

(11)

PACKAGE STORING A MEDICAL CONTAINER

This invention relates to a package storing a plastics medical container. More particularly, this invention relates to a package storing a plastics medical container such as a blood bag or a trans-
5 fusion solution bag which contains therein a medicinal fluid.

Plastics medical containers such as blood bag and transfusion bags contain therein anticoagulants such as ACD solution and CPD solution which serve to prevent
10 the blood from being coagulated during collection or transfusion of blood. The medical containers containing such chemical solutions are stowed in tightly closed packages of synthetic resin designed exclusively for the purpose of storage. Since the medical containers are made of plastics
15 materials and therefore are pervious to gases, there is a possibility that oxygen gas, for example, will penetrate through these containers and pass into the solutions contained therein to cause oxidative degradation of the chemical solutions. The wetting components, particularly
20 the moisture, present in the chemical solutions penetrate through the walls of the containers and add to the humidity within the packages. If aerobic microorganisms survive by some reason or other within the chemical solutions, there is the possibility that the microorganisms,

which collect on the surface of the containers between the time these containers are manufactured and the time they are put to use, will proliferate because of the heightened humidity.

5 It has been recently proposed to put deoxidizer in the packages to effect quick reduction of concentration of oxygen within the tightly closed packages and prevent the contents of the containers from oxidising. As a tightly closed package suited to the
10 prevention of its contents from oxidising, there has been proposed a bag-shaped package which is obtained by vacuum depositing aluminum on the opposed surfaces of two superposed polyester type resin sheets and heat sealing the corresponding peripheries of the two sheets by way
15 of a hot melt type adhesive agent (Japanese Published Unexamined Patent No. SHO 53(1978)-113693). Since the bag-shaped package is deficient in shape-retaining property, the inner volume of the package decreases and its walls collapse as the oxygen therein is gradually
20 absorbed by the deoxidizer. When the contents of the package and the walls of the package adhere fast to the surfaces of the deoxidizer, the absorption of oxygen by the deoxidizer fails to proceed at the expected rate and the concentration of oxygen in the package fails
25 to fall to the prescribed level (less than 0.1%/50 hrs.), frequently with the result that microorganisms which by chance have found their way into the containers in the course of fabrication will enjoy growth in the presence of

②
oxygen. Since the bag-shaped package has an inferior shape-retaining property, it tends to be inconvenient for storage. When such bag-shaped packages are piled up during storage or in transit, they can collapse with adverse effects upon their contents. If the prior package is molded three-dimensionally, the conditions involved in the molding deform and crack the conventional gas and steam barrier layers formed of aluminum and the package thus is non effective as a gas barrier.

10 A known powdered deoxidizer is composed of a metal such as iron and a halogenated metal.

Such a deoxidizer is used contained in a bag-like container pervious to gases. As the deoxidizer absorbs oxygen, the metal used therein corrodes

15 Particularly when the metal happens to be iron, it rusts red. The red rust exudes through the walls of the bag-like container, comes into contact with the medical container and soils it. To eliminate this problem, a membrane impervious to gases is attached to one of the walls of the
20 aforementioned bag-like container. This bag-like container is used with the membrane side thereof facing the medical container held in the package and the gas-pervious wall side thereof in contact with the bottom surface of the package. Consequently, the overall area of the deoxidizer
25 container exposed to contact with the ambient gas is notably decreased, and the concentration of oxygen is not reduced within a prescribed length of time to a prescribed level, namely to not more than 0.1% by volume

within 72 hours, as is required for the prevention of growth of aerobic microorganisms. Thus, the interior of the package cannot be brought to a substantially oxygen-free condition. The package, therefore fails
5 to keep the medical container held therein from growth of aerobic microorganisms.

The present invention provides a
tightly sealed package holding a) a medical
container and b) a deoxidizer which is covered on one
10 side with a gas-impervious sheet and on at least one other side with a gas-pervious sheet, said deoxidizer resting with a gas-pervious sheet side on an inner side of the package and being provided at this inner side with at least one passage for gas communication
15 between the gas-pervious sheet side of the deoxidizer and the atmosphere enclosed within the package.

20 This package may comprise a tray provided round the opening thereof with a flange portion, a sheet-like lid member and a hot melt adhesive layer forming a peelable seal between the flange portion and the lid member. At least the tray is preferably
25 transparent. The tray is suitably formed of a laminated sheet comprising a polyolefin layer, a layer to act as a barrier to passage of gases and steam and a polyolefin layer, the lid member may be a laminated sheet comprising

a polyamide layer, a layer to act as a barrier to passage of gases and steam and a layer of sufficient thermal resistance to withstand the conditions of heat sealing, and the hot melt adhesive layer may comprise

5 a plurality of materials of dissimilar melting point and including at least one material substantially the same as polyolefin in the tray; when the adjacent polyolefin layer in the tray is of polypropylene, the hot melt adhesive layer is suitably a blend of poly-
10 ethylene with polypropylene, preferably in a weight ratio of polyethylene to polypropylene in the range of 20 : 80 to 50 : 50; the thermally resistant layer may be of polyester, polyamide or polypropylene; the tray barrier layer may be of ethylene-vinyl alcohol copolymer,
15 and that of the lid member may be of polyvinylidene chloride or ethylene-vinyl alcohol copolymer.

The passage(s) giving communication between the gas pervious sheet and the package interior may be a recess or recesses (e.g. grooves) formed in the
20 bottom portion of the package.

The invention is illustrated, by way of example only, by the accompanying drawings, in which

(6)

like numerals denote like parts and in which :

Figure 1 is a perspective view illustrating one package of this invention for the storage of a medical container;

5 Figure 2 is a cross section taken along the line II-II in the diagram of Fig.1;

Figure 3 is a plan view illustrating the condition of the package without the lid member and medical container;

10 Figure 4 is an enlarged cross section of part of the diagram of Fig.2; and

Figure 5 is a cross section similar to Fig.2 illustrating another package of this invention.

15 The package of Figs.1 to 4 has a tray part 2 provided with a flange portion 1, a recessed portion 3 for receiving a deoxidizer 7, and at least one groove 4 in the bottom of the recess portion.

20 Within this deoxidizer receiving portion 3, the deoxidizer 7 covered on at least one side thereof with a gas-impervious sheet 5 (such as aluminum foil, synthetic resin film, paper or cloth impregnated or coated with wax or synthetic resin) and on at least one
25 other side thereof, generally the side opposite the aforementioned side, with a gas-pervious sheet 6 (such as paper or cloth) is received in such a manner that the gas-pervious sheet 6 is positioned on the groove 4 side.

(19)

- 7 -

The aforementioned groove 4 is formed so as to reach the outside of the deoxidizer receiving portion 3 and form a free passage for gases. After the deoxidizer 7 and the medical container 8 have been set in position within the tray part 2, the lid member 10 is peelably heat sealed to the tray flange via the hot melt adhesive layer 9.

In the illustrated type of passage any materials which are capable of resisting passage of gases and steam and are highly heat sealable can be used for relevant parts of tray 2 and lid member 10. Examples are shown below. They are particularly excellent in shape-retaining property, ability to resist passage of gases and steam and heat sealability and are transparent. As illustrated in Fig.4, the tray part 2 is producible by molding in the shape of a tray a laminated sheet comprising a polyolefin layer (outer layer) 11, a layer capable of resisting passage of gases and steam (intermediate layer 12) and a polyolefin layer (inner layer) 13. The lid member 10 is formed by laminating a polyamide layer (inner layer) 14, a layer capable of resisting passage of gases and steam (intermediate layer 15) and a layer of sufficient thermal resistance to withstand the conditions of heat sealing (outer layer 16). The hot melt adhesive 9 is formed of a blend of polyethylene with polypropylene.

Examples of the polyolefin which forms the outer layer 11 and the inner layer 13 of the tray part 2 are polyethylene and polypropylene. Polypropylene is preferred because of its excellent shape-retaining property and thermal resistance compared to polyethylene. For use herein the polyethylene advantageously has a molecular weight of 3,000 to 200,000, preferably 50,000 to 100,000, and the polypropylene a molecular weight of 5,000 to 1,000,000, preferably 100,000 to 500,000.

10 The thickness of each of the polyolefin layers is e.g. 500 to 600 μ m. The intermediate layer 12 of the tray part 2 which is capable of resisting passage of gases and steam is desirably formed of ethylene-vinyl alcohol copolymer; The thickness of this layer is e.g. about 50 μ m. The vinyl

15 alcohol content of the copolymer is desirably 20 to 80 mol%, preferably 40 to 70 mol%. The molecular weight of the copolymer is desirably 5,000 to 100,000, preferably 10,000 to 50,000.

The layer 9 which at least in use can be the innermost layer of the lid member 10 is desirably formed of a blend of polyethylene with polypropylene. The weight ratio of the polyethylene to the polypropylene in the blend, when the inner layer 13 of the tray part 2 is of polypropylene, is desirably in the range of 20 : 80 to

25 50 : 50 to give a good heat sealing which yet is peelable open. The thickness of layer 9 is e.g. 30 to 60 μ m, preferably 40 to 50 μ m. The layer of blend is superposed by a layer of polyamide, such as nylon 6 or nylon-6,6;

this permits the lid member to retain its strength. The intermediate layer 15 is desirably formed of polyvinylidene chloride or ethylene-vinyl alcohol copolymer.

Generally, polyvinylidene chloride is used superposed
5 on a polyolefin film, particularly a biaxially drawn polypropylene film. Generally, the molecular weight of the polypropylene is 5,000 to 1,000,000, e.g. 100,000 to 500,000. The thickness of the polyolefin film is e.g. 20 to 40 μm . The molecular weight of the polyvinylidene
10 chloride is e.g. 8,000 to 20,000, preferably 10,000 to 15,000, and its thickness may for example be 5 to 10 μm .

This film exhibits an outstanding ability to resist passage of gases and steam. A still better barrier property is obtained by using a plurality of such layers
15 superposed. To ensure safe storage of a plastics medical container holding a medicinal fluid therein, the intermediate layer 15 desirably has not more than 1 $\text{g}/\text{m}^2 \cdot 24 \text{ hr}$ (40°C , 90% RH), preferably 0.1-0.2 $\text{g}/\text{m}^2 \cdot 24 \text{ hr}$ (40°C , 90% RH), perviousness to humidity. To ensure
20 prevention of growth of aerobic microorganisms, the gas barrier property of the intermediate layer 15 is desirably not more than 0.1%/72 hr, preferably not more than 0.1%/50 hr of oxygen concentration in the package. Examples of the resin of the outer layer 16

25 of thermal resistance enough to withstand the conditions of heat sealing include polyesters such as polyethylene terephthalate and polybutylene terephthalate, polyamides such as nylon 6 and nylon-6,6, and polypropylene.

Among other polymers mentioned above, polyethylene terephthalate proves to be particularly desirable. The thickness of the layer 16 is e.g. 10 to 30 μm , preferably 12 to 25 μm .

5 The weight ratio of the polyethylene to the polypropylene in the hot melt adhesive layer is from 20 : 80 to 50 : 50 where the inner layer 13 of tray part 2 is formed of polypropylene and from 80 : 20 to 50 : 50 where the inner layer 13 is formed of polyethylene. This
10 is because the seal is peeled open with great difficulty when the proportion in the blend of the material identical with the polyolefin forming the inner layer of the tray part 2 is too high and the adhesiveness of the flange portion and the lid member is insufficient when the
15 proportion is too low.

 The medical container stored in the package of the present invention usually holds a medicinal fluid therein.

 Examples of medical container for which the
20 package of this invention is advantageously usable include blood bags, transfusion bags, etc. containing therein anticoagulants, fluids or transfusion, and other medicinal fluids such as ACD-A solution (containing 2.20 g of sodium citrate, 0.80 g of citric acid and
25 2.20 g of grape sugar in 100 ml of aqueous solution, for example) and CPD solution (containing 0.327 g of citric acid, 2.63 g of sodium citrate, 0.251 g of disodium citrate and 2.32 g of dextrose in 100 ml of aqueous

solution, for example); these bags may have their accessories such as tubes, connectors and syringes integrally molded therewith or connected thereto.

5 The package provided by this invention contains a deoxidizer 7, in any of numerous forms; at least one compound selected from iron carbide, iron carbonyl, ferrous oxide, ferrous hydroxide and iron silicate and halogenated metal (containing water when necessary) (Japanese Published Unexamined Patent No. 10 SHO 54(1979)-37088), and deoxidizer which is obtained by coating powdered metal with halogenated metal (Japanese Published Unexamined Patent No. SHO 54(1979)-35189) are examples.

15 Figure 5 illustrates another package of the present invention. This package has at the bottom of the tray part 2 a deoxidizer receiving portion 19 defined by raised strips 18 instead of by the depression 3 of Fig. 2. The aforementioned deoxidizer receiving portion may be formed at one or more positions on the 20 lateral sides of the tray part 2 or may not be formed at all. In the diagrams of Figs. 1-5, the component layers of the packages are illustrated in exaggerated thicknesses.

25 Storage of a medical container 8 in the package constructed as described above is accomplished by first placing the deoxidizer 7 in the tray part 2 in such a manner that the gas-pervious sheet 6 side thereof falls on the grooves 4 side, setting the medical

container 8 (usually containing therein a medicinal fluid) in the tray part 2, then applying the lid member 10 by way of hot melt adhesive layer 9 to the flange portion 1 of the tray part 2, and tightly heat sealing the lid member 10 and the flange portion 1 by high frequency or some other heating means. In this case, at least one small segment of the corner 20 of the flange portion 1 may be partially left intact by the heat sealing so that it will facilitate the peeling of the seal when the medical container is to be removed for use. The aforementioned hot melt adhesive layer 9 is generally supplied bonded (under application of heat and pressured) to the flange 1 of the tray part 2 or to the periphery of the inner layer 14 of the lid member 10. Optionally, the adhesive layer 9 may be superposed on the lid member and extend outwardly and down and around the flange portion to seal the lid when wrapped fully around flange portion. The adhesive layer may be superposed over the entire surface of the lid member. Of course, any deoxidizer may be placed in the tray 2 before or simultaneously with the medical container 8.

The present invention is illustrated more specifically below in working Examples 1 to 7:

As illustrated in FIGS. 1 to 4, in a tray part 2 formed of a laminated sheet comprising an outer layer 11 of polypropylene (having a molecular weight of 100,000 to 500,000) 500 μ m in thickness, an intermediate

layer 12 of ethylene-vinyl alcohol copolymer (having a molecular weight of 10,000 to 50,000) 5 μ m in thickness, and an inner layer 13 of polypropylene (having a molecular weight of 100,000 to 500,000) 500 μ m in thickness, was set a pack of deoxidizer in a bag-like container having as one wall a gas-impervious sheet 5 obtained by vacuum depositing aluminum on a film of polyester (having a molecular weight of 100,000 to 500,000) and as the other wall thereof a gas-pervious sheet 6 of paper, with the latter sheet 6 against the grooves. Further a blood bag 8 made polyvinyl chloride and containing therein an anticoagulant was set in position in the tray part 2. Then a lid member 10, obtained by laminating a layer 14 composed of nylon and 15 μ m in thickness, an intermediate layer 15 composed of two layers each of a film of biaxially drawn polypropylene (having a molecular weight of 100,000 to 500,000) 20 μ m in thickness superposed by a layer of polyvinylidene chloride (having a molecular weight of 10,000 to 15,000) 10 μ m in thickness, and an outer layer 16 of polyethylene terephthalate (having a molecular weight of 100,000 to 500,000), was heat sealed by high frequency to the flange portion 1 of the tray part 2 by way of a hot melt adhesive layer 9 of a blend of polyethylene (having a molecular weight of 50,000 to 100,000) and polypropylene (having a molecular weight of 100,000 to 500,000) in a weight ratio of 30 : 70 and superposed in advance on the flange portion 1 of the

24

tray part 2. The packages thus produced were tested for concentration of oxygen contained therein by the use of a zirconia type analyzer (made by Toray Ltd). The results were as shown in Table 1. When the procedure described above was repeated by using ethylene-vinyl alcohol copolymer as the material for the layer of the lid member capable of resisting passage of gases and steam, there were obtained similar results.

Comparative Experiments 1-5

The procedure of Example 1 was repeated, except that the tray part, though made of the same materials, had no grooves formed in the bottom side thereof and the bag-like container of the deoxidizer was set in position so that the gas-pervious sheet side thereof fell on the bottom side. The packages thus obtained were tested as in Example 1. The results were as shown in Table 1.

Table 1

Oxygen concentration (% by volume)

Example No.	After 24 hrs.	After 33 hrs.	After 48 hrs.	After 53 hrs.	After 57 hrs.
20					
1	11.0	6.4	0.163	-	-
2	-	7.0	0.310	0.093	-
3	-	-	0.067	0.048	-
4	-	-	0.055	-	-
5	-	-	0.080	-	-
25					
6	-	-	0.187	0.070	-
7	-	-	0.076	0.054	-



Comparative
Experiment

1	15.2	12.5	7.6	-	-
2	-	13.7	9.9	8.7	-
3	-	10.9	5.4	3.68	2.06
4	-	-	6.3	4.86	3.37
5	-	-	-	4.17	2.67

Since the surface of the deoxidizer cover which comes into contact with the medical container stored in the package is impervious to gases, there is no possibility that the red rust produced by the deoxidizer upon absorption of oxygen will adhere to the medical container. On the gas-pervious side of the deoxidizer, at least one passage communicating with the atmosphere enclosed with the package is formed in the package, and constitutes a path through which the oxygen in the package is delivered to the deoxidizer and absorbed thereby. Consequently, the interior of the package can be brought to a substantially oxygen-free condition within a very short length of time. Owing to this quick deoxidization, even when the medical container stored within the package happens to be formed of a material such as polyvinyl chloride which is highly pervious, the medicinal fluid held in the medical container is not subjected to oxidative degradation. Even if some aerobic microorganisms have by chance found their way into the container in the course of fabrication, they are not allowed to grow. Thus, the package can keep the medical container in a substantially

sterilized state for a long time.

When the package, namely, the tightly sealed container, is composed of the specific laminated materials as described above, the tray can enjoy high shape-retaining property and transparency, and the contents can be inspected without opening the package.

The lid member has a high ability to resist passage of gases and steam when polyvinylidene chloride or ethylene-vinyl alcohol copolymer is used as or in the intermediate layer. When polyester, polyamide or polypropylene is selected as the resin for the outer layer required to withstand the conditions of heat sealing, the lid member has ample shape-retaining property in spite of the conditions of heat sealing. When all these layers are transparent, the condition of the medical container inside the package can be readily inspected without opening the package. When polypropylene is selected for the polyolefin layers in the tray part and a blend of polyethylene with polypropylene is selected for the hotmelt adhesive layer, with the weight ratio of polyethylene to polypropylene falling in the range of 20 : 80 to 50 : 50, the package has ample adhesive strength and excels in peel openability. The production of packages of this invention can be mechanized, and when the package is adopted for the storage of a medical container such as a blood bag or transfusion bag holding therein an anticoagulant or some other medicinal fluid, it offers the advantage that possible growth of aerobic



- 17 -

microorganisms under the wet conditions due to the
aforementioned medicinal fluid can be precluded because
the interior of the package is brought to a
substantially oxygen-free state within a very short
5 length of time after the medical container is placed
in the package.

10

15

20

25



(28)

C L A I M S :

1. A tightly sealed package holding a) a medical container and b) a deoxidizer which is covered on one side with a gas-impervious sheet and on at least one other side with a gas-pervious sheet, said deoxidizer resting with a gas-pervious sheet side on an inner side of the package and being provided at this inner side with at least one passage for gas communication between the gas-pervious sheet side of the deoxidizer and the atmosphere enclosed within the package.
2. A package according to claim 1 wherein the medical container and deoxidiser are held in a tray provided round the opening thereof with a flange, a hot melt adhesive layer forming a peelable heat seal between the flange and a sheet shaped lid member.
3. A package according to claim 2 wherein the tray is a laminate comprising a polyolefin layer, an intermediate layer to act as a barrier to passage of gases and steam, and a polyolefin layer, the lid member is a laminate comprising a polyamide layer, a layer to act as a barrier to passage of gases and steam, and an outer



layer of sufficient thermal resistance to withstand the conditions of heat sealing, and the hot melt layer comprises a plurality of materials of dissimilar melting points and including at least one material substantially the same as a polyolefin of the tray layer in contact therewith.

5

4. A package according to claim 3 wherein the polyolefin inner layer of the tray is of polypropylene and the hot melt adhesive layer is of a blend of polyethylene with polypropylene.

10

5. A package according to claim 4 wherein the weight ratio of polyethylene to polypropylene in the hot melt adhesive layer is in the range of 20 : 80 to 50 : 50.

15

6. A package according to any of claims 3 to 5 wherein the thermally resistant layer is of polyester, polyamide or polypropylene.

20

7. A package according to any of claims 3 to 6 wherein the barrier layer of the lid member comprises polyvinylidene chloride or ethylene-vinyl alcohol copolymer.

25

8. A package according to any of claims 3 to 7 wherein the barrier layer of the tray comprises



(20)

ethylene-vinyl alcohol copolymer.

9. A package according to any of claims 2 to 8 wherein at least the tray is transparent.

5 10. A package according to any preceding claim having a said passage or passages along the bottom of the package.

11. A package according to any preceding claim
10 having a groove or grooves providing said passage or passages.

12. A package according to any preceding claim wherein the medical container stored in the package
15 contains a medical fluid.

13. A package substantially as hereinbefore described with reference to Fig.3 taken in conjunction with Figs.1, 2 and 4 of the accompanying drawings.
20

14. A package substantially as hereinbefore described with reference to Fig.5 of the accompanying drawings.
25

3

- 21 -



15. A package
substantially as hereinbefore described in any one of
Examples 1 to 7.

5

10

15

20

25