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(56) Documents cited
GB 1487875 GB 1133282 JP A 56–41420
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GB 1163278

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C3V

(54) Vinyl chloride polymer composition and medical devices made thereof

(57) The present invention provides a vinyl chloride resin composition for medical use, which is stabilised against degradation by radiation, comprising 100 parts by weight of vinyl chloride resin, at least 0.001 part by weight of metal oxide selected from magnesium, calcium and zinc oxides, and 5 to 200 parts by weight of plasticizer. It also provides radiation sterilisable medical devices made of such vinyl chloride resin composition.

The term "vinyl chloride resin" includes polyvinylidene chloride.

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Formulae in the printed specification were reproduced from drawings submitted after the date of filing, in accordance with Rule 20(14) of the Patents Rules 1982.

FIG.1

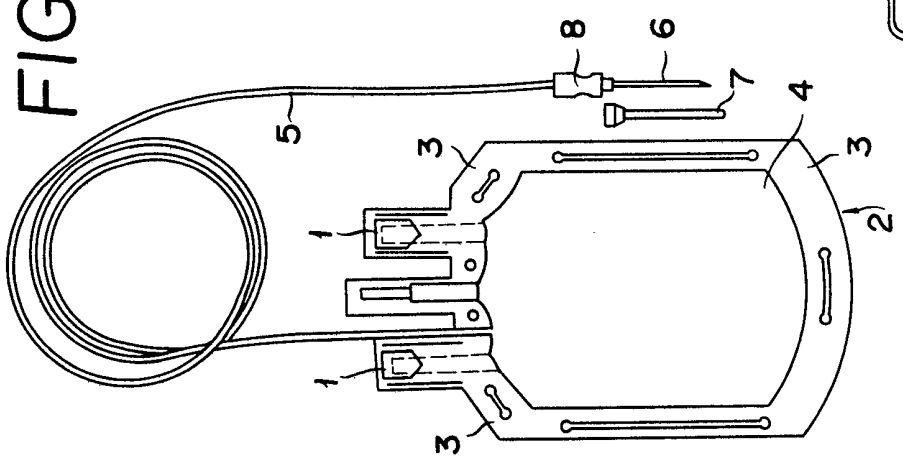


FIG.2

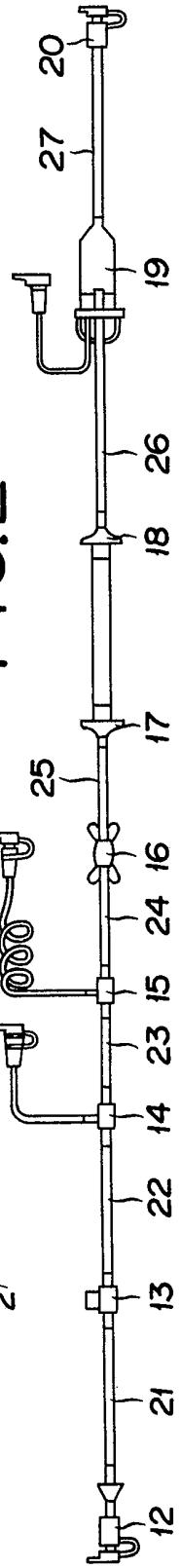
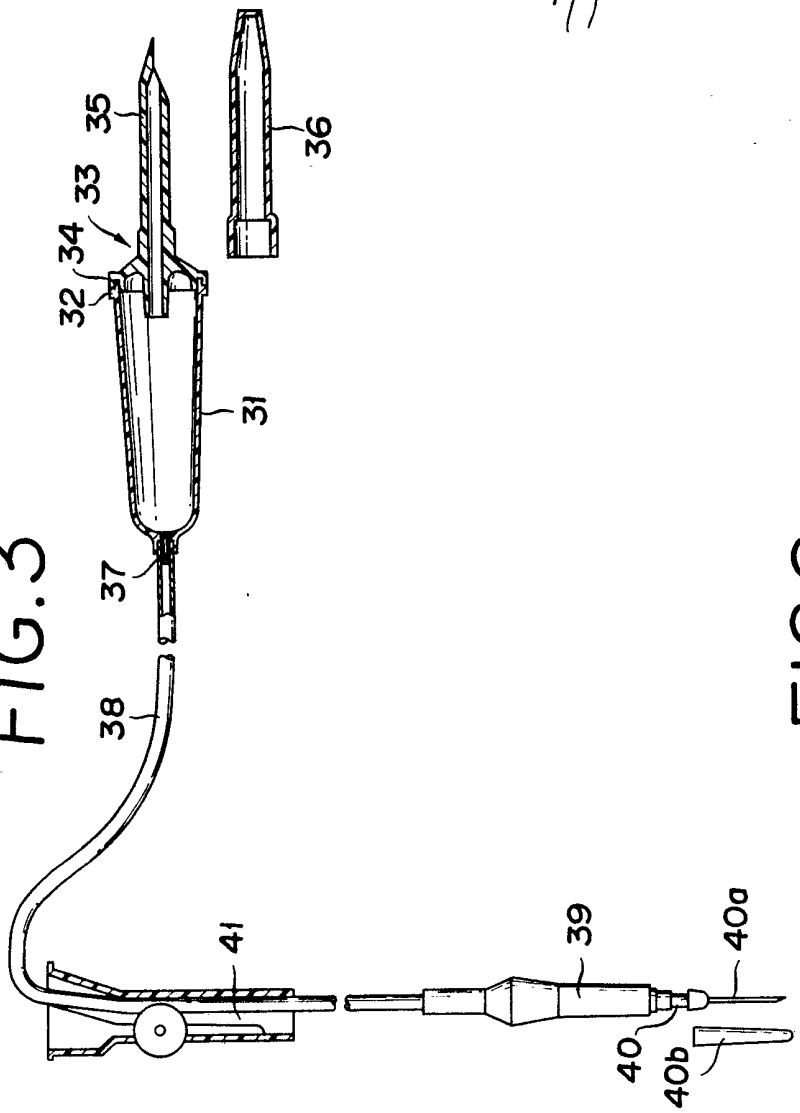


FIG.3



SPECIFICATION

Polymer composition and medical devices made thereof

This invention relates to a vinyl chloride polymer composition and to radiation sterilizable medical devices made of this composition.

Heretofore, it has been customary for medical devices (e.g. blood bags, solution administration sets and catheters) to be first sterilized thermally or by the action of a sterilizing agent such as ethylene oxide gas and then stowed in respective packages similarly sterilized in advance or for them to be first contained in respective packages and thereafter subjected in situ to sterilization. In the case of thermal sterilization, however, there has been the problem that the synthetic resin used in such medical devices is required to resist thermal degeneration and deformation. In the case of sterilization with ethylene oxide gas, there has been the problem that, after the sterilization, a good deal of time is wasted before the sterilized medical devices are free from ethylene oxide gas.

As a method for effecting sterilization without heat or sterilizing agent, sterilization by radiation has recently been proposed. Since this method is carried out at low temperatures, it no longer entails the requirement that the materials of medical devices should be capable of withstanding heat and resisting thermal deformation. The use of radiation nevertheless causes irradiated medical devices to suffer from adverse effects such as deterioration and discoloration. Particularly, medical devices made of or using flexible vinyl chloride resin, when sterilized by radiation, have failed in the safety test which all medical devices are required to pass. For example, the vinyl chloride resin composition which has found popular acceptance for use in medical devices comprises 100 parts by weight of polyvinyl chloride, 30 to 80 parts by weight of di-2-ethylhexyl phthalate, about 0.01 to 5 parts by weight of a calcium-zinc type metallic soap as a stabilizer, about 0 to 10 parts by weight of epoxidized soybean oil as an assistant stabilizer, and optionally about 0 to 5 parts by weight of slidant. When a moulded article of such flexible vinyl chloride resin was sterilized by exposure to radiation and thereafter tested by the "Standard for Blood Bag Set made of Vinyl Chloride Resin" (Ministry of Health and Welfare Standard), Notification No. SHOWA 40(1965)–448 of the Japanese Ministry of Health and Welfare or the "Method for Testing Plastic Containers for Transfusion (Pharmacopoeial Standard)" of the Tenth Amended General Testing Methods, No. 42, of the Japanese Pharmacopoeia, to determine whether or not the moulded article would discharge any extract and whether the extract, if any, would cause hemolysis, the results obtained (with irradiation at a dosage of 3 Mrads) were found to exceed the tolerable limits. Thus, the resin proved to be unsuitable as a material for medical devices destined to be sterilized by radiation. When an extract from the moulded article was subjected to a cell toxicity test it was found to possess discernible toxicity.

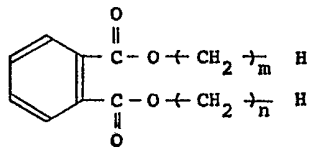
A stabilizer such as zinc stearate, calcium stearate or magnesium stearate has hitherto been incorporated with the vinyl chloride resin, but the amount used was large. Such stabilizer also acts as a lubricant, and bleeds out on the surface during the moulding.

As a resin composition for medical use, a composition comprising 100 parts by weight of a vinyl chloride resin, 5 to 200 parts by weight of an ethylene-carbon monoxide-vinyl acetate copolymer and 0.001 to 10 parts by weight of powdered magnesium oxide or calcium oxide is known (Japanese Patent Open No. Sho 56[1981]–41420). The ethylene-carbon monoxide-vinyl acetate copolymer, a softening agent, is apt to yield acetic acid during heat moulding and the acetic acid is neutralized by magnesium oxide or calcium oxide. However, the above composition can be moulded only below 120°C. If the composition is heated above 120°C. diacetic acid is formed. Further, if a medical device made of the composition is sterilized by radiation, acetic acid is apt to form, and may be extracted into medical solution or blood when the device is used.

The present invention provides a vinyl chloride resin composition for medical use comprising 100 parts by weight of vinyl chloride resin, at least 0.001 (preferably up to 5) parts by weight of metal oxide selected from magnesium, calcium and zinc oxides, and 5 to 200 parts by weight of plasticizer; it also provides medical devices made of such a composition.

The composition according to the invention most preferably contains from 0.005 to 3 parts by weight of said metal oxide. The plasticizer preferably comprises dialkyl phthalate, which preferably has the same or different alkyl groups of 6 to 13 carbon atoms. The composition preferably contains from 10 to 100 parts by weight of dialkyl phthalate plasticizer. The compositions according to the invention are suitable for making radiation sterilizable medical devices, e.g. a container for preserving body fluid, particularly blood; a catheter; a blood administration set; a solution administration set; or a blood line.

A preferred amount of said metal oxide in said resin composition falls in the range of 0.005 to 3 parts by weight based on 100 parts by weight of said vinyl chloride resin. Preferred dialkyl phthalate plasticizers include those of general formula I:



(I)

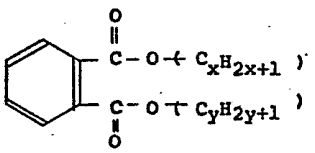
wherein m and n are independently integers of substantially 6 to 12 and the average of m and n, (m + n)/2 is not more than 11.5. A preferred amount of dialkyl phthalate in said resin compound is in the range of 10 to 100 parts by weight based on 100 parts by weight of said vinyl chloride resin content. In formula I, m and n may stand independently for integers of at least 7, with the average of m and n, (m + n)/2, not more than 11. The dialkyl phthalate may be di-n-decyl phthalate or a mixture of n-decyl-(n-dodecyl) phthalate, di-n-decyl phthalate and di-n-dodecyl phthalate.

The medical devices contemplated by the present invention are such medical devices as bags and tubes for use in catheters, blood administration sets, solution administration sets, blood lines and blood bags; catheters themselves; tubes for dialysis and solution administration sets; containers for packaging such medical devices as described above; and containers for packaging tablets and other forms of medicine.

Examples of the vinyl chloride resin contained in the resin composition of this invention include, besides homo-polymers of vinyl chloride, polyvinylidene chloride and copolymers between at least 40% by weight, more desirably at least 65% by weight, and most desirably at least 75% by weight, of vinyl chloride and monomer copolymerizable therewith. The average polymerization degree of the vinyl chloride resin is usually 400 to 3,000 more desirably 600 to 2,700 and most desirably 800 to 1,700. Examples of the comonomer to be copolymerized with vinyl chloride include vinylidene chloride, ethylene, propylene, vinyl acetate, vinyl bromide, vinyl fluoride, styrene, vinyl toluene, vinyl pyridine, acrylic acid, alkyl acrylates (such as, for example, methyl acrylate, ethyl acrylate, isopropyl acrylate, n-butyl acrylate and 2-ethylhexyl acrylate), methacrylic acid, alkyl methacrylates (such as, for example, methyl methacrylate, ethyl methacrylate and 2-ethylhexyl methacrylate), acrylonitrile, and methacrylonitrile. Optionally, the vinyl chloride resin may be used in combination with styrene acrylonitrile copolymer or styrene-methacrylonitrile copolymer.

The most prominent characteristic of the present invention is the fact that the vinyl chloride resin is used in combination with at least one metal oxide selected from the group consisting of magnesium oxide, calcium oxide and zinc oxide. Of the three metal oxides, magnesium oxide is the most desirable choice. The amount of the metal oxide to be contained in the resin composition is usually 0.001 to 5 parts by weight, preferably 0.005 to 3 parts by weight, based on 100 parts by weight of the vinyl chloride resin content. If the metal oxide content is less than 0.001 part by weight, adequate results in the extraction test are not attained. If this content exceeds 5 parts by weight, further improvement may no longer be obtained.

As the plasticizer for use in the resin composition of this invention, any of the plasticizers which are generally suitable for use with vinyl chloride resin can be adopted. This plasticizer, however, preferably comprises dialkyl phthalate; the alkyl groups thereof may be the same or different and of 6 to 13 carbon atoms. Suitable dialkyl phthalate plasticizers include those of the general formula II:



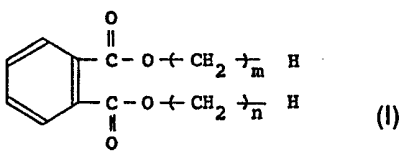
(II)

In the general formula, x and y are independently integers of at least 6 and the average of x and y, (x + y)/2, is not more than 13, and more desirably x and y are independently integers of substantially 7 to 13 and the average of x and y, (x + y)/2, is not more than 12. If either or both of x and y are not more than 4, the diester may manifest toxicity. If x and y are both 5, the diester is not commercially available and is hard to obtain. If the average, (x + y)/2, exceeds 13, the diester exhibits poor miscibility with the vinyl chloride resin and is poor as a plasticizer. The ester may issue from a mixture of two alcohols of different chain lengths.

It is imperative that the vinyl chloride resin composition containing the plasticizer described above should incorporate the aforementioned metal oxide. If the metal oxide content in the resin composition is less than 0.001 part by weight, the resin composition no longer passes the standard test of Japanese Ministry of Health and Welfare and is not suitable for the production

of the medical devices contemplated by the present invention.

The dialkyl phthalates described above include phthalic diesters of fatty alcohols represented by the general formula I:



(I)

In the general formula, m and n are independently integers of substantially 6 to 12 and the average of m and n, $(m + h)/2$, is not more than 11.5; and more desirably m and n are independently integers of substantially 7 to 12 and the average of m and n, $(m + n)/2$, is not more than 11. If the average of m and n, $(m + n)/2$, exceeds 11.5, the phthalic diester may have poor miscibility with the vinyl chloride resin. The ester may come from a mixture of two alcohols of different chain lengths. If the alcohols as components of the phthalic diester are alcohols of straight chains, the composition during sterilization by radiation discharges extract at a tolerable level (fixed by the Japanese Pharmacopoeia) and this extract does not produce cell toxicity. Dialkyl phthalates from linear alcohols are thus preferred plasticizers for use in this invention.

Examples of the dialkyl phthalate of the aforementioned general formula I are esters of phthalic anhydride with single alcohols or mixed alcohols and include, for example, di-n-hexyl phthalate, di-n-heptyl phthalate, di-n-octyl phthalate, di-n-nonyl phthalate, di-n-decyl phthalate, di-n-undecyl phthalate, di-n-dodecyl phthalate, n-hexyl-(n-heptyl) phthalate, n-hexyl-(n-octyl) phthalate, n-hexyl-(n-nonyl) phthalate, n-hexyl-(n-decyl) phthalate, n-hexyl-(n-undecyl) phthalate, n-hexyl-(n-dodecyl) phthalate, n-heptyl-(n-octyl) phthalate, n-heptyl-(n-nonyl) phthalate, n-heptyl-(n-decyl) phthalate, n-heptyl-(n-undecyl) phthalate, n-heptyl-(n-dodecyl) phthalate, n-octyl-(n-nonyl) phthalate, n-octyl-(n-decyl) phthalate, n-octyl-(n-undecyl) phthalate, n-octyl-(n-dodecyl) phthalate, n-nonyl-(n-decyl) phthalate, n-nonyl-(n-undecyl) phthalate, n-nonyl-(n-dodecyl) phthalate, n-decyl-(n-undecyl) phthalate, n-decyl-(n-dodecyl) pthalate, n-octyl-(n-decyl)-(dodecyl) phthalate and mixtures thereof. Of these dialkyl phthalates, the most desirable choices are di-n-decyl phthalate; a mixture of n-decyl-(n-dodecyl) phthalate, di-n-decyl phthalate and di-n-dodecyl phthalate; and di-ethylhexyl phthalate.

The amount of the plasticizer can fall in the range of 5 to 200 parts by weight, more desirably 8 to 120 parts by weight, and most desirably 10 to 100 parts by weight, based on 100 parts by weight of the vinyl chloride resin content. Particularly, the plasticizer represented by the aforementioned general formula II manifests an advantageous effect. The plasticizer represented by the aforementioned general formula I can give a better effect.

When required, the vinyl chloride resin compound may further incorporate a metallic soap of calcium or zinc with stearic acid, lauric acid, ricinoleic acid, or naphthenic acid; an epoxidized vegetable oil such as epoxidized soybean oil or epoxidized linseed oil; a slidant; and/or an antioxidant. An additive may be used, as conventionally known, in the form of a high molecular weight compound. For example, polychloroprene resin or thermoplastic polyurethane resin may be incorporated by the technique of polymer blending.

Medical devices according to the invention are described below, by way of example only, with reference to the drawing in which:

Figure 1 is a front view illustrating a blood bag;

Figure 2 is a schematic side view illustrating an arterial blood line; and

Figure 3 is a cross sectional view illustrating a solution administration set.

Fig. 1 illustrates a blood bag 2 made of vinyl chloride resin composition and provided with a plurality of outlets 1 each fitted with a peel tab whose peripheral edge is sealed by high-frequency heating or some other heating means. A tube 5 made of vinyl chloride resin composition is connected to the blood bag so as to communicate with an inner space 4 of the blood bag. The tube 5 is provided at the leading end thereof with a needle base 8. To this needle base 8 is fastened a piercing needle 6. This piercing needle 6 is adapted to be sheathed with a cap 7.

Fig. 2 illustrates a typical arterial blood line which comprises a shunt adapter 12 provided with a priming cap 11, self-sealing injection port 13, T-shaped tubes 14, 15, a negative pressure pillow 16, pump-segment connectors 17, 18, a drip chamber 19, and a port connector 20, and tubes 21, 22, 23, 24, 25, 26 and 27 made of the aforementioned vinyl chloride resin composition and adapted to interconnect the components described above.

Fig. 3 shows a solution administration set in which an instillator is formed by placing a flange member 34 formed near the tip of an opening of a rigid cap member 33 produced by injection moulding polypropylene, for example, in contact with a flange member 32 formed near the tip

of an opening of a flexible, transparent tubular member 31 produced by injection moulding a propylene-α-olefin copolymer and joining these two flange members by ultrasonic fusion by causing an oscillator of an ultrasonic welder (not shown) to act upon the flange member 34 side. The cap member has a vial needle 35 integrally formed therewith. When necessary, the vial needle 35 is sheathed with a protective cap 36. At one end of the aforementioned flexible, transparent tubular member 31, there is formed a port 37. To this port 37 is connected a flexible tube 38 made of the aforementioned vinyl chloride resin composition and adapted to transfer a medical liquid. When necessary, a flexible connector 39 made of rubber and a connector 40 made of a rigid material are connected to the tip of the flexible tube 38. To the leading end of the connector 40 is connected, when necessary, a piercing needle 40*a* adapted to be plunged into a vein. Optionally, the piercing needle 40*a* is sheathed with a protective cap 40*b*. In the intervening portion, a pinch 41 is fitted so as to clamp the aforementioned flexible tube 38.

The medical device of this present invention has been described by citing e.g. a blood bag, a blood line, and a solution administration set each embodying the present invention. This invention can further be embodied as a container for preserving blood, a blood administration system, a solution administration system, a catheter, and a tube for dialysis in much the same way as described above. Since the aforementioned moulded article made of vinyl chloride resin can well withstand sterilization by radiation, tubes, catheters, and particularly tubes for solution administration sets can show satisfactory results when they are made of this resin compound.

The medical devices contemplated by the present invention prove particularly advantageous when they are sterilized by radiation.

Examples of the radiation which may be used for the sterilization of medical devices are electromagnetic radiations such as gamma ray and electron beam. The intensity of this radiation may e.g. be from 1 to 5 Mrads, preferably 1.5 to 3 Mrds.

The present invention is illustrated more specifically by the following working Examples and Controls.

Example 1 and Control 1

With rolls of surface temperature kept at 160°C, 100 parts by weight of polyvinyl chloride of an average polymerization degree of about 1,250, 50 parts by weight of a phthalic diester of branched configuration satisfying the general formula II by having substantially 8 as the value of each of x and y (di-2-ethyhexyl phthalate) [DOP: made by Kyowa Hakko Kogyo Co. Ltd.], 0.5 part by weight of magnesium oxide (MgO), and suitable amounts of a stabilizer and a slidant of the grade generally accepted for use in medical grade vinyl chloride resin were blended and the resultant blend was moulded to produce a pressed sheet about 0.4 mm in thickness (Example 1).

By following the procedure described above, except that magnesium oxide was omitted, there was similarly produced a pressed sheet (Control 1).

These pressed sheets were irradiated with 3 Mrads of gamma ray and were then tested by the "Standard for Blood Bag Set made of Vinyl Chloride Resin (Ministry of Health and Welfare Standard), Notification No. SHOWA 40 (1965)–448 of Japanese Ministry of Health and Welfare. The results were as shown in Table 1.

The Example 1 vinyl chloride resin composition had excellent radiation sterilization resistance; it passed the above Standard which is the most severe standard for medical devices enacted by Pharmaceutical Affairs Law, and can be used as catheter, solution administration set, blood line and blood bag material.

Table 1

Item of test	Toleration	Control 1	Example 1
Appearance	Colorless and transparent	Colorless and transparent	Colorless and transparent
Change in pH	2.0 max	2.41	0.64
0.01 $NKMnO_4$ consumed	2.0 ml max.	1.57	0.77
Chloride	1.1 ml max.	1.1 ml max.	1.1 ml max.
Sulfate	1.0 ml max.	1.0 ml max.	1.0 ml max.
Ammonium	1.0 ml max.	1.0 ml max.	1.0 ml max.
Residue on evaporation	5 mg max.	0.4 mg	0.4 mg

Example 2 and Control 2

With rolls of surface temperature kept at 160°C, 100 parts by weight of polyvinyl chloride of an average polymerization degree of about 1,250, 50 parts by weight of a phthalic diester satisfying the general formula I by having substantially 10 as the value of each of m and n (di-n-decyl phthalate) (Vinysize #105 made by Kao Soap Co., Ltd.), 0.5 parts by weight of magnesium oxide (MgO), and suitable amounts of a stabilizer and a slidant generally accepted for use with medical grade vinyl chloride resin were blended and the resultant blend was molded to produce a pressed sheet about 0.4 mm in thickness (Example 2). By following the procedure described above, except that magnesium oxide was omitted, there was similarly obtained a pressed sheet (Control 2).

These pressed sheets and the pressed sheet of Control 1 were irradiated with 3 Mrads of gamma ray and then tested by the "Method for Testing Plastic Containers for Transfusion (Pharmacopoeial Standard)" of the Tenth Amended General Testing Methods, No. 42, of the Japanese Pharmacopoeia. The results were as shown in Table 2. Further, a cell toxicity test was carried out to obtain the results of Table 3. The results show that phthalic diesters esterified with alcohol having straight chain can provide a medical vinyl chloride resin composition which can satisfy the Pharmacopeia standard, does not show cell toxicity, has high safety and can be sterilized by radiation; the composition can pass the Pharmacopeia standard which requires the highest level of safety for medical vinyl chloride resin and also can pass the cell toxicity test which has the highest sensitivity as a screening test for toxicity. The medical vinyl chloride resin composition is not limited in use and can be sterilized by radiation.

The cell toxicity test was carried out in accordance with the Toplin Method (Toplin, I; Cancer Res. *19*, 959 (1959) "Method for Toxicity Test, Explanation, Evaluation, and Problems, pp 171–172, 186–189).

The usefulness of this cell toxicity test is described in 82/1 Polymer Feasibility Lectures, collection of Summaries of Lectures, "Method for Testing Plastic Materials and Problems Encountered" pp 74–76. Although this method has not yet been officially adopted, it is useful in ascertaining safety of a given material.

Specifically, this test was conducted by placing 1 g of sliced test pieces in 3 ml of culture medium, keeping the medium at 121°C for 20 minutes to induce possible extraction, diluting the resultant extraction medium with a reference medium, and administering the diluted medium to a subject cell. The cell used in this test was HeLa.

Table 2

Test item	Tolerance	Control 1*	Example 2**	Control 2***
Appearance	Colorless and transparent	Colorless and transparent	Colorless and transparent	Colorless and transparent
Change in pH	1.5 max.	2.48	0.71	2.30
0.01N $KMnO_4$ consumed (ml)	1.0 max.	1.71	0.66	0.92
Foaming	Extinction of foam within 3 minutes	Foam vanished within 3 minutes	Foam vanished within 3 minutes	Foam vanished within 3 minutes
Chloride (ml)	0.7 max.	0.7 max.	0.7 max.	0.7 max.
Sulfate (ml)	2.0 max.	2.0 max.	2.0 max.	2.0 max.
Ammonium (ml)	0.5 max.	0.5 max.	0.5 max.	0.5 max.
Phosphate (ml)	0.3 max.	0.3 max.	0.3 max.	0.3 max.
Distillation residue (ml)	1 max.	0.5	0.4	0.4
Ultraviolet absorption				
230–241 nm	0.08 max.	0.19	0.05	0.06
241–350 nm	0.05 max.	0.10	0.02	0.02
Hemolysis	No hemolysis detected	Hemolysis occured	No hemolysis detected	Hemolysis occured

* Di-2-ethylhexyl phthalate incorporated as plasticizer and addition of MgO omitted.
** Di-n-decyl phthalate incorporated as plasticizer.
*** Di-n-decyl phthalate incorporated as plasticizer and addition of MgO omitted.

Table 3

Concentration of extracted medium	Control 1	Example 2	Control 2
100% (no dilution involved)	2	0	0
67%	0	0	0
33%	0	0	0

Scale for rating toxicity:

0: Absence of cell toxicity (absolutely no difference from blank recognized).

1: Increase of dead cells (conspicuous signs of malformation and poor propagation, while the number of surviving cells was large).

2: Death of nearly all cells or all the cells verging on death.

3: Complete extinction of all the cells.

Examples 3–5

Medical grade vinyl chloride resin compositions were prepared by following the procedure of Example 1 except that the kind and amount of plasticizer and the kind and amount of metal oxide as a stabilizer were varied as indicated in Table 4. In the three compositions thus produced, only that of Example 5 was white and translucent.

A sheet for a blood bag was produced from the composition of Example 3, a tube 5 from the composition of Example 4, and a needle base 8 from the composition of Example 5, for the blood bag illustrated in Fig. 1. This blood bag was sterilized by exposure to 3 Mrads of gamma ray. Then, the parts were subjected to the same test as indicated in Example 2. The results were as shown in Tables 5–6.

Table 4

	Example 3	Example 4	Example 5
Plasticizer			
(kind)	Di-n-decyl phthalate	Phthalic diester mixture obtained by n-decyl alcohol and n-dodecyl alcohol	Phthalic diester mixture obtained by n-decyl alcohol and n-dodecyl alcohol
(amount)	60	70	15
Stabilizer			
(kind)	Magnesium oxide	Calcium oxide	Zinc oxide
(amount)	0.1	0.3	0.05

Table 5

Test item	Example 3	Example 4	Example 5
Appearance	Colorless and transparent	Colorless and transparent	Colorless and transparent
Change of pH	0.80	0.92	0.57
0.01N $KMnO_4$ consumed (ml)	0.58	0.70	0.41
Foaming	Foam vanished within 3 minutes	Foam vanished within 3 minutes	Foam vanished within 3 minutes
Chloride (ml)	0.7 max.	0.7 max.	0.7 max.
Sulfate (ml)	2.0 max.	2.0 max.	2.0 max.
Ammonium (ml)	0.5 max.	0.5 max.	0.5 max.
Phosphate (ml)	0.3 max.	0.3 max.	0.3 max.
Distillation residue (ml)	0.2	0.4	0.2
Ultraviolet absorption			
230–241 nm	0.06	0.05	0.05
241–350 nm	0.02	0.02	0.02
Hemolysis	No hemolysis detected	No hemolysis detected	No hemolysis detected

Table 6

Concentration of extracted medium	Example 3	Example 4	Example 5
100% (no dilution involved)	0	0	0
67%	0	0	0
33%	0	0	0

Medical devices made from resin compositions of the invention withstand sterilization by radiation. When a dialkyl phthalate represented by the general formula II is used as a plasticizer, then the composition can exhibit excellent properties in the standard tests specified by the Japanese Ministry of Health and Welfare. When a di-n-alkyl phthalate represented by the general formula I is used as a plasticizer, the composition can exhibit excellent properties in the tests specified by the Japanese Pharmacopoeia and also show quite satisfactory results in the cell toxicity test.

When the amount of the metal oxide in the resin composition falls in the range of 0.005 to 3 parts by weight and the amount of the plasticizer to be incorporated in the resin composition is in the range of 10 to 100 parts by weight, medical devices made of the resin composition can exhibit outstanding mechanical strength and flexibility. When this resin composition is used in the production of body fluid containers such as containers for the preservation of blood and medical devices such as catheters, blood administration sets, solution administration sets and blood lines, which are exposed to direct contact with body fluids or solutions for administration, the radiation sterilized devices have little or no tendency to discharge extracts or cause hemolysis or manifest toxicity.

As a standard on safety of medical synthetic resin, there is the "Standard for Blood Bag Set made of Vinyl Chloride Resin" Ministry of Health and Welfare Standard of Japan, Notification No. SHOWA 40 (1965) 448 which is the most severe standard, in addition to the standard about blood administration set, solution administration set, blood bag, etc. notified by Ministry of Health and Welfare enacted based on Pharmaceutical Affairs Law, such as "Standard for Disposable Solution and Blood Administration Sets" (Notification No. SHOWA 45(1970)–301 of Ministry of Health and Welfare of Japan) and "Standard for Disposable Blood Collecting Instrument" (Notification No. SHOWA 45(1970)–300 of Ministry of Health and Welfare of Japan), and the medical vinyl chloride resin composition incorporating said metal oxide can provide a material having excellent radiation resistance which can satisfy the stanard even after

sterilization by radiation. An example of the plasticizer for the medical vinyl chloride composition is di-2-ethylhexyl phthalate.

Especially high safety is required in a plastics container for solution administration which is expected to be sterilized by high pressure steam; it is necessary to pass the standard described in "Method for Testing Plastic Containers for Transfusion" of the Tenth Amended General Testing Methods, No. 42 of Japanese Pharmacopeia. Devices made from a vinyl chloride resin composition according to the present invention can pass all of these standards.

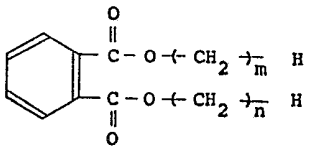
CLAIMS

1. A vinyl chloride resin composition for medical use comprising 100 parts by weight of vinyl chloride resin, at least 0.001 parts by weight of metal oxide selected from magnesium, calcium and zinc oxides, and 5 to 200 parts by weight of plasticizer.

2. A composition according to claim 1 wherein the plasticizer comprises dialkyl phthalate.

3. A composition according to claim 2 wherein the alkyl groups of the dialkyl phthalate are the same or different alkyl groups of 6 to 13 carbon atoms.

4. A composition according to claim 3 wherein the dialkyl phthalate is represented by the general formula



wherein m and n are the same or different integers of 6 to 12 and $(m + n)/2$ is not more than 11.5.

5. A composition according to claim 4 wherein m and n are the same or different integers of at least 7 and $(m + n)/2$ is not more than 11.

6. A composition according to claim 5 wherein the dialkyl phthalate is di-n-decyl phthalate, or a mixture of n-decyl-(n-dodecyl) phthalate, di-n-decyl phthalate and di-n-dodecyl phthalate.

7. A composition according to any of claims 2 to 6 containing from 10 to 100 parts by weight of dialkyl phthalate plasticizer.

8. A composition according to any preceding claim containing from 0.005 to 3 parts by weight of said metal oxide.

9. A composition according to any preceding claim wherein said metal oxide is magnesium oxide.

10. A composition according to any preceding claim sterilized by radiation.

11. A vinyl chloride resin composition for medical use and substantially as hereinbefore described in any one of Examples 1–5.

12. A medical device made of a vinyl chloride resin composition according to any preceding claim.

13. A medical device according to claim 12 which has been sterilized by radiation.

14. A medical device according to claim 12 which has been sterilized by gamma radiation.

15. A tubular medical device according to any of claims 12 to 14.

16. A medical device according to any of claims 12 to 15 which is selected from bags and tubes for use as or on catheters, dialysis tubes, blood administration sets, solution administration sets, blood lines and blood bags; catheters; and packaging for medicine.

17. A medical device made of a vinyl chloride resin composition and substantially as hereinbefore described with reference to any one of Figs. 1–3 of the accompanying drawings.

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