temperature of 30-80°C, an injection pressure of 600-1800 bar and a moderate injection speed. Preferably, a low moulding speed is used initially and slowly increased during the moulding process. Preferably, the back pressure is as low as technically possible. Preferably, the material for injection moulding is pre-dried, for example at 75-80°C for up to 4 hours, for example 2-4 hours.

Thus, in a further aspect the present invention provides a method of constructing a component for use in an inhalation apparatus comprising moulding a component from a carbon black loaded polymeric material.

When the carbon black loaded polymeric material is a coating on another polymer, it may be co-moulded with the other polymeric material, for example using two extruders, to produce a moulded component in which the carbon black loaded polymeric material is surrounded by the other material; i.e., the "inner" surface of the component is of the carbon black loaded polymeric material and the "outer" surface of the component is of the other polymer. The outer material may be provided with any desired pigmentation, to mask the black colour of the carbon black in circumstances where this would be considered undesirable.

The thickness of the component or carbon black loaded polymeric layer may vary according to the nature of the moulded component. Where the component is a spacer device, for example, the thickness of the carbon black loaded polymeric material might be for example up to about 10 mm, for example between 1 mm and 5 mm thick.

The invention further described in the following non-limiting Examples.

Example 1

A carbon black loaded polymeric material, "PP 1381" (formerly "Pre-Elec TP 4474"), Premix Oy, Finland, comprising polypropylene "Hostalen PPU 1734S1", Hoechst, and 9% "Printex XE2", Degussa, was used to manufacture a spacer device for use with a dry

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powder inhaler device, by injection moulding using a "Ferromatic" injection moulder, with a cylinder nozzle temperature of 240°C, a mould cavity temperature of 30°C, an injection pressure of 1700 bar, a back pressure of 1600 bar and a moderate injection speed.

The specific volume resistivity obtained was 100 Ohmcm. (Surface resistance 1300 Ohm.)

Example 2

A carbon black loaded polymeric material, "Pre-Elec TP 4479", Premix Oy, Finland, comprising polypropylene "Hostalen PPU 1734S1", Hoechst, and 22% "Black Pearls 4750", Cabot Plastics, was used to manufacture a spacer device for use with a dry powder inhaler device, by injection moulding as in Example 1.

The specific volume resistivity obtained was 30 Ohmcm. (Surface resistance 800 Ohm.)

Example 3

A carbon black loaded polymeric material, "Pre-Elec TP 4480", Premix Oy, Finland, comprising polypropylene "Hostalen PPU 1734S1", Hoechst, and 37% "Channel Black MPC", was used to manufacture a spacer device for use with a dry powder inhaler device, by injection moulding as in Example 1.

The specific volume resistivity obtained was 10000 Ohmcm. (Surface resistance 100000 Ohm.)

Example 4

Doses of budesonide from a dry powder inhaler (Pulmicort Turbuhaler ®) containing 200 unit doses each comprising 400 µg of budesonide were expelled by means of a suction flow

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into a spacer device according to Example 1 above. After a 2 second delay, suction flow means were employed to expel the dose from the spacer device onto a filter.

The experiment was repeated using a spacer device constructed of polypropylene only. The means of manufacture of the polypropylene-only spacer was as in Example 1, but with an injection pressure of 900 bar and a back pressure of 600 bar.

The amount of budesonide on the filter after expulsion from the carbon black loaded polypropylene spacer of Example 1 was 2.4 times greater than the amount resulting from expulsion from the conventional polypropylene spacer. This was taken as an indication of the greatly reduced amount of medicament which had been retained in the spacer according to the present invention as compared with a conventional spacer.

Example 5

Doses of budesonide from a dry powder inhaler (Pulmicort Turbuhaler ®) containing 200 unit doses each comprising 400 μg of budesonide were expelled by means of a suction flow into a spacer device according to Example 1 above. After a 30 second delay, suction flow means were employed to expel the dose from the spacer device onto a filter.

The experiment was repeated using a spacer device constructed of polypropylene only.

The amount of budesonide on the filter after expulsion from the carbon black loaded polypropylene spacer of Example 1 was 2.8 times greater than the amount resulting from expulsion from the conventional polypropylene spacer. This was taken as an indication of the greatly reduced amount of medicament which had been retained in the spacer according to the present invention as compared with a conventional spacer.

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Claims

1. A component for use in an inhalation apparatus, said component being made of or coated with a polymeric material, characterised in that the polymeric material is loaded with carbon black in an amount sufficient to impart to the polymeric material a specific volume resistivity of less than 10^9 Ohmcm.

2. A component as claimed in claim 1, wherein the specific volume resistivity is less than 10^6 Ohmcm.

3. A component as claimed in claim 1, wherein the specific volume resistivity is less than 10^2 Ohmcm.

4. A component as claimed in any one of the preceding claims, wherein the carbon black is a carbon black dispersion.

5. A component as claimed in any one of the preceding claims, wherein the carbon black-loaded polymeric material comprises a homogeneous mixture of the carbon black and the polymer.

6. A component as claimed in any one of the preceding claims, wherein the said component is selected from the body of an inhaler, the mouthpiece of an inhaler and the channel of an inhaler.

7. A component as claimed in any one of claims 1-5, wherein the said component is a spacer device.

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8. A component as claimed in any one of the preceding claims, wherein the carbon black loaded polymeric material comprises carbon black in an amount of up to 40% by weight of the said material.

9. A component as claimed in claim 8, wherein the carbon black loaded polymeric material comprises carbon black in an amount of between 3% and 15% by weight of the said material.

10. A component as claimed in claim 9, wherein the carbon black loaded polymeric material comprises carbon black in an amount of between 8% and 10% by weight of the said material.

11. A component as claimed in claim 11, wherein the carbon black has a DBP number of at least 50 ml/100 g.

12. A component as claimed in any one of the preceding claims, wherein the carbon black has a DBP value of at least 110 ml/100 g.

13. A component as claimed in any one of the preceding claims, wherein the polymeric material is a polypropylene, a polyethylene, a polyester, a polycarbonate, a polystyrene, or a copolymer.

14. A component as claimed in claim 13, wherein the polymeric material is a polypropylene or a polyethylene.

15. A polymeric component for use in an inhalation apparatus, said component having a specific volume resistivity of less than 10^9 Ohmcm.

16. A polymeric component as claimed in claim 15, wherein said polymeric component is a spacer device.

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17. A polymeric component as claimed in claim 15 or claim 16, wherein the specific volume resistivity is less than 10^6 Ohmcm.

18. A polymeric component as claimed in claim 15 or claim 16, wherein the specific volume resistivity is less than 10^2 Ohmcm.

19. An inhalation apparatus comprising a component as claimed in any one of the preceding claims.

20. An inhalation apparatus as claimed in claim 19, wherein the inhalation apparatus comprises a spacer device.

21. A method of constructing a component for use in an inhalation apparatus comprising moulding a component from a carbon black loaded polymeric material.

22. A method of constructing an inhalation apparatus from at least the component of claim 21.

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