



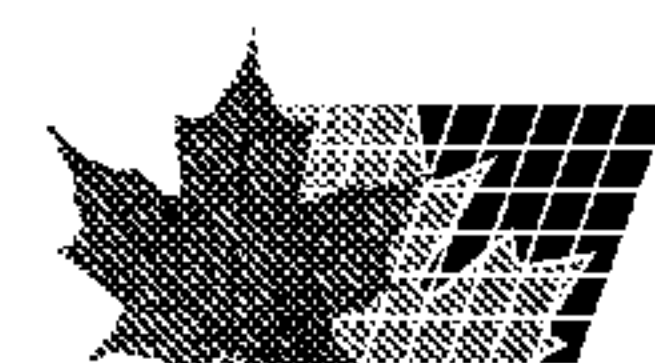
(86) Date de dépôt PCT/PCT Filing Date: 2006/05/12
(87) Date publication PCT/PCT Publication Date: 2006/11/16
(85) Entrée phase nationale/National Entry: 2007/11/07
(86) N° demande PCT/PCT Application No.: GB 2006/001754
(87) N° publication PCT/PCT Publication No.: 2006/120469
(30) Priorités/Priorities: 2005/05/13 (GB0509824.9);
2005/08/24 (GB0517361.2)

(51) Cl.Int./Int.Cl. *A61K 9/12* (2006.01)
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(54) Titre : MOUSSE THERAPEUTIQUE
(54) Title: THERAPEUTIC SCLEROSING FOAM MADE PREFERABLY XENON

(57) **Abrégé/Abstract:**

A foam for the treatment of varicose veins is disclosed, comprising a sclerosant solution, e.g. polidocanol, foamed with a gas mixture which includes greater than 41 % of a lipid soluble gas such as xenon. The aim is to provide a foam which may be injected into a varicose vein in large quantities because the gas component is dissipated quickly after the foam has acted on the varicose vein.



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

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
16 November 2006 (16.11.2006)

PCT

(10) International Publication Number
WO 2006/120469 A3

(51) International Patent Classification:
A61K 9/12 (2006.01)

(21) International Application Number:
PCT/GB2006/001754

(22) International Filing Date: 12 May 2006 (12.05.2006)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0509824.9 13 May 2005 (13.05.2005) GB
0517361.2 24 August 2005 (24.08.2005) GB

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

(88) Date of publication of the international search report:
21 December 2006

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: THERAPEUTIC SCLEROSING FOAM MADE PREFERABLY XENON

(57) Abstract: A foam for the treatment of varicose veins is disclosed, comprising a sclerosant solution, e.g. polidocanol, foamed with a gas mixture which includes greater than 41 % of a lipid soluble gas such as xenon. The aim is to provide a foam which may be injected into a varicose vein in large quantities because the gas component is dissipated quickly after the foam has acted on the varicose vein.



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Therapeutic foam

The present invention relates to a therapeutic foam e.g. for treatment of varicose veins.

5 In recent years the use of sclerosing chemicals in the form of foams has become a popular way of treating varicose veins. Foam is injected into the affected vein whilst its progress is monitored using ultrasound scanning. The process causes sclerosis and functional elimination of the vein. Other disorders such as venous malformations may also be treated this way.

10 Most practitioners make foam extemporaneously using ambient air as the gaseous component. As extensively discussed in copending patent applications nos. PCT/GB04/004824, PCT/GB04/004831, PCT/GB04/004846 and PCT/GB04/004848, the use of air foams is potentially harmful and, in the view of the inventors, is to be avoided. The inventors have followed the key disclosure by the Cabrerias in their
15 patent EP0656203B who first proposed a microfoam with oxygen or carbon dioxide as the gas component. Carbon dioxide and oxygen are respectively dissolved in blood in or absorbed by haemoglobin, thus making both considerably more attractive than air.

There are other gases which are very soluble, e.g. nitrous oxide. Helium has
20 also been considered since it passes easily across pulmonary gas exchange membranes and hence is exhaled from the body quickly.

The inventors have now surprisingly realised that the gas need not be soluble and need not necessarily be absorbed only by the blood: it is possible to overcome the problem of foam treatment leaving residual gas in the body by using a gas component
25 which dissolves into tissue other than blood, e.g. the vein walls. In this context, they have conceived of the possibility of using a lipid soluble gas, e.g. one or more of the noble gases, as a substantial proportion (greater than 40%) of the gas component of the foam. The higher molecular weight noble gases, especially xenon, are known to dissolve in lipid, e.g. in cell walls. Thus it appears that these gases may be taken up
30 by the body quickly if injected into the venous system, both into the cells of the vein walls and into the blood cells. This dual mode of uptake may give rise to very fast absorption, especially if the gas also has a degree of solubility in water as well. Speed of uptake is critical because if gas is taken up slowly, this may give the opportunity for nitrogen which is already dissolved in the blood to diffuse into the foam,

potentially causing enduring bubbles. Again, this is discussed at length in the copending applications mentioned above.

According to the present invention a foam is provided comprising a liquid phase and a gas phase wherein the liquid phase comprises at least one sclerosing agent and the gas phase comprises between 41% and 100% of a gas which is lipid soluble, preferably between 50 and 100%, more preferably between 60 and 100%, still more preferably between 70 and 100%, 80 and 100% or 90 and 100%.

The lipid soluble gas may be argon, krypton or xenon or a mixture of these. The most preferred of these is xenon. Xenon is used as an anaesthetic, and its behaviour in body tissue is well understood: see for example "Xenon Anesthesia": Lynch et al, *Anesthesiology*, v92, No.3, March 2000. Xenon has the further advantage that it is moderately soluble in water (mole fraction solubility 7.9×10^{-5} , which is three times as soluble as oxygen).

If the lipid soluble gas does not make up 100% of the gas phase, then it is preferred that the remainder of the gas phase consist essentially of oxygen, carbon dioxide or a mixture of the two.

Example

A fume cupboard is filled with greater than 99% pure xenon gas, after placing in the cupboard a small (100ml) beaker containing 10ml 1% polidocanol solution, together with a small hand held electric motor with a chuck in which is mounted a small (10mm diameter) dental brush. The motor is switched on and the speed adjusted to 12,000 r.p.m. The dental brush is then gently inserted into the liquid in the beaker, such that a vortex is formed in the surface of the liquid in the beaker. After a few seconds a foam forms, which becomes finer and more homogeneous as time goes on. After 90 seconds the brush is removed. In the beaker is a stiff, homogeneous foam whose bubbles are in the main part invisible to the naked eye (a "microfoam"). The beaker may be inverted for a few seconds without the foam falling out. 30ml of the foam is then drawn out of the beaker using a syringe for use in the treatment of a human patient's varicose veins using methodology which is generally known in this field.

Claims

1. A foam having a liquid phase and a gas phase wherein the liquid phase comprises at least one sclerosing agent and the gas phase comprises between 41% and
5 100% of a gas which is lipid soluble

2. A foam as claimed in claim 1 wherein the gas phase comprises between 50 and 100%, more preferably between 60 and 100%, still more preferably between 70 and 100%, 80 and 100% or 90 and 100% of gas which is lipid soluble.
10

3. A foam as claimed in claim 1 or claim 2 wherein the lipid soluble gas is a noble gas or mixture of noble gases.

4. A foam as claimed in claim 3 wherein the lipid soluble gas is argon, krypton or xenon or a mixture of two or more of these gases.
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5. A foam as claimed in any preceding claim wherein the remainder of the gas phase is substantially made up by oxygen, carbon dioxide or a mixture of oxygen and carbon dioxide.
20

6. A foam as claimed in any preceding claim wherein the sclerosing agent is polidocanol solution.

7. A method of treating varicose veins comprising injecting into an affected vein a foam as claimed in any of the preceding claims.
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8. A method as claimed in claim 7 wherein substantially an entire greater saphenous vein is treated in one injection.

9. A method as claimed in claim 7 or claim 8 wherein between 15ml and 50ml of foam are injected.
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