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[Continued on next page]

(54) Title: DRUG CONTAINER AND DRUG DELIVERY DEVICE

(57) Abstract: The invention relates to a drug container (2), comprising a flexible bag with a distal end (2.1) connectable to a discharge nozzle (5), wherein the bag is compressible by a compression means (3), wherein the compression means (3) is arranged as an axle (3) attached to an opposite end of the bag and arranged to be rotated so as to spirally wind the bag about the axle (3).

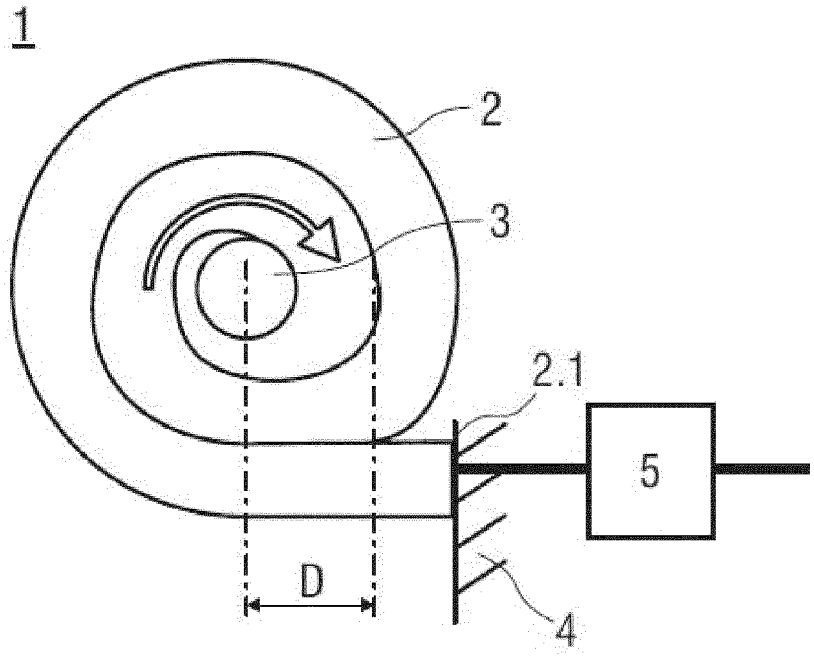

FIG 1

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TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— *of inventorship (Rule 4.17(iv))*

Published:

— *with international search report (Art. 21(3))*

Drug container and drug delivery device

Technical Field

The invention relates to a drug container and a drug delivery device.

Background of the Invention

Many medicaments or drugs are injected into the body. This applies in particular to medicaments, which are deactivated or have their efficiency remarkably decreased by oral administration, e.g. proteines (such as insulin, growth hormones, interferons), carbohydrates (e.g. heparin), antibodies and the majority of vaccines. Such medicaments are predominantly injected by means of syringes, medicament pens or medicament pumps.

Summary of the Invention

It is an object of the present invention to provide an improved drug container and an improved drug delivery device.

The object is achieved by a drug container according to claim 1 and by a drug delivery device according to claim 2.

Preferred embodiments of the invention are given in the dependent claims.

According to the invention a drug container comprises a flexible bag with a distal end connectable to a discharge nozzle, wherein the bag is compressible by a compression means, wherein the compression means is arranged as an axle attached to an end of the bag opposite the distal end and arranged to be rotated so as to spirally wind the bag about the axle.

If the axle is rotated, the spirally wound drug container is squeezed such that an amount of drug depending on an angle of rotation of the axle is displaced from the drug container through the discharge nozzle.

The drug container according to the invention has less weight than a glass ampoule. As opposed to conventional ampoules and syringes, where stopper friction has to be overcome in order to displace the drug, the drug container according to the invention does not have a stopper and hence no stopper related friction. The drug may be easily dosed by rotating the axle about a defined angle. Due to the simplicity and low part count the drug container is particularly inexpensive. The drug container according to the invention minimizes space requirement other than conventional drug containers which require a piston rod about the same length as the container itself.

The drug container may be applied in a drug delivery device, wherein a distal end of the flexible drug container is attached to a housing and in fluid communication with a discharge nozzle.

A guide may be arranged for shifting or allowing to shift the axle towards the housing, where the distal end of the drug container is attached. For example, a linear guide may be arranged for radially shifting the axle towards the housing.

As the diameter of the spirally wound drug container progressively decreases when emptying the drug container the guide is arranged for shifting or allowing to shift the axle towards the housing such that an amount of residual drug in the drug container is minimized which is particularly important when delivering expensive drugs.

The guide may comprise slot holes for bearing the axle, wherein the slot holes are aligned to allow movement (e.g. radial movement) of the axle towards and away from the fixing point of the container, for example to the housing or the needle. This embodiment passively allows radial movement of the axle and is particularly simple and inexpensive.

In another embodiment the linear guiding comprises a gear radially moving the axle towards and away from the housing depending on the angle of rotation of the axle. This embodiment is active and allows for precisely shifting the axle.

The axle may be manually rotated. In another embodiment the axle may be rotated by a motor such as an electric motor, a torsion spring, a constant force spring, etc.

The discharge nozzle may be arranged as an injection needle or a jet nozzle. Further, a meter measuring the flow through the nozzle may be provided, such that defined amounts of medicament may be expelled through the nozzle with high accuracy.

The drug delivery device may be arranged as an inhaler device or an injection device.

The term “drug” or “medicament“, as used herein, means a pharmaceutical formulation containing at least one pharmaceutically active compound,

wherein in one embodiment the pharmaceutically active compound has a molecular weight up to 1500 Da and/or is a peptide, a proteine, a polysaccharide, a vaccine, a DNA, a RNA, an enzyme, an antibody or a fragment thereof, a hormone or an oligonucleotide, or a mixture of the above-mentioned pharmaceutically active compound,

wherein in a further embodiment the pharmaceutically active compound is useful for the treatment and/or prophylaxis of diabetes mellitus or complications associated with diabetes mellitus such as diabetic retinopathy, thromboembolism disorders such as deep vein or pulmonary thromboembolism, acute coronary syndrome (ACS), angina, myocardial infarction, cancer, macular degeneration, inflammation, hay fever, atherosclerosis and/or rheumatoid arthritis,

wherein in a further embodiment the pharmaceutically active compound comprises at least one peptide for the treatment and/or prophylaxis of diabetes mellitus or complications associated with diabetes mellitus such as diabetic retinopathy,

wherein in a further embodiment the pharmaceutically active compound comprises at least one human insulin or a human insulin analogue or derivative, glucagon-like peptide (GLP-1) or an analogue or derivative thereof, or exendin-3 or exendin-4 or an analogue or derivative of exendin-3 or exendin-4.

Insulin analogues are for example Gly(A21), Arg(B31), Arg(B32) human insulin; Lys(B3), Glu(B29) human insulin; Lys(B28), Pro(B29) human insulin; Asp(B28) human insulin; human insulin, wherein proline in position B28 is replaced by Asp, Lys, Leu, Val or Ala and wherein in position B29 Lys may be replaced by Pro; Ala(B26) human insulin; Des(B28-B30) human insulin; Des(B27) human insulin and Des(B30) human insulin.

Insulin derivates are for example B29-N-myristoyl-des(B30) human insulin; B29-N-palmitoyl-des(B30) human insulin; B29-N-myristoyl human insulin; B29-N-palmitoyl human insulin; B28-N-myristoyl LysB28ProB29 human insulin; B28-N-palmitoyl-LysB28ProB29 human insulin; B30-N-myristoyl-ThrB29LysB30 human insulin; B30-N-palmitoyl-ThrB29LysB30 human insulin; B29-N-(N-palmitoyl-Y-glutamyl)-des(B30) human insulin; B29-N-(N-lithocholyl-Y-glutamyl)-des(B30) human insulin; B29-N-(ω-carboxyheptadecanoyl)-des(B30) human insulin and B29-N-(ω-carboxyheptadecanoyl) human insulin.

Exendin-4 for example means Exendin-4(1-39), a peptide of the sequence H-His-Gly-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH2.

Exendin-4 derivatives are for example selected from the following list of compounds:

H-(Lys)4-des Pro36, des Pro37 Exendin-4(1-39)-NH2,
H-(Lys)5-des Pro36, des Pro37 Exendin-4(1-39)-NH2,
des Pro36 Exendin-4(1-39),
des Pro36 [Asp28] Exendin-4(1-39),
des Pro36 [IsoAsp28] Exendin-4(1-39),
des Pro36 [Met(O)14, Asp28] Exendin-4(1-39),
des Pro36 [Met(O)14, IsoAsp28] Exendin-4(1-39),
des Pro36 [Trp(O2)25, Asp28] Exendin-4(1-39),
des Pro36 [Trp(O2)25, IsoAsp28] Exendin-4(1-39),
des Pro36 [Met(O)14 Trp(O2)25, Asp28] Exendin-4(1-39),
des Pro36 [Met(O)14 Trp(O2)25, IsoAsp28] Exendin-4(1-39); or

des Pro36 [Asp28] Exendin-4(1-39),
des Pro36 [IsoAsp28] Exendin-4(1-39),
des Pro36 [Met(O)14, Asp28] Exendin-4(1-39),
des Pro36 [Met(O)14, IsoAsp28] Exendin-4(1-39),
des Pro36 [Trp(O2)25, Asp28] Exendin-4(1-39),
des Pro36 [Trp(O2)25, IsoAsp28] Exendin-4(1-39),
des Pro36 [Met(O)14 Trp(O2)25, Asp28] Exendin-4(1-39),
des Pro36 [Met(O)14 Trp(O2)25, IsoAsp28] Exendin-4(1-39),
wherein the group -Lys6-NH2 may be bound to the C-terminus of the Exendin-4 derivative;

or an Exendin-4 derivative of the sequence
des Pro36 Exendin-4(1-39)-Lys6-NH2 (AVE0010),
H-(Lys)6-des Pro36 [Asp28] Exendin-4(1-39)-Lys6-NH2,
des Asp28 Pro36, Pro37, Pro38Exendin-4(1-39)-NH2,
H-(Lys)6-des Pro36, Pro38 [Asp28] Exendin-4(1-39)-NH2,
H-Asn-(Glu)5des Pro36, Pro37, Pro38 [Asp28] Exendin-4(1-39)-NH2,
des Pro36, Pro37, Pro38 [Asp28] Exendin-4(1-39)-(Lys)6-NH2,
H-(Lys)6-des Pro36, Pro37, Pro38 [Asp28] Exendin-4(1-39)-(Lys)6-NH2,
H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Asp28] Exendin-4(1-39)-(Lys)6-NH2,
H-(Lys)6-des Pro36 [Trp(O2)25, Asp28] Exendin-4(1-39)-Lys6-NH2,
H-des Asp28 Pro36, Pro37, Pro38 [Trp(O2)25] Exendin-4(1-39)-NH2,
H-(Lys)6-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-NH2,
H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-NH2,
des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-(Lys)6-NH2,
H-(Lys)6-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-(Lys)6-NH2,
H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Trp(O2)25, Asp28] Exendin-4(1-39)-(Lys)6-NH2,
H-(Lys)6-des Pro36 [Met(O)14, Asp28] Exendin-4(1-39)-Lys6-NH2,
des Met(O)14 Asp28 Pro36, Pro37, Pro38 Exendin-4(1-39)-NH2,
H-(Lys)6-desPro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-NH2,
H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-NH2,
des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-(Lys)6-NH2,
H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-(Lys)6-NH2,
H-Asn-(Glu)5 des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-(Lys)6-NH2,
H-Lys6-des Pro36 [Met(O)14, Trp(O2)25, Asp28] Exendin-4(1-39)-Lys6-NH2,

H-des Asp28 Pro36, Pro37, Pro38 [Met(O)14, Trp(O2)25] Exendin-4(1-39)-NH2,
H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Asp28] Exendin-4(1-39)-NH2,
H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(O)14, Trp(O2)25, Asp28] Exendin-4(1-39)-NH2,
des Pro36, Pro37, Pro38 [Met(O)14, Trp(O2)25, Asp28] Exendin-4(1-39)-(Lys)6-NH2,
H-(Lys)6-des Pro36, Pro37, Pro38 [Met(O)14, Trp(O2)25, Asp28] Exendin-4(S1-39)-(Lys)6-NH2,
H-Asn-(Glu)5-des Pro36, Pro37, Pro38 [Met(O)14, Trp(O2)25, Asp28] Exendin-4(1-39)-(Lys)6-NH2;

or a pharmaceutically acceptable salt or solvate of any one of the afore-mentioned Exendin-4 derivative.

Hormones are for example hypophysis hormones or hypothalamus hormones or regulatory active peptides and their antagonists as listed in Rote Liste, ed. 2008, Chapter 50, such as Gonadotropine (Follitropin, Lutropin, Choriongonadotropin, Menotropin), Somatropine (Somatropin), Desmopressin, Terlipressin, Gonadorelin, Triptorelin, Leuprorelin, Buserelin, Nafarelin, Goserelin.

A polysaccharide is for example a glucosaminoglycane, a hyaluronic acid, a heparin, a low molecular weight heparin or an ultra low molecular weight heparin or a derivative thereof, or a sulphated, e.g. a poly-sulphated form of the above-mentioned polysaccharides, and/or a pharmaceutically acceptable salt thereof. An example of a pharmaceutically acceptable salt of a poly-sulphated low molecular weight heparin is enoxaparin sodium.

Antibodies are globular plasma proteins (~150 kDa) that are also known as immunoglobulins which share a basic structure. As they have sugar chains added to amino acid residues, they are glycoproteins. The basic functional unit of each antibody is an immunoglobulin (Ig) monomer (containing only one Ig unit); secreted antibodies can also be dimeric with two Ig units as with IgA, tetrameric with four Ig units like teleost fish IgM, or pentameric with five Ig units, like mammalian IgM.

The Ig monomer is a "Y"-shaped molecule that consists of four polypeptide chains; two identical heavy chains and two identical light chains connected by disulfide bonds between

cysteine residues. Each heavy chain is about 440 amino acids long; each light chain is about 220 amino acids long. Heavy and light chains each contain intrachain disulfide bonds which stabilize their folding. Each chain is composed of structural domains called Ig domains. These domains contain about 70-110 amino acids and are classified into different categories (for example, variable or V, and constant or C) according to their size and function. They have a characteristic immunoglobulin fold in which two β sheets create a "sandwich" shape, held together by interactions between conserved cysteines and other charged amino acids.

There are five types of mammalian Ig heavy chain denoted by α, δ, ε, γ, and μ. The type of heavy chain present defines the isotype of antibody; these chains are found in IgA, IgD, IgE, IgG, and IgM antibodies, respectively.

Distinct heavy chains differ in size and composition; α and γ contain approximately 450 amino acids and δ approximately 500 amino acids, while μ and ε have approximately 550 amino acids. Each heavy chain has two regions, the constant region (C_H) and the variable region (V_H). In one species, the constant region is essentially identical in all antibodies of the same isotype, but differs in antibodies of different isotypes. Heavy chains γ, α and δ have a constant region composed of three tandem Ig domains, and a hinge region for added flexibility; heavy chains μ and ε have a constant region composed of four immunoglobulin domains. The variable region of the heavy chain differs in antibodies produced by different B cells, but is the same for all antibodies produced by a single B cell or B cell clone. The variable region of each heavy chain is approximately 110 amino acids long and is composed of a single Ig domain.

In mammals, there are two types of immunoglobulin light chain denoted by λ and κ. A light chain has two successive domains: one constant domain (CL) and one variable domain (VL). The approximate length of a light chain is 211 to 217 amino acids. Each antibody contains two light chains that are always identical; only one type of light chain, κ or λ, is present per antibody in mammals.

Although the general structure of all antibodies is very similar, the unique property of a given antibody is determined by the variable (V) regions, as detailed above. More specifically, variable loops, three each the light (VL) and three on the heavy (VH) chain,

are responsible for binding to the antigen, i.e. for its antigen specificity. These loops are referred to as the Complementarity Determining Regions (CDRs). Because CDRs from both VH and VL domains contribute to the antigen-binding site, it is the combination of the heavy and the light chains, and not either alone, that determines the final antigen specificity.

An “antibody fragment” contains at least one antigen binding fragment as defined above, and exhibits essentially the same function and specificity as the complete antibody of which the fragment is derived from. Limited proteolytic digestion with papain cleaves the Ig prototype into three fragments. Two identical amino terminal fragments, each containing one entire L chain and about half an H chain, are the antigen binding fragments (Fab). The third fragment, similar in size but containing the carboxyl terminal half of both heavy chains with their interchain disulfide bond, is the crystalizable fragment (Fc). The Fc contains carbohydrates, complement-binding, and FcR-binding sites. Limited pepsin digestion yields a single F(ab')2 fragment containing both Fab pieces and the hinge region, including the H-H interchain disulfide bond. F(ab')2 is divalent for antigen binding. The disulfide bond of F(ab')2 may be cleaved in order to obtain Fab'. Moreover, the variable regions of the heavy and light chains can be fused together to form a single chain variable fragment (scFv).

Pharmaceutically acceptable salts are for example acid addition salts and basic salts. Acid addition salts are e.g. HCl or HBr salts. Basic salts are e.g. salts having a cation selected from alkali or alkaline, e.g. Na+, or K+, or Ca2+, or an ammonium ion N+(R1)(R2)(R3)(R4), wherein R1 to R4 independently of each other mean: hydrogen, an optionally substituted C1-C6-alkyl group, an optionally substituted C2-C6-alkenyl group, an optionally substituted C6-C10-aryl group, or an optionally substituted C6-C10-heteroaryl group. Further examples of pharmaceutically acceptable salts are described in "Remington's Pharmaceutical Sciences" 17. ed. Alfonso R. Gennaro (Ed.), Mark Publishing Company, Easton, Pa., U.S.A., 1985 and in Encyclopedia of Pharmaceutical Technology.

Pharmaceutically acceptable solvates are for example hydrates.

Further scope of applicability of the present invention will become apparent from the detailed description given hereinafter. However, it should be understood that the detailed description and specific examples, while indicating preferred embodiments of the invention,

are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.

Brief Description of the Drawings

The present invention will become more fully understood from the detailed description given hereinbelow and the accompanying drawings which are given by way of illustration only, and thus, are not limitive of the present invention, and wherein:

Figure 1 is a schematic view of a drug delivery device prior to drug delivery, and

Figure 2 is a schematic view of a drug delivery device after drug delivery.

Corresponding parts are marked with the same reference symbols in all figures.

Detailed Description of Preferred Embodiments

Figure 1 is a schematic view of a drug delivery device 1 prior to drug delivery. The drug delivery device 1 comprises a flexible drug container 2 spirally wound about an axle 3. A distal end 2.1 of the flexible drug container 2 is attached to a housing 4 and in fluid communication with a discharge nozzle 5, which may be arranged as an injection needle or a jet nozzle.

If the axle 3 is rotated clockwise, the spirally wound drug container 2 is squeezed such that an amount of drug depending on an angle of rotation of the axle 3 is displaced from the drug container 2 through the discharge nozzle 5.

As the diameter of the spirally wound drug container 2 progressively decreases when emptying the drug container 2 a linear guiding is arranged for radially shifting or allowing to radially shift the axle 3 towards the housing 4, where the distal end 2.1 of the drug container 2 is attached.

The linear guiding may be arranged as slot holes for bearing the axle 3, wherein the slot holes are aligned to allow radial movement of the axle 3 towards and away from the housing 4.

Likewise the linear guiding may comprise a gear radially moving the axle 3 towards and away from the housing 4 depending on the angle of rotation of the axle 3.

The axle 3 may be manually rotated. In another embodiment the axle 3 may be rotated by a motor such as an electric motor, a torsion spring, a constant force spring, etc.

Figure 2 is a schematic view of the drug delivery device 1 after drug delivery with the drug container 2 fully emptied and the axle 3 hence moved by a distance D towards the housing 4, where the distal end 2.1 of the drug container 2 is attached, so that an amount of residual drug in the drug container 2 is minimized. The axle 3 may move straight or at an angle towards the housing 4, where the distal end 2.1 of the drug container 2 is attached.

In the illustrated embodiment the axle 3 is rotated in the clockwise sense for emptying the drug container 2. It goes without saying that an alternative embodiment could be arranged to empty the drug container 2 on counter-clockwise rotation of the axle 3.

List of References

1	drug delivery device
2	drug container
2.1	distal end
3	axle
4	housing
5	discharge nozzle
D	distance

Claims

1. Drug delivery device (1) comprising a flexible drug container (2) , wherein a distal end (2.1) of the flexible drug container (2) is attached to a housing (4) and in fluid communication with a discharge nozzle (5), wherein the bag is compressible by an axle (3) attached to an opposite end of the bag and arranged to be rotated so as to spirally wind the bag about the axle (3), wherein a motor is arranged for driving the axle (3), characterized in that the motor is arranged as an electric motor.

2. Drug delivery device (1) according to claim 1, characterized in that a guide is arranged for shifting or allowing shifting the axle (3) towards a fixing point of the container at the housing (4), where the distal end (2.1) of the drug container (2) is attached.

3. Drug delivery device (1) according to claim 2, characterized in that the guide comprises slot holes for bearing the axle (3), wherein the slot holes are aligned to allow movement of the axle (3) towards and away from the fixing point of the container at the housing (4).

4. Drug delivery device (1) according to claim 2, characterized in that the guide comprises a gear radially moving the axle (3) towards and away from the housing (4) depending on the angle of rotation of the axle (3).

5. Drug delivery device (1) according to one of the claims 1 to 4, characterized in that the discharge nozzle (5) is arranged as an injection needle.

6. Drug delivery device (1) according to one of the claims 1 to 4, characterized in that the discharge nozzle (5) is arranged as a jet nozzle.

7. Drug delivery device (1) according to one of the claims 1 to 4 arranged as an inhaler device.

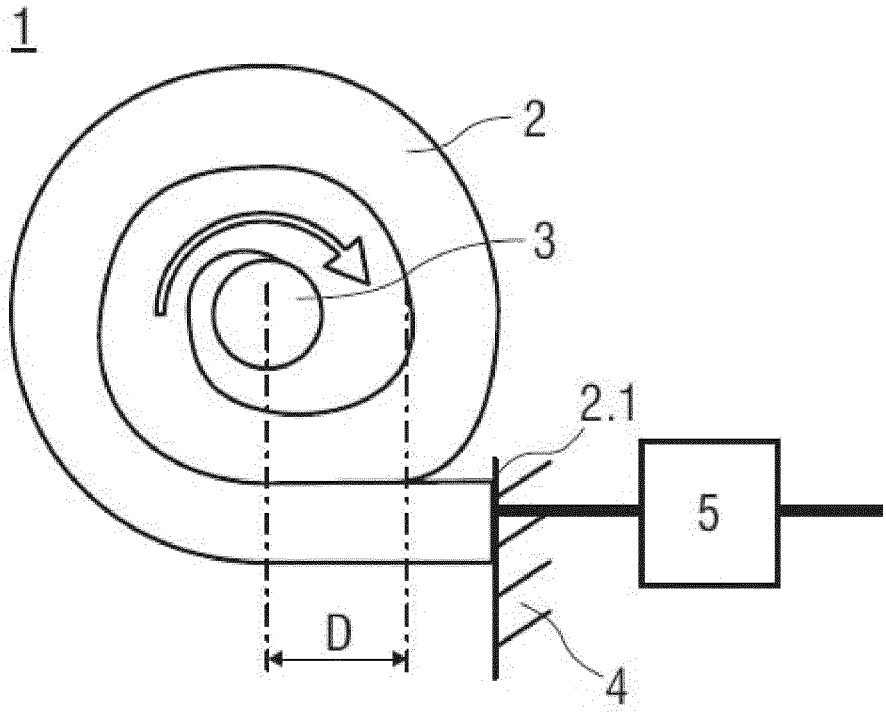

FIG 1

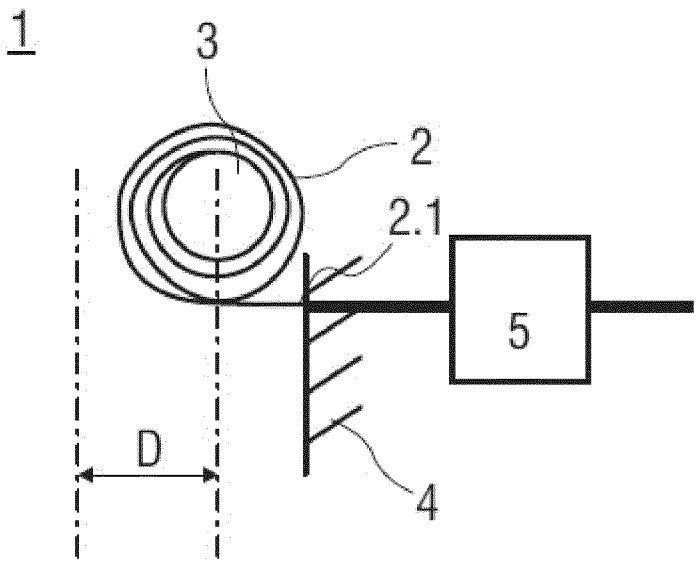

FIG 2

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/063239

A. CLASSIFICATION OF SUBJECT MATTER
INV. A61M5/148 A61M5/24 A61M5/28 A61J1/05 B65D35/28
ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
A61M A61B A61J B65D

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 187 860 A (VILLARI FRANK K [US]) 12 February 1980 (1980-02-12)	1
Y	figures 1-3	2-7

X	US 2 907 326 A (WILLIAM GERARDE HORACE) 6 October 1959 (1959-10-06)	1
Y	figure 3	2-7

X	EP 0 080 179 A1 (INTERMEDICAT GMBH [CH]) 1 June 1983 (1983-06-01)	1
Y	figures	2-7

A	US 2 727 516 A (LOCKHART MARSHALL L) 20 December 1955 (1955-12-20) figures	1-7

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[X] Further documents are listed in the continuation of Box C.

[X] See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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Date of the actual completion of the international search	Date of mailing of the international search report
18 July 2013	25/07/2013

Name and mailing address of the ISA/	Authorized officer
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1

Form PCT/ISA/210 (second sheet) (April 2005)

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2013/063239

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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