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(54) **Container and closure for sterilised or low bacterial load products free of preservatives**

Konservierungsmittelfreie Behälter und Verschluss für sterilisierte Produkte oder Produkte mit niedriger Bakterienzahl

Conteneur et fermeture pour produits stérilisés ou à faible teneur en bactéries sans conservateurs

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(73) Proprietor: **S.M.P. S.r.l.**
23881 Airuno (LC) (IT)

(72) Inventors:
• **Stucchi, Diego**
23881 AIRUNO (LC) (IT)

• **Montani, Fiorenzo**
20020 ARESE (MI) (IT)

(74) Representative: **Finetti, Claudia**
Barzanò & Zanardo
Via Borgonuovo 10
20121 Milano (IT)

(56) References cited:
EP-A1- 2 113 466 JP-A- 3 150 122
JP-A- 3 289 476 JP-A- 8 151 083
US-A- 5 518 774 US-B1- 6 179 141

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Description

[0001] The present invention relates to a container and a relative closing element for sterilised products or products with low bacterial load free of preservatives.

[0002] In particular, the present invention relates to a container and relative closing element suitable for limiting and/or reducing the growth of bacteria within a sterile product and/or with low bacterial load free of preservatives, during usage.

[0003] The present invention further relates to a primary packaging device for the above-mentioned products as well as to the use of the above-mentioned device for limiting and/or reducing the growth of bacteria within these products during usage. Examples of products that may be stored in the containers of the present invention are pharmaceutical products, medical devices, cosmetic products, dietetic and food products. Such products may be in form of liquid, gel, suspension, paste, powder or granules.

[0004] The microorganisms, naturally present in large amounts and various species, may contaminate products packaged in sterile conditions or with low bacterial load (for example pharmaceutical products) once the container is opened by the consumer and they can multiply very quickly, especially if the environmental conditions are not such as to favour the growth and proliferation thereof.

[0005] The presence of such microorganisms (for example, bacteria, fungi, yeasts, mildews, etc.) negatively affects the hygienic, life and quality conditions of the packaged product, leading to degradation of the product, to the proliferation of pathogenic agents and consequently, to serious risks for the health of the product's end user.

[0006] For these reasons, the packaging of pharmaceutical, cosmetic, dietetic and food products should prevent the product contamination by the microorganisms present in the environment outside the container as much as possible once it has been opened for the first time, that is, after the user has used the first product dose and has closed the container back to store the remaining product thereof for the subsequent administrations. The reclosable containers suitable for containing products intended for being used in portions (doses) at subsequent times are called pluridose or multidose containers.

[0007] In order to reduce the risks associated to the product contamination by microorganisms, the formulations of the products of the above-mentioned type in the prior art are generally admixed with preserving substances, suitable for limiting or preventing the microbial growth that may develop within the same products during the usage thereof. Preservatives suitable for such purpose are, for example, benzalkonium chloride, sodium thiomersal, clorexidin, methylparaben, ethylparaben, propylparaben, phenol, polyhexamethylenebiguanide (PHMB), N-hydroxymethylglycinate, chlorbutanol.

[0008] The use of preservatives in the formulations of sterile products or with a low bacterial load, however, is undesired since their presence may also affect the consumer's health in an unexpected manner, generating undesired reactions.

[0009] In order to obviate the use of preservatives, the use of containers provided with filters, or other mechanical devices that prevent the passage of microorganisms, has been proposed in the prior art. When the product, for example a collyrium, is used, the filters or other mechanical devices present in the container allows the output to the outside of the product and at the same time they prevent the inlet of microorganisms within the container.

[0010] While this technical solution prevents the product contamination within the container and thus favours the storage thereof in optimum conditions, it has the drawback of not preventing the use of the contaminated product by the user. From the second use on, in fact, the product is forced to cross a filter or the subsequent dispensing zone (for example, the drop dispenser tip in the case of a collyrium container) contaminated by microorganisms, in turn becoming contaminated.

[0011] An alternative solution to the addition of preservatives proposed in the prior art is that described in patent application WO0026100. This document describes the use of a closing element for containers intended for containing drinks for babies, such as for example a feeding bottle, made of a plastic material admixed with an inorganic antimicrobial agent, such as an antibacterial zeolite.

[0012] The containers having closing elements of the type described in WO0026100 ensure higher hygienic conditions than those of the containers having conventional closing elements; however, they are only suitable for containing products that do not require sterility or particularly low bacterial load conditions (for example food liquids), as on the other hand are the conditions required for the pharmaceutical or cosmetic products.

[0013] In fact, it is known that the plastics generally used for making food containers have the drawback of allowing the bacterial proliferation. Therefore, using a closing device of an antibacterial material on containers made of plastic of the conventional type does not adequately ensure the product preservation at the desired low bacterial load conditions.

[0014] Besides the specific drawbacks described above, it is important that the antibacterial agents described in the prior art are not always capable of ensuring the desired bactericide and/or bacteriostatic action towards all types of microorganisms. In particular, the Applicant does not know any container for sterile products or with a low bacterial load, made of a plastic material, capable of reducing and/or preventing the concurrent proliferation of bacteria and fungi, such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Candida albicans* and *Aspergillus niger* according to the requirements set forth by the European Pharmacopoeia, by the United States Pharmacopoeia and by the Japanese Pharma-

copoeia.

[0015] US 6 179 141 B1 discloses a container according to the preamble of claim 1.

[0016] The object of the present invention is to overcome the drawbacks highlighted by the prior art.

[0017] Therefore, the object of the present invention is a reclosable container according to claim 1.

[0018] A further object of the present invention is the use of said primary packaging device for packaging sterile products or with low bacterial load free of preservatives, according to claim 14, and its use in combination with ophthalmic liquid in accordance with claim 15.

[0019] In particular, the primary packaging device according to the present invention is a dispensing device of the multidose type comprising a container, which contains a sterile product and/or with low bacterial load free of preservatives, and the relative closing element. The device may be opened by the user for taking a dose of the contents and then closed back for storing the product until the next use. The device prevents the product contamination by external microorganisms both during the pick up of a dose and between one pick up and the next one.

[0020] To better understand the features of the present invention, reference shall be made to the following figures in the description:

- figure 1 shows a schematic view of a container and of the relative closing element according to a first embodiment of the present invention;
- figure 2 shows a schematic view of a container and of the relative closing element according to a second embodiment of the present invention.

[0021] The Applicant has surprisingly perceived that the use of a thermoplastic material wherein an antibacterial composition is dispersed for making a reclosable container and the relative closing element allows making a packaging device suitable for containing sterile products or with low bacterial load that are preserved over time and also during the different usage steps (administration) of the product, preventing the addition of preservatives of any kind to the formulation of the product to be preserved.

[0022] According to the present invention, the container is an enclosure wherein at least the inner surface is made of a material consisting of a thermoplastic resin comprising an antibacterial composition. Hereinafter in the present description, the terms "resin" and "thermoplastic material" are used as synonyms.

[0023] By inner surface of the container it is meant the surface that may come to contact with the product during the product packaging steps and the subsequent use by the end user. Typically, the enclosure that makes up the container is made entirely of said thermoplastic resin comprising an antibacterial composition.

[0024] The thermoplastic material suitable for making the container of the present invention and the relative closing element is a thermoplastic material comprising, or consisting of, a polymeric resin for example selected from: polyethylene (PE), polypropylene (PP), polyethylene terephthalate (PET), polyvinylchloride (PVC), polycarbonate (PC) and thermoplastic rubber (for example, poly-butadiene-styrene (PBS)).

[0025] The antibacterial composition is a chemical composition capable of exerting a prevention action in the proliferation of microorganisms and/or of reduction of the number thereof where these are present. Hereinafter in the present description, such action shall be indicated as "antibacterial action". For the purposes of the present invention, the term microorganisms refers to unicellular organisms classified as bacteria, fungi, yeasts, mildews and spores.

[0026] The antibacterial composition present in the thermoplastic resin comprises metal ions with antibacterial action. The metal ions with antibacterial action are selected from the group consisting of silver, copper, zinc, gold and mixtures thereof. Preferably, silver ions are used due to the higher antibacterial efficacy thereof. Even more preferably, mixtures of silver ions and zinc ions are used.

[0027] Metal ions are supported on solid supports, such as ceramic structures based on zirconium phosphate and/or on supports of the aluminium silicate type (zeolites).

[0028] Examples of aluminium silicates that may be used to this end are the following: zeolite A, zeolite X, zeolite Y, zeolite T, sodalite, mordenite, analcite, clinoptilolite, cabazit, erionite and mixtures thereof. Preferably, zeolites A are used due to the higher ionic exchange capability thereof. Particularly preferred are zeolites A containing silver ions, even more preferably those containing silver and zinc ions at the same time due to the antibacterial efficacy against a larger number of microorganisms.

[0029] Examples of compositions containing metal ions supported on structures based on zirconium phosphate are described in US 5296238.

[0030] The ions with antibacterial action are deposited on said supports based on zirconium phosphate or of the aluminium silicate type through deposition and/or ionic exchange reactions according to the known prior art techniques.

[0031] Generally, the content of metal ions with antibacterial action present in the zeolites is lower than the ionic exchange saturation capability of zeolites. Therefore, besides containing the metal ions having a specific antibacterial action, the zeolites used for the purposes of the present invention may also contain other ions (metal and non metal), such as for example alkaline metals, alkaline-earth metals, protons and ammonium ions.

[0032] The total content of metal ions with antibacterial action in zeolite is generally variable within the range 2-25% by weight referred to the weight of the dried zeolite, preferably within the range 5-20% by weight. As it is known, the drying temperature of zeolites may vary according to the thermal stability of the different zeolites and of the type of counter-ions present; in the case of zeolite A, the reference drying temperature is within the range 400-800°C.

[0033] Zeolites containing metal ions are available on the market.

[0034] When it is desired to prepare a resin incorporating two or more different metal ions, these may be supported on the same support (zeolite or structure based on zirconium phosphate) or on different supports.

[0035] The Applicant has unexpectedly observed that the antibacterial action exerted by the thermoplastic material comprising the antibacterial compositions described above may be intensified by suitably selecting the metal ions and the relative support.

[0036] In particular, the studies conducted by the Applicant have shown that the best results in terms of efficacy in preventing, limiting and/or reducing the proliferation of microorganisms that come to contact with the product stored in the containers object of the present invention are obtained for the thermoplastic resins wherein an antibacterial composition comprising silver ions and zinc ions has been dispersed.

[0037] Preferably, the weight ratio between silver ions and zinc ions (Ag/Zn) in the antibacterial composition varies within the range $0.04 < \text{Ag/Zn} < 20$, preferably within the range $0.15 < \text{Ag/Zn} < 10$, more preferably within the range $0.31 < \text{Ag/Zn} < 1$.

[0038] This combination of ions is preferably supported on zeolitic structures, in particular on zeolites of the type A.

[0039] When added to the thermoplastic resins described above, the antibacterial compositions comprising silver and zinc ions allow obtaining packaging that meets the antimicrobial efficacy requirements set forth by the European Pharmacopoeia, by the United States Pharmacopoeia and by the Japanese Pharmacopoeia.

[0040] In particular, the antibacterial compositions comprising silver and zinc ions, preferably supported on zeolites A, are capable of ensuring an effective action in limiting the proliferation and reducing the number of microorganisms *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Candida albicans* and *Aspergillus niger*.

[0041] The antibacterial compositions may contain one or more zeolites and/or supports based on zirconium phosphate exchanged with metal ions having an antibacterial action.

[0042] An antibacterial composition having a given concentration of one or more metal ions may be prepared by mixing different supports having different concentrations of the metal ions, up to obtaining the desired concentration of ions with antibacterial action in the composition. As an alternative, it is possible to use a single support comprising two or more metal ions with antibacterial action.

[0043] When two or more zeolites and/or supports based on zirconium phosphate are used, the antibacterial composition may be prepared by mixing the respective supports exchanged with the metal ions (for example one type of ion per each support) in solid form (granules or powders).

[0044] The antibacterial compositions described above may be incorporated in the thermoplastic resins using the techniques and the equipment known in the field of thermoplastic material processing.

[0045] Incorporating the antibacterial composition in the resin prior to forming the container and the relative closing element reduces the extent of the possible yield of the metal ions towards the product contained therein.

[0046] The containers and the relative closing elements may be obtained in various shapes and dimensions.

[0047] The antibacterial composition is generally added to the thermoplastic material in such amount as to have an overall concentration of metal ions with antibacterial action variable within the range 0.01-10.0% by weight referred to the weight of the thermoplastic material that makes up the container (and the relative closing element), preferably within the range 0.01-7.0% by weight, even more preferably within the range 0.1-5.0% by weight.

[0048] The antibacterial compositions, both those based on zirconium phosphate and those based on zeolites, may be dispersed as a solid (granular or powder) in the thermoplastic resin, also at the solid state (granules) by mechanical mixing. The mixture of thermoplastic granules and antibacterial composition is then transformed into the end product (container and/or closing element) with the usual techniques for processing thermoplastic materials.

[0049] As an alternative, the antibacterial compositions may be combined to the thermoplastic resin during the melting operation.

[0050] The usual processing techniques of thermoplastic materials comprise drawing (extrusion), moulding, injection, injection-blowing, extrusion-blowing and Blow-Fill-Seal.

[0051] The thermoplastic resin containing the antibacterial composition may also be extruded in the shape of small "pellets" (granules), usable subsequently as starting material for producing the containers and the relative closing elements with above-mentioned the techniques.

[0052] While there is no intention herein to refer to any specific theory, it is deemed that the mechanism at the basis of the antibacterial action in the containers object of the present invention is essentially related to the contact between the antibacterial composition present on the surface of the thermoplastic material the container and the product contained therein are made of. In this case, the antibacterial efficacy depends in particular on the extension of the container surface in contact with the product and on the duration of such contact.

[0053] While the above-indicated concentrations for the antibacterial composition within the thermoplastic material the containers and the relative closing elements are made of are generally sufficient for ensuring the desired antibacterial action for a period of time compatible with the product usage time, in some particular cases however, the antibacterial performances of the container may not be sufficient for the intended use. This may happen, for example, if the container has walls with reduced thickness and thus exhibits reduced amounts of ions of the antibacterial composition on the inner surface in contact with the product.

[0054] In these cases it is possible to obviate the lower efficacy of the thermoplastic material comprising the antibacterial composition making containers with a suitable shape, such as those exemplified in figures 1 and 2.

[0055] Figure 1 schematically shows a primary packaging device 1 suitable for containing ophthalmic liquids (for example a collyrium) comprising a container 2 and the relative closing element 3. Device 1 also comprises a dropper 4, fixed on the closing element 3. Elements 2-4 of device 1 are made of a thermoplastic resin comprising an antibacterial composition according to the present invention. A liquid product 5 is present inside container 1 whose aseptic features obtained with the product sterilisation upon the packaging thereof are to be preserved.

[0056] In order to ensure a more effective antibacterial action, a projection 6 (in the specific case having a tubular shape) associated to the closing element 3 is provided within the container. Projection 6 is also made of a thermoplastic resin comprising an antibacterial composition and therefore it also has an antibacterial action when its surface comes to contact with the product 5 contained in container 2. The presence of projection 6, in practice, increases the overall surface the product can come to contact with during its preservation period inside container 2 during the use of the contained product.

[0057] Figure 2 shows a second embodiment of the technical solution exemplified in figure 1. Figure 2 shows a primary packaging device 21 comprising a container 22 and the relative closing element 23. Device 21 also comprises a dropper 24, fixed to the closing element 23. Elements 22, 23 and 24 are made of a thermoplastic resin comprising an antibacterial composition according to the present invention. A product 5 (for example an ophthalmic liquid), the low bacterial load features whereof are to be preserved, is present inside container 22. According to this second embodiment of the invention, container 22 may comprise one or more moveable bodies 25 therein, having at least the outer surface made of a thermoplastic resin comprising an antibacterial composition according to the invention. The moveable bodies 25, in particular the outer surface containing the antibacterial composition, are in contact with product 5. The moveable bodies have such dimensions as to not come out of the packaging through the dropper opening, which only allows the spilling of product 5 for the administration to the user.

[0058] In addition to the moveable bodies 25, the container may also have projections 27, associated for example to the bottom wall of the container, which extend inwards of the container. Also in the case of the device shown in figure 2, the presence of the moveable bodies 25 and optionally of projections 27 increases the overall surface the product may come in contact with, during the storage within container 2, thus intensifying the own antibacterial action of the inner surface of container 22.

[0059] The following exemplary embodiments are only given by way of an illustration of the present invention, and are not to be intended as limiting of the scope of protection as it appears from the annexed claims.

EXAMPLE 1

[0060] A first primary packaging device comprising a container and relative closing element (packaging A) was prepared using a polyethylene resin for both components (container and closing element). An antibacterial composition comprising silver and zinc ions supported on a zeolite A was dispersed in the resin.

[0061] Zeolite A contained 5% by weight of silver ions, 12% by weight of zinc ions (percentages by weight referred to the weight of exchanged and dried zeolite) and optional residual ammonium or hydrogen ions (that is, the original synthesis counter-ions of zeolite).

[0062] The antibacterial composition was mixed with the resin in amounts equal to 2% by weight referred to the overall weight of the thermoplastic resin.

EXAMPLE 2

[0063] A second primary packaging device comprising a container and the relative closing element (packaging B) was prepared with the same methods described in Example 1, using a polyethylene resin admixed with the same antibacterial composition as in Example 1. The antibacterial composition was mixed with the resin in amounts equal to 5% by weight referred to the overall weight of the thermoplastic resin.

EXAMPLE 3

[0064] A third primary packaging device comprising a container and the relative closing element (packaging C) was

prepared with the same methods described in Example 1, but using a polyethylene resin admixed with an antibacterial composition consisting of silver ions dispersed on a ceramic structure based on zirconium phosphate. The concentration of Ag ions on the support was equal to 30% by weight referred to the overall weight of the exchanged and dried support.

[0065] The antibacterial composition was mixed with the resin in amounts equal to 8% by weight referred to the overall weight of the thermoplastic resin.

Antimicrobial efficacy test

[0066] The antimicrobial efficacy of packagings A-C was tested according to the provisions of the European Pharmacopoeia ("Efficacy of Antimicrobial Preservation", Ph. Eur. Current Edition - 5.1.3).

[0067] The efficacy was assessed in terms of logarithmic reduction of the number of vital microorganisms compared to the number of microorganisms introduced with the inoculum.

[0068] The acceptability criteria for parenteral and ophthalmic preparations defined by the European Pharmacopoeia are shown in Table 1. Acceptability criteria comparable to those of the European Pharmacopoeia are also defined by the United States Pharmacopoeia and by the Japanese Pharmacopoeia.

Table 1

<i>Microrganisms</i>	<i>Assessment criterion</i>	<i>LOGARITHMIC REDUCTION</i>				
		<i>6 h</i>	<i>24 h</i>	<i>7 dd</i>	<i>14 dd</i>	<i>28 dd</i>
<i>Bacteria</i>	A	2	3	-	-	NR
	B	-	1	3	-	NI
<i>Fungi</i>	A	-	-	2	-	NI
	B	-	-	-	1	NI
NR = no recovery NI = no increase						

[0069] The results of the tests run on packagings A-C are respectively shown in Tables 2-4.

[0070] The experimental data show that the antibacterial composition of packagings A and B, wherein silver and zinc ions are present at the same time, is capable of meeting the requirements of the European Pharmacopoeia of Table 1. The data further show that the efficacy of the compound increases as its concentration in the resin increases.

[0071] It should be noted that containers made with the same thermoplastic resin as in example 1 but containing the antibacterial composition in amounts equal to 1% by weight referred to the overall weight of the thermoplastic resin show an antibacterial efficacy comparable to that of packaging A.

[0072] On the other hand packaging C, wherein the antibacterial composition only contains silver ions supported on zirconium phosphate, it is only partly effective against the tested bacteria and mildews, not respecting the reduction values expected in the case of the *Aspergillus niger*.

[0073] The examples shows the efficacy of the devices of the present invention in limiting and reducing the growth of microorganisms; in particular, the experimental results confirm that the container and the relative closing element of Examples 1 and 2 may be used as packaging for the primary packaging of sterile products or with a low bacterial load free from preservatives in compliance with the requirements set forth by the European Pharmacopoeia, by the United States Pharmacopoeia and by the Japanese Pharmacopoeia.

EXAMPLE 4

[0074] The yield test was run on some samples of device A of Example 1 according to the guidelines of the European Pharmacopoeia for the primary packaging devices of plastic material for pharmaceutical use. The test showed an average yield value of 12 ppm, lower than the maximum value allowed of 50 ppm.

[0075] Tests were further run on the same packaging samples for assessing the extent of the release of ions Ag and Zn from the material of the device. To this end, each device was filled with 10 ml of distilled water and stored sealed at controlled temperature of 25°C or 40°C for 10 days. The concentration of Ag and Zn ions present in the water was measured at the end of the storage period using the methods for determining zinc and silver IRSA CNR 3320 and IRSA CNR 3070. The content of Ag ions in the distilled water was of 0.006 micrograms/device, in the samples stored at 25°C, and of 0.002 micrograms/device in the samples stored at 40°C. The content of Zn ions was of 0.069 micrograms/device (25°C) and 1.167 micrograms/device (40°C). Ag and Zn ions are released in the product in negligible amounts.

[0076] On the whole, the above described tests show that the devices according to the present invention may be used as primary packaging devices for pharmaceutical use according to the criteria set forth by the European Pharmacopoeia.

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Table 2 - Packaging A

	Inoculation value UFC/ml	T0	T 6h	R 6h	T 24h	R 24h	T 7d	R 7d	T 14d	R 14d	T 28d	R 28d	T 35d	R 35d	T 42d	R 42d
<i>S. aureus</i> ATCC 6538	5.7x10 ⁶	3.6x 10 ⁶	2.9x 10 ⁶	0.30	2.0x 10 ²	4.46	0	>6.76	--	--	0	>6.76	0	>6.76	0	>6.76
<i>P.aeruginosa</i> ATCC 9027	4.5x10 ⁶	1.8x 10 ⁶	<1.0x 10 ²	>4.65	0	>6.65	--	--	--	--	0	>6.65	0	>6.65	0	>6.65
<i>C. albicans</i> ATCC 10231	4.9x10 ⁵	4.6x 10 ⁵	-				2.0x 10 ³	2.39	0	>5.69	0	>5.69	0	>5.69	0	>5.69
<i>A.niger</i> ATCC 16404	2.3x10 ⁶	3.5x 10 ⁵	-		-		2.0x 10 ⁵	1.06	4.8x 10 ⁴	1.68	2.0x 10 ³	3.06	3.7x 10	4.80	3.1x 10	4.87
T = time R = reduction																

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[illegible]

Table 4 - Packaging C

	Inoculum value UFC/ml	T0	T 6h	R 6h	T 24h	R 24h	T 7d	R 7d	T 14d	R 14d	T 28d	R 28d	T 35d	R 35d
<i>S. aureus</i> ATCC 6538	3.5x10 ⁶	1.6x 10 ⁶	1.1x 10 ⁶	0.50	1.0x 10 ⁶	0.54	6.8x 10 ³	2.71	6	5.77	0	6.54	0	6.54
<i>P.aeruginosa</i> ATCC 9027	2.4x10 ⁶	2.2x 10 ⁶	1.6x 10 ⁶	0.18	7.1x 10 ⁵	0.53	2.0x 10 ⁵	1.08	4.5x 10 ⁴	1.73	2.5x 10 ⁴	1.98	3.8x 10 ³	2.80
<i>C. albicans</i> ATCC 10231	5.4x10 ⁵	5.1x 10 ⁵	-		-		6.7x 10 ⁴	0.91	6.0x 10 ³	1.95	0	5.73	0	5.73
<i>A. niger</i> ATCC 16404	2.2x10 ⁵	1.9x 10 ⁵	-		-		1.0x 10 ⁵	0.34	1.0x 10 ⁵	0.34	8.5x 10 ⁴	0.41	8.0x 10 ⁴	0.44
T = time														
R = reduction														

Claims

- 5 1. Reclosable container for sterilised products or products with low bacterial load free of preservatives, suitable for limiting and/or reducing the growth of bacteria within said products, **characterised in that** it is entirely made of a thermoplastic material comprising an antibacterial composition dispersed therein, said antibacterial composition comprising at least silver ions and zinc ions borne on a solid support.
- 10 2. Container according to claim 1, **characterised in that** said support is a ceramic structure based on zirconium phosphate or a support of the aluminium silicate type.
3. Container according to claim 2, **characterised in that** said support of aluminium silicate type is a zeolite selected from the group consisting of zeolite A, zeolite X, zeolite Y, zeolite T, sodalite, mordenite, analcite, clinoptilolite, chabazite, erionite and mixtures thereof.
- 15 4. Container according to the preceding claim, **characterised in that** said zeolite is a zeolite A.
5. Container according to any one of the preceding claims, **characterised in that** said antibacterial composition further comprises copper and/or gold ions.
- 20 6. Container according to any one of the preceding claims, **characterised in that** the weight ratio between silver ions and zinc ions (Ag/Zn) varies in the range $0.04 < \text{Ag/Zn} < 20$.
7. Container according to the preceding claim, **characterised in that** the weight ratio between silver ions and zinc ions (Ag/Zn) varies in the range $0.15 < \text{Ag/Zn} < 10$.
- 25 8. Container according to the preceding claim, **characterised in that** the weight ratio between silver ions and zinc ions (Ag/Zn) varies in the range $0.31 < \text{Ag/Zn} < 1$.
9. Container according to any one of the preceding claims, **characterised in that** the overall concentration of metal ions with antibacterial action is variable in the range between 0.01 and 10.0% in weight referring to the weight of the thermoplastic material, preferably in the range between 0.01 and 7.0% in weight, even more preferably in the range between 0.1 and 5.0%.
- 30 10. Container according to any one of the preceding claims, **characterised in that** said thermoplastic material is a material comprising, or consisting of, a polymeric resin selected from: polyethylene (PE), polypropylene (PP), polyethylene terephthalate (PET), polyvinylchloride (PVC), polycarbonate (PC) and thermoplastic rubber.
- 35 11. Container according to any one of the preceding claims, **characterised in that** its inner surface comprises a projection extended towards the interior of said container, said projection having a surface that may come to contact with said product made of a thermoplastic material comprising an antibacterial composition as defined in any one of the preceding claims.
- 40 12. Primary packaging device for sterilised products or with low bacterial load free of preservatives comprising a container according to any one of claims 1 to 10 and a closing element associable to said container, said closing element being made of thermoplastic material comprising an antibacterial composition as defined in any one of claims 1 to 9.
- 45 13. Device according to claim 12, **characterised in that** it comprises a moveable body arranged inside the container, said body having at least the outer surface made of thermoplastic material comprising an antibacterial composition as defined in any one of claims 1 to 6.
- 50 14. Use of a primary packaging device according to claim 12 or 13 for packaging sterilised products or with low bacterial load free of preservatives, limiting and/or reducing the growth of bacteria therein.
- 55 15. Use of a primary packaging device according to the preceding claims wherein said sterilized product is an ophthalmic liquid.

Patentansprüche

- 5 1. Wiederverschließbarer Behälter für sterilisierte Produkte oder Produkte mit niedriger Bakterienbelastung ohne Konservierungsmittel, der geeignet ist, das Bakterienwachstum in diesen Produkten zu begrenzen und/oder zu verringern, **dadurch gekennzeichnet, dass** er vollständig aus einem thermoplastischen Material besteht, das eine darin fein verteilte antibakterielle Zusammensetzung umfasst, wobei diese antibakterielle Zusammensetzung mindestens Silberionen und Zinkionen umfasst, die auf einem festen Träger getragen werden.
- 10 2. Behälter nach Anspruch 1, **dadurch gekennzeichnet, dass** der Träger eine keramische Struktur auf der Basis von Zirkoniumphosphat oder ein Träger vom Typ Aluminiumsilikat ist.
- 15 3. Behälter nach Anspruch 2, **dadurch gekennzeichnet, dass** der Träger vom Typ Aluminiumsilikat ein Zeolith ist, der aus der Gruppe ausgewählt ist, die aus Zeolith A, Zeolith X, Zeolith Y, Zeolith T, Sodalith, Mordenit, Analcim, Klinoptilolith, Chabasit, Erionit und Gemischen davon besteht.
- 20 4. Behälter nach dem vorhergehenden Anspruch, **dadurch gekennzeichnet, dass** der Zeolith ein Zeolith A ist.
- 5 5. Behälter nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet, dass** die antibakterielle Zusammensetzung ferner Kupfer- und/oder Goldionen umfasst.
- 25 6. Behälter nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet, dass** das Gewichtsverhältnis zwischen Silberionen und Zinkionen (Ag/Zn) im Bereich $0,04 < \text{Ag/Zn} < 20$ variiert.
7. Behälter nach dem vorhergehenden Anspruch, **dadurch gekennzeichnet, dass** das Gewichtsverhältnis zwischen Silberionen und Zinkionen (Ag/Zn) im Bereich $0,15 < \text{Ag/Zn} < 10$ variiert.
- 30 8. Behälter nach dem vorhergehenden Anspruch, **dadurch gekennzeichnet, dass** das Gewichtsverhältnis zwischen Silberionen und Zinkionen (Ag/Zn) im Bereich $0,31 < \text{Ag/Zn} < 1$ variiert.
- 35 9. Behälter nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet, dass** die Gesamtkonzentration an Metallionen mit antibakterieller Wirkung im Bereich von 0,01 bis 10,0 Gew.-% bezogen auf das Gewicht des thermoplastischen Materials, vorzugsweise im Bereich von 0,01 bis 7,0 Gew.-%, noch bevorzugter im Bereich von 0,1 bis 5,0%, variabel ist.
- 40 10. Behälter nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet, dass** das thermoplastische Material ein Material ist, das einen Polymerharz umfasst oder aus ihm besteht, der ausgewählt ist aus: Polyethylen (PE), Polypropylen (PP), Polyethylenterephthalat (PET), Polyvinylchlorid (PVC), Polycarbonat (PC) und thermoplastischer Elastomer.
- 45 11. Behälter nach einem der vorhergehenden Ansprüche, **dadurch gekennzeichnet, dass** seine Innenfläche einen Ansatz umfasst, der sich in Richtung des Inneren des Behälters erstreckt, wobei dieser Ansatz eine Oberfläche, die in Kontakt mit dem Produkt kommen kann, aufweist, die aus einem thermoplastischen Material besteht, das eine antibakterielle Zusammensetzung umfasst, wie sie in einem der vorhergehenden Ansprüche definiert ist.
- 50 12. Primärverpackungsvorrichtung für sterilisierte oder eine niedrige Bakterienbelastung aufweisende Produkte ohne Konservierungsmittel, die einen Behälter nach einem der Ansprüche 1 bis 10 und ein Verschlusselement umfasst, das mit diesem Behälter verbunden werden kann, wobei dieses Verschlusselement aus einem thermoplastischen Material besteht, das eine antibakterielle Zusammensetzung umfasst, wie sie in einem der Ansprüche 1 bis 9 definiert ist.
- 55 13. Vorrichtung nach Anspruch 12, **dadurch gekennzeichnet, dass** sie einen beweglichen Körper umfasst, der in dem Behälter angeordnet ist, wobei bei diesem Körper zumindest die Außenfläche aus einem thermoplastischen Material besteht, das eine antibakterielle Zusammensetzung umfasst, wie sie in einem der Ansprüche 1 bis 6 definiert ist.
14. Verwendung einer Primärverpackungsvorrichtung nach Anspruch 12 oder 13 zum Verpacken von sterilisierten oder eine niedrige Bakterienbelastung aufweisenden Produkten ohne Konservierungsmittel, die das Bakterienwachstum darin begrenzt und/oder verringert.

15. Verwendung einer Primärverpackungsvorrichtung nach den vorhergehenden Ansprüchen, wobei das sterilisierte Produkt eine ophthalmische Flüssigkeit ist.

5 Revendications

1. Conteneur refermable pour des produits stérilisés ou des produits à faible teneur en bactéries sans conservateurs, adapté pour limiter et/ou réduire la croissance de bactéries à l'intérieur desdits produits, **caractérisé en ce qu'il** est entièrement constitué d'un matériau thermoplastique comprenant une composition antibactérienne dispersée dans celui-ci, ladite composition antibactérienne comprenant au moins des ions argent et des ions zinc supportés sur un support solide.
2. Conteneur selon la revendication 1, **caractérisé en ce que** ledit support est une structure céramique à base de phosphate de zirconium ou un support du type silicate d'aluminium.
3. Conteneur selon la revendication 2, **caractérisé en ce que** ledit support de type silicate d'aluminium est une zéolithe sélectionnée à partir du groupe comprenant zéolithe A, zéolithe X, zéolithe Y, zéolithe T, sodalite, mordénite, analcite, clinoptilolite, chabazite, ériolite et leurs mélanges.
4. Conteneur selon la revendication précédente, **caractérisé en ce que** ladite zéolithe est une zéolithe A.
5. Conteneur selon l'une quelconque des revendications précédentes, **caractérisé en ce que** ladite composition antibactérienne comprend en outre des ions cuivre et/ou or.
6. Conteneur selon l'une quelconque des revendications précédentes, **caractérisé en ce que** le rapport de poids entre ions argent et ions zinc (Ag/Zn) varie dans la plage de $0,04 < \text{Ag/Zn} < 20$.
7. Conteneur selon la revendication précédente, **caractérisé en ce que** le rapport de poids entre ions argent et ions zinc (Ag/Zn) varie dans la plage de $0,15 < \text{Ag/Zn} < 10$.
8. Conteneur selon la revendication précédente, **caractérisé en ce que** le rapport de poids entre ions argent et ions zinc (Ag/Zn) varie dans la plage de $0,31 < \text{Ag/Zn} < 1$.
9. Conteneur selon l'une quelconque des revendications précédentes, **caractérisé en ce que** la concentration totale d'ions métalliques avec action antibactérienne est variable dans la plage entre 0,01 et 10,0% en poids en référence au poids du matériau thermoplastique, de préférence dans la plage entre 0,01 et 7,0% en poids, de manière encore plus préférée dans la plage entre 0,1 et 5,0%.
10. Conteneur selon l'une quelconque des revendications précédentes, **caractérisé en ce que** ledit matériau thermoplastique est un matériau comprenant, ou constitué par, une résine polymère sélectionnée parmi : polyéthylène (PE), polypropylène (PP), polyéthylène téréphtalate (PET), chlorure de polyvinyle (PVC), polycarbonate (PC) et caoutchouc thermoplastique.
11. Conteneur selon l'une quelconque des revendications précédentes, **caractérisé en ce que** sa surface intérieure comprend une saillie étendue vers l'intérieur dudit conteneur, ladite saillie ayant une surface susceptible de venir en contact avec ledit produit qui est constituée d'un matériau thermoplastique comprenant une composition antibactérienne telle que définie dans l'une quelconque des revendications précédentes.
12. Dispositif de conditionnement primaire pour produits stérilisés ou à faible teneur en bactéries sans conservateurs comprenant un conteneur selon l'une quelconque des revendications 1 à 10 et un élément de fermeture associable audit conteneur, ledit élément de fermeture étant constitué de matériau thermoplastique comprenant une composition antibactérienne telle que définie dans l'une quelconque des revendications 1 à 9.
13. Dispositif selon la revendication 12, **caractérisé en ce qu'il** comprend un corps mobile disposé à l'intérieur du conteneur, ledit corps ayant au moins la surface extérieure constituée de matériau thermoplastique comprenant une composition antibactérienne telle que définie dans l'une quelconque des revendications 1 à 6.
14. Utilisation d'un dispositif de conditionnement primaire selon la revendication 12 ou 13 pour conditionner des produits

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stérilisés ou à faible teneur en bactéries sans conservateurs, pour limiter et/ou réduire la croissance de bactéries à l'intérieur.

- 5 **15.** Utilisation d'un dispositif de conditionnement primaire selon les revendications précédentes, dans lequel ledit produit stérilisé est un liquide ophtalmique.

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Fig.2

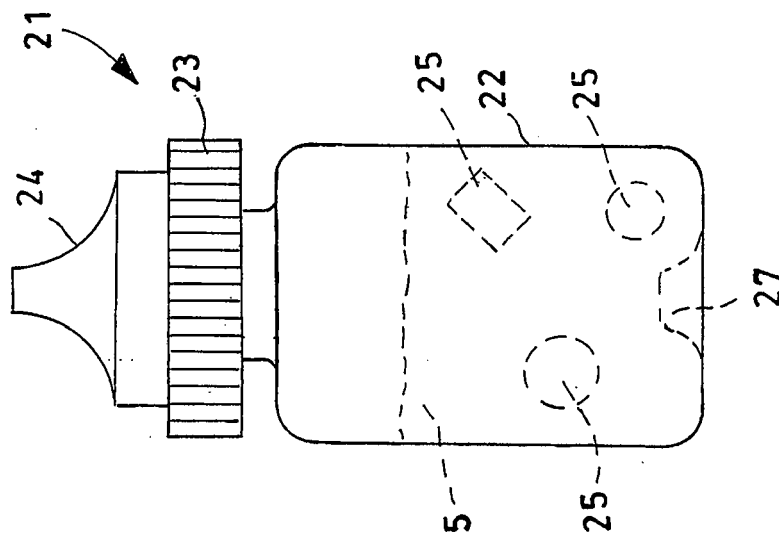
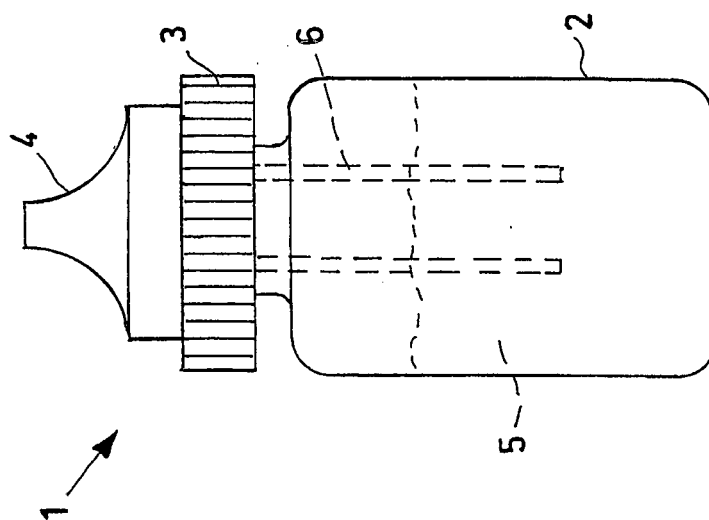


Fig.1



REFERENCES CITED IN THE DESCRIPTION

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Patent documents cited in the description

- WO 0026100 A [0011] [0012]
- US 6179141 B1 [0015]
- US 5296238 A [0029]

Non-patent literature cited in the description

- Efficacy of Antimicrobial Preservation. *Ph. Eur. Current Edition* - 5.1.3 [0066]