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(54) Title: GLASS FOR PHARMACEUTICAL CONTAINERS

(57) Abstract: An object of the present invention is to provide a glass for pharmaceutical containers, which is resistant to delamination and has excellent processibility. The glass for pharmaceutical containers of the present invention comprises, in mol% on an oxide basis, 69 to 81% of SiO₂, 4 to 12% of Al₂O₃, 0 to 5% of B₂O₃, 5 to 20% of Li₂O + Na₂O + K₂O, 0.1 to 12% of Li₂O, and 0 to 10% of MgO + CaO + SrO + BaO. The glass has a hydrolytic resistance of Class 1 in a test in accordance with the European pharmacopoeia.



WO 2014/196655 A1

DESCRIPTION

GLASS FOR PHARMACEUTICAL CONTAINERS

5 Technical Field

The present invention relates to a glass for pharmaceutical containers, which has excellent chemical durability and also has excellent processibility.

Background Art

10 As containers for packing and storing pharmaceuticals, glasses made of various materials have been used. Pharmaceuticals are roughly divided into oral agents and parenteral agents. Among them, in the case of parenteral agents, a liquid medicine packed/stored in a glass container is directly administered into the patient's blood. Therefore, there are extremely rigorous quality requirements for such glass containers. In particular, extractables from the glass into the liquid medicine may change the properties of the liquid medicine, seriously affecting the life and health of the patient. Therefore, the pharmacopoeia of each country prescribes the amount of extractables from the glass. In addition, for processing into various forms such as ampoules, vials, prefilled syringes, and cartridges, excellent viscosity characteristics are necessary.

15 20 As a glass material that meets these requirements, borosilicate glass has generally been used. Borosilicate glass for pharmaceutical containers normally contains, as constituents, SiO₂, Al₂O₃, B₂O₃, Na₂O, K₂O, CaO, and BaO together with a small amount of fining agent.

25 Citation List

Patent Literature

[PTL 1] WO 2013/063275

Non-Patent Literature

[NPTL 1] PDA J Pharm Sci and Tech 2012, 66 116

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Summary of Invention

Technical Problem

In recent years, with the rapid advance of pharmaceutical sciences, a wide variety of medicines have been produced, and medicines to be packed in pharmaceutical containers have been changing, which is accompanied by an increase in the number of powerful medicines that corrode glass containers. When such a medicine is
5 packed/stored in a glass container, the inner surface of the container peels off and floats as flakes in the liquid medicine. This phenomenon, called delamination, has been a serious problem.

Various studies have been conducted to find out the causes of delamination. As in NPTL 1, the boron component contained in borosilicate glass used as a glass for
10 pharmaceutical containers evaporates during thermal processing, resulting in the formation of a silica rich layer, or the evaporated component recondenses on the container inner surface, which occasionally causes phase separation on the inner surface of the glass container; this is believed to be one of the causes of delamination.

Accordingly, as glasses for pharmaceutical containers for suppressing
15 delamination, boron free and low boron glasses have been proposed as in PTL 1, and some delamination suppressing effects can be seen. However, there is a problem in that the working points of these glasses are so high that processing into various forms is difficult.

An object of the present invention is to provide a glass for pharmaceutical
20 containers, which is resistant to delamination and has excellent processibility.

Solution to Problem

The present inventors have conducted various studies, and, as a result, found that the problems mentioned above can be solved by the limitation of the B_2O_3 content
25 and the addition of Li_2O . This finding is proposed as the present invention.

That is, the glass for pharmaceutical containers of the present invention comprises, in mol% on an oxide basis, 69 to 81% of SiO_2 , 4 to 12% of Al_2O_3 , 0 to 5% of B_2O_3 , 5 to 20% of $Li_2O + Na_2O + K_2O$, 0.1 to 12% of Li_2O , and 0 to 10% of $MgO + CaO + SrO + BaO$.

The " $Li_2O + Na_2O + K_2O$ " herein means the total content of Li_2O , Na_2O , and K_2O . The " $MgO + CaO + SrO + BaO$ " herein means the total content of MgO , CaO ,
30 SrO , and BaO .

In the present invention, it is preferable that B_2O_3 is 0 to 4% in mol% on an oxide basis.

In the present invention, it is preferable that Na_2O is 0 to 11% and K_2O is 0 to 5% in mol% on an oxide basis.

5 In the present invention, it is preferable that MgO is 0 to 9%, CaO is 0 to 4%, SrO is 0 to 4%, and BaO is 0 to 4% in mol% on an oxide basis.

In the present invention, it is preferable that the glass further comprises 0 to 2 mol% of ZrO_2 .

10 In the present invention, it is preferable that the glass has a hydrolytic resistance of Class 1 in a test in accordance with the European pharmacopoeia (i.e., a hydrolytic resistance of Class 1 in a test in accordance with ISO 720). The “hydrolytic resistance in a test in accordance with the European pharmacopoeia” refers to the degree of alkali extraction determined by the follow method.

(1) A glass sample is ground in an alumina mortar and classified into 300 to 425 μm through a sieve.

(2) The obtained powder sample is washed with distilled water and ethanol and dried in an oven at 140°C.

(3) 10 g of the dried powder sample is placed in a quartz flask, further 50 mL of distilled water is added, and the flask is capped and treated in an autoclave. The treatment is performed under the following conditions: the temperature is raised from 100°C to 121°C at 1°C/min, then maintained at 121°C for 30 minutes, and lowered to 100°C at 0.5°C/min.

(4) After autoclaving, the solution in the quartz flask is transferred to another beaker. Further, the inside of the quartz flask is washed three times with 15 mL of distilled water, and the washing water is also added to the beaker.

(5) A methyl red indicator is added to the beaker, followed by titration with a 0.02 mol/L hydrochloric acid solution.

(6) With 1 mL of the 0.02 mol/L hydrochloric acid solution equivalent to 620 μg of Na_2O , the amount of alkali extracted per g of glass is calculated.

30 In addition, the “hydrolytic resistance of Class 1 in a test in accordance with the European pharmacopoeia” means that the amount of alkali extracted as Na_2O determined as above is 62 $\mu g/g$ or less.

In the present invention, it is preferable that the alkali resistance in a test in accordance with ISO 695 is at least Class 2. The “test in accordance with ISO 695” herein refers to the follow test.

- (1) A 15 cm² glass sample piece with an entirely mirror finished surface is prepared. First, as a pretreatment, the sample is immersed in a solution containing fluoric acid (40 wt%) and hydrochloric acid (2 mol/L) mixed in a volume ratio of 1:9, followed by stirring for 10 minutes with a magnetic stirrer, and then taken out. Next, the sample is ultrasonically cleaned for 2 minutes with ultrapure water three times, and then ultrasonically cleaned for 1 minute with ethanol twice.
- (2) Subsequently, the sample is dried in an oven at 110°C for 1 hour and allowed to cool for 30 minutes in a desiccator.
- (3) The mass of sample m1 is measured to an accuracy of ±0.1 mg and recorded.
- (4) A 800 mL solution containing an aqueous sodium hydroxide solution (1 mol/L) and an aqueous sodium carbonate solution (0.5 mol/L) mixed in a volume ratio of 1:1 is placed in a stainless steel container and heated to boiling using a mantle heater. After boiling, the sample suspended on a platinum wire is placed therein and maintained boiling for 3 hours.
- (5) The sample is taken out, ultrasonically cleaned for 2 minutes with ultrapure water three times, and then ultrasonically cleaned for 1 minute with ethanol twice. Subsequently, the sample is dried in an oven at 110°C for 1 hour and allowed to cool for 30 minutes in a desiccator.
- (6) The mass of sample m2 is measured to an accuracy of ±0.1 mg and recorded.
- (7) From the masses of sample before and after placed in the boiling alkaline solution, m1 and m2 (mg), and the total surface area of sample A (cm²), the mass loss per unit area is calculated by the following equation as a measurement value of the alkali resistance test.

$$(\text{Mass loss per unit area}) = 100 \times (m1 - m2)/A$$

The “alkali resistance of Class 2 in a test in accordance with ISO 695” means that the measured value determined as above is 175 mg/dm² or less. Incidentally, when the measured value determined as above is 75 mg/dm² or less, the glass has “an alkali resistance of Class 1 in a test in accordance with ISO 695”.

In the present invention, it is preferable that the working point is 1260°C or less. The “working point” herein means the temperature at which the viscosity of the glass is 10⁴ dPa·s.

The glass for pharmaceutical containers of the present invention comprises, in
5 mol% on an oxide basis, 69 to 81% of SiO₂, 4 to 12% of Al₂O₃, 0 to 5% of B₂O₃, 5 to
20% of Li₂O + Na₂O + K₂O, 0.1 to 12% of Li₂O, 0 to 11% of Na₂O, 0 to 5% of K₂O,
and 0 to 10% of MgO + CaO + SrO + BaO, in which the Li₂O content is higher than the
K₂O content.

The glass tube for pharmaceutical containers of the present invention is made
10 of the glass for pharmaceutical containers mentioned above.

Advantageous Effects of Invention

The glass for pharmaceutical containers of the present invention is resistant to
delamination and also can be easily processed into a complex shape. In addition, it has
15 excellent hydrolytic resistance and is suitable as a glass material for pharmaceutical
containers, such as ampoules, vials, prefilled syringes, and cartridges.

Description of Embodiments

The reasons for controlling the range of composition for each component will
20 be described. Incidentally, “%” means “mol%” unless otherwise noted.

SiO₂ is one of the components forming the network of the glass. When the
content of SiO₂ is too low, vitrification is difficult to occur, and also the coefficient of
thermal expansion becomes too high, whereby thermal shock resistance is likely to
decrease. In addition, the acid resistance of the glass tends to be deteriorated.
25 Meanwhile, when the content of SiO₂ is too high, meltability and formability are likely
to decrease. Therefore, the content is 69 to 81%, preferably 69 to 80%, still more
preferably 70 to 79%, particularly preferably 70 to 78%, and most preferably 73 to 76%.

Al₂O₃ is one of the components forming the network of the glass and is
effective in improving the hydrolytic resistance of the glass. The content is 4 to 12%,
30 preferably 4.5 to 11%, still more preferably 5 to 10%, and most preferably 5.5 to 7%.
When the content of Al₂O₃ is low, it is difficult to achieve the hydrolytic resistance of
Class 1 in a test in accordance with the European pharmacopoeia. Meanwhile, when the
content of Al₂O₃ is high, it is difficult to achieve the working point of 1260°C or less.

B₂O₃ is effective in reducing the viscosity of the glass. It is preferable that the content is 0 to 5%, 0 to 4%, 0 to 3%, 0 to 2%, 0 to 1%, and particularly 0 to 0.5%. B₂O₃ is believed to be one of the causes of delamination. When the content is high, delamination resistance decreases, and flakes likely to occur. That is, this easily results in a greater amount of SiO₂ extracted in a delamination resistance test in accordance with the method described in NPTL 1 than in the case of conventional borosilicate glass. Incidentally, it is preferable that B₂O₃ is contained as an essential component in view of the meltability and processability. In this case, it is preferable that the content of B₂O₃ is 0.01% or more, particularly 0.05% or more.

Li₂O, Na₂O, and K₂O, which are alkali metal oxides (R₂O), are effective in reducing the viscosity of the glass. However, when the total content of these components is high, the amount of alkali extracted from the glass increases, and also the coefficient of thermal expansion increases, resulting in a decrease in thermal shock resistance. The total content of R₂O is 5 to 20%, preferably 7 to 17%, 10 to 15%, 10 to 14.5%, and still more preferably 10.5 to 14.5%.

Among R₂O, Li₂O is the most effective in reducing the viscosity of the glass, followed by Na₂O, and then K₂O. In addition, when the contents are the same, K₂O results in the greatest amount of alkali extracted from the glass, and Li₂O the smallest. Therefore, in the present invention, it is preferable that the content of R₂O is controlled to be Li₂O ≥ Na₂O ≥ K₂O, particularly Li₂O > Na₂O > K₂O.

In addition, in the present invention, Li₂O is contained as an essential component. The specific content of Li₂O is 0.1 to 12%, preferably 1.5 to 12%, still more preferably 3 to 11.5%, and particularly 4.5 to 11.5%. It is preferable that the content of Na₂O is 0 to 11%, 1 to 10%, 1 to 8% and particularly 1 to 6%, and the content of K₂O is 0 to 5%, 0.1 to 5% and particularly 1 to 5%.

BaO, SrO, CaO, and MgO, which are alkaline earth metal oxides (R'O), are effective in reducing the viscosity of the glass. They also affect the amount of alkali extracted. However, in the case where these components are included in the glass composition, during use as a pharmaceutical container, an extremely small amount of R'O may be extracted from the glass into the liquid medicine, resulting in the precipitation of a carbonate or sulfate thereof. When the medicine is administered to a human body, such a precipitate may cause a thrombus, or the like, and thus is harmful.

Therefore, the total content of R'O is 0 to 10%, preferably 0.1 to 10%, and more preferably 1 to 9%.

Incidentally, whether a carbonate or sulfate of R'O precipitates depends on the solubility of each salt. Specifically, the solubility of MgO is the highest, followed by
5 CaO, SrO, and then BaO. That is, MgO has the lowest likelihood of salt precipitation, and BaO the highest. In addition, when the contents are the same, the amount of alkali extracted from the glass increases in the order of MgO, CaO, SrO, and then BaO. Accordingly, it is preferable that the content of R'O is controlled to be $MgO \geq CaO \geq SrO \geq BaO$, particularly $MgO > CaO > SrO > BaO$.

10 In addition, in the present invention, the glass can contain MgO. Particularly, it is preferable that MgO is contained as an essential component. Specifically, it is preferable that the content of MgO is 0 to 9%, 0.1 to 9%, 0.5 to 8.5%, and particularly 1 to 5%.

It is preferable that the content of CaO is 0 to 4%, 0 to 2%, 0.1 to 2%, and
15 particularly 0.1 to 1%.

It is preferable that the content of SrO is 0 to 4%, particularly 0 to 1%, and, if possible, it is desirable that no SrO is contained. It is preferable that the content of BaO is 0 to 4%, particularly 0 to 1%, and, if possible, it is desirable that no BaO is contained.

ZrO₂ is effective in improving the alkali resistance of the glass. However,
20 when much ZrO₂ is added, this results in an increase in viscosity and causes deterioration in devitrification resistance. Although ZrO₂ is not an essential component in the present invention, when added, it is preferable that the content is 0 to 2%, particularly 0 to 1%.

As a fining agent, one or more of F, Cl, Sb₂O₃, As₂O₃, SnO₂, Na₂SO₄, and the
25 like may also be contained. In this case, the total fining agent content is normally 5% or less, particularly preferably 1% or less, and still more preferably 0.5% or less.

Other components may also be contained in addition to the above components. For example, in order to improve chemical durability, high temperature viscosity, or the like, TiO₂, Fe₂O₃, ZnO, P₂O₅, Cr₂O₃, Sb₂O₃, SO₃, Cl₂, PbO, La₂O₃, WO₃, Nb₂O₃, Y₂O₃,
30 and the like may be added each in an amount up to 3%.

Incidentally, when the glass is to be colored, TiO₂ and Fe₂O₃ may be added to the batch raw material. In this case, the total content of TiO₂ and Fe₂O₃ is normally 10% or less.

In addition, as impurities, components such as H₂, CO₂, CO, H₂O, He, Ne, Ar, N₂, and the like may be contained each in an amount up to 0.1%. Further, it is preferable that the contents of noble metal elements incorporated as impurities, such as Pt, Rh, and Au, are each 500 ppm or less, preferably 300 ppm or less.

5 The glass for pharmaceutical containers of the present invention has a hydrolytic resistance of Class 1 in a test in accordance with the European pharmacopoeia. This means that the amount of alkali extracted as Na₂O in the above test is 62 µg/g or less. In the case where the amount of alkali extracted is more than 62 µg/g, when the glass is processed into an ampoule or vial, and a medicine is packed and
10 stored therein, the alkali extracted from the glass may change the properties of medicine components.

In addition, it is preferable that the glass of the present invention has an alkali resistance of at least Class 2 in a test in accordance with ISO 695. This means that the mass loss per unit area in the above test is 175 mg/dm² or less. The mass loss per unit
15 area is preferably 130 mg/dm² or less, particularly 75 mg/dm² or less. Delamination often occurs when a medicine using a citrate or phosphate buffer, or the like, which shows a strong alkaline behavior even at near neutral pH, is packed/stored in a glass container. Thus, the alkali resistance of a glass can be an index of resistance to delamination. When the mass loss per unit area is more than 175 mg/dm², the
20 possibility of delamination increases.

In addition, it is preferable that the glass of the present invention has a working point of 1260°C or less, 1240°C or less, 1230°C or less, and particularly 1220°C or less. When the working point is high, the processing temperature at which a material glass tube is processed into an ampoule or vial increases, whereby a significantly increased
25 amount of alkali component evaporates from the glass. The evaporated alkali component adheres to the inner surface of the glass container and causes the change of properties of the medicine packed and stored therein. In addition, when the glass contains boron, boron evaporates and condensates, which can be the cause of delamination.

30 Next, a method for producing the glass tube for pharmaceutical containers of the present invention will be described. The following explains an example using the Danner method.

First, glass raw materials are formulated in the above glass composition to produce a glass batch. Subsequently, the glass batch is continuously fed into a melting furnace at 1550 to 1700°C to perform melting and fining. Then, while winding the obtained molten glass around a rotatory refractory, air is blown out from the tip of the refractory, and the glass is drawn from the tip in the form of a tube. The drawn tubular glass is cut into a predetermined length to give a glass tube for pharmaceutical containers. The glass tube thus obtained is used for the production of a vial or ampoule.

Incidentally, the glass tube for pharmaceutical containers of the present invention can be produced not only by the Danner method but also using any of known techniques. For example, the Vello method and a down draw method are also effective as production methods for the glass tube for pharmaceutical containers of the present invention.

Examples

Hereinafter, the present invention will be described based on the examples.

Tables 1 to 4 show the examples of the present invention (Samples No.1 to 34) and Table 5 shows comparative examples (Samples No. 35 to 42).

Table 1

Sample No.	1	2	3	4	5	6	7	8	9	10
Glass Composition [mol%]										
SiO ₂	75.6	69.9	75.1	73.6	72.3	78.9	74.9	74.9	74.9	74.9
Al ₂ O ₃	5.9	11.0	4.8	6.0	6.1	6.0	6.0	6.0	6.0	6.0
B ₂ O ₃										
MgO	4.9	4.5	4.5	4.6	4.6	0.9	4.5	4.5	1.5	1.5
CaO	0.5	0.5	0.5	0.5	0.6	0.1	0.5	0.5	1.5	1.5
SrO									1.0	1.0
BaO									1.0	1.0
Li ₂ O	3.1	6.1	6.1	6.2	6.2	6.1	11.1	4.6	6.1	11.1
Na ₂ O	8.8	5.9	5.9	5.9	6.0	5.9	1.4	4.7	5.9	1.4
K ₂ O	1.0	1.9	1.9	2.0	2.0	1.9	1.4	4.6	1.9	1.4
ZrO ₂			1.0	1.0	2.0					
SnO ₂	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Cl										
ΣR ₂ O	12.9	13.9	13.9	14.1	14.2	13.9	13.9	13.9	13.9	13.9
ΣR'O	5.4	5.1	5.1	5.1	5.2	1.0	5.0	5.0	5.0	5.0
Strain Point Ps (°C)	495	535	478	490	509	465	477	480	464	465
Annealing Point Ta (°C)	543	584	524	536	555	513	521	528	507	507
Softening Point Ts (°C)	799	840	764	777	799	763	780	780	733	725
Working Point 10 ⁴ (°C)	1216	1250	1163	1177	1185	1212	1152	1211	1136	1109
Hydrolytic Resistance [μg/g]		44	62	50	49	34	47	52	59	52
Alkali Resistance [mg/dm ²]	52	72	43	47	32	107	64	82	66	65
Delamination Resistance [μg/cm ²]					1.84					

Table 2

	11	12	13	14	15	16	17	18	19	20
Glass Composition [mol%]										
SiO ₂	74.9	74.9	74.9	74.2	73.6	73.0	71.4	75.0	75.0	73.9
Al ₂ O ₃	6.0	6.0	6.0	5.9	5.9	5.8	5.7	7.0	7.0	6.0
B ₂ O ₃				0.9	1.8	2.6	4.4			
MgO	1.5	1.5	4.5	4.5	4.4	4.4	4.4	2.4	2.4	8.1
CaO	1.5	1.5	0.5	0.5	0.5	0.5	0.5	2.0	2.0	0.9
SrO	1.0	1.0								
BaO	1.0	1.0								
Li ₂ O	8.1	8.1	6.1	6.1	5.9	5.9	5.9	5.0	7.0	4.6
Na ₂ O	1.4	4.4	5.9	5.8	5.8	5.7	5.6	5.0	5.0	4.6
K ₂ O	4.4	1.4	1.9	1.9	1.9	1.9	1.9	3.4	1.4	1.7
ZrO ₂										
SnO ₂	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Cl										
ΣR_2O	13.9	13.9	13.9	13.8	13.6	13.5	13.4	13.4	13.4	10.9
$\Sigma R'O$	5.0	5.0	5.1	5.1	4.9	4.9	4.9	4.4	4.4	9.0
Strain Point Ps (°C)	472	461	472	471	472	472	473	484	478	528
Annealing Point Ta (°C)	516	503	518	514	514	512	511	531	524	575
Softening Point Ts (°C)	743	724	758	745	737	726	710	781	764	825
Working Point 10 ⁴ (°C)	1140	1118	1171	1152	1144	1130	1116	1207	1191	1234
Hydrolytic Resistance [μg/g]	58	54	49	49	48	44	40			
Alkali Resistance [mg/dm ²]	71	62	64	66	68	72	73	64	60	
Delamination Resistance [μg/cm ²]		2.15	1.82	2.07	2.38	2.41	2.89			

Table 3

	21	22	23	24	25	26	27	28	29	30
Glass Composition [mol%]										
SiO ₂	70.9	76.0	74.4	71.4	77.5	77.5	77.5	77.5	77.5	77.5
Al ₂ O ₃	6.0	5.9	6.0	9.0	6.0	6.0	6.0	6.0	6.0	6.0
B ₂ O ₃										
MgO	8.1	4.9	4.5	4.5	1.5	1.5	2.5	2.5	2.5	3.5
CaO	0.9	0.6	0.5	0.5	0.3	0.3	0.3	0.3	0.3	0.3
SrO										
BaO										
Li ₂ O	6.1	1.9	6.1	6.1	6.0	7.5	5.5	6.5	7.5	6.5
Na ₂ O	5.9	10.1	5.9	5.9	5.5	4.0	5.0	4.0	3.0	3.0
K ₂ O	1.9	0.4	1.9	1.9	2.5	2.5	2.5	2.5	2.5	2.5
ZrO ₂			0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
SnO ₂	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
Cl										
ΣR ₂ O	13.9	12.4	13.9	13.9	14.0	14.0	13.0	13.0	13.0	12.0
ΣR'O	9.0	5.5	5.0	5.0	1.8	1.8	2.8	2.8	2.8	3.8
Strain Point	486	516	480	517	473	474			495	
Ps (°C)										
Annealing Point	529	566	527	565	520	521			544	
Ta (°C)										
Softening Point	752	827	770	815	773	770			804	
Ts (°C)										
Working Point	1137	1253	1182	1225	1207	1198	1247	1230	1226	1257
10 ⁴ (°C)										
Hydrolytic Resistance	62		46	39	46	44			41	
[μg/g]										
Alkali Resistance	81		51	52	56	57	55	57	51	57
[mg/dm ²]										
Delamination Resistance			2.24	2.04	1.56	1.55			1.56	
[μg/cm ²]										

Table 4

	31	32	33	34
Glass Composition [mol%]				
SiO ₂	77.0	74.0	74.3	77.0
Al ₂ O ₃	6.0	6.0	6.0	6.0
B ₂ O ₃		0.4	0.1	
MgO	3.5	4.5	4.5	3.5
CaO	0.3	0.5	0.5	0.3
SrO				
BaO				
Li ₂ O	7.0	6.1	6.1	6.0
Na ₂ O	3.0	5.9	5.9	4.0
K ₂ O	2.5	1.9	1.9	2.5
ZrO ₂	0.5	0.5	0.5	0.5
SnO ₂	0.2	0.2	0.2	0.2
Cl				
ΣR ₂ O	12.5	13.9	13.9	12.5
ΣR'O	3.8	5.0	5.0	3.8
Strain Point Ps (°C)	486	478	481	
Annealing Point Ta (°C)	534	523	527	
Softening Point Ts (°C)	794	761	769	
Working Point 10 ⁴ (°C)	1240	1171	1179	1241
Hydrolytic Resistance [μg/g]	41		53	
Alkali Resistance [mg/dm ²]	52	55	54	50
Delamination Resistance [μg/cm ²]	1.47	1.84		

Table 5

	35	36	37	38	39	40	41	42
Glass Composition [mol%]								
SiO ₂	76.3	76.3	77.9	74.9	74.9	74.9	68.2	64.7
Al ₂ O ₃	4.5	6.0	6.1	6.0	6.0	6.0	5.4	5.2
B ₂ O ₃	10.0						8.8	13.3
MgO		5.0	5.1	4.5	0.5	0.5	4.1	4.0
CaO	1.0	0.6	0.6	0.5	0.5	0.5	0.5	0.4
SrO					4.0			
BaO	0.5					4.0		
Li ₂ O				1.4	6.1	6.1	5.6	5.4
Na ₂ O	6.0	11.8	6.1	1.4	5.9	5.9	5.4	5.1
K ₂ O	1.5	0.1	4.0	11.1	1.9	1.9	1.8	1.7
ZrO ₂								
SnO ₂		0.2	0.2	0.2	0.2	0.2	0.2	0.2
Cl	0.2							
ΣR_2O	7.5	11.9	10.1	13.9	13.9	13.9	12.7	12.2
$\Sigma R'O$	1.5	5.5	5.6	5.0	5.0	5.0	4.7	4.4
Strain Point	525	562	606	540	466	455	478	479
Ps (°C)								
Annealing Point	570	615	667	596	508	497	513	512
Ta (°C)								
Softening Point	785	876	967	879	724	709	689	675
Ts (°C)								
Working Point	1170	1297	1404	1313	1115	1093	1032	1014
10 ⁴ (°C)								
Hydrolytic Resistance	17	58	40	96	74	88	41	50
[$\mu\text{g/g}$]								
Alkali Resistance	130	70	74	100	76	80	94	
[mg/dm^2]								
Delamination Resistance	2.73	1.98					3.05	6.16
[$\mu\text{g/cm}^2$]								

The samples were prepared as follows.

First, a 500 g batch was formulated in the composition shown in the table and melted using a platinum crucible at 1650°C for 3.5 hours. Incidentally, stirring was performed twice during the melting process in order to reduce bubbles in the sample.

5 After melting, an ingot was produced, processed into a shape required for measurement, and subjected to various kinds of evaluation. The results are shown in the tables.

As is clear from the tables, with respect to Samples No.1 to 34, which are examples of the present invention, the working point was 1257°C or less, the amount of alkali extracted in a hydrolytic resistance test was 62 µg/g or less, and the amount of
10 alkali extracted in an alkali resistance test was 107 mg/dm² or less. In addition, the amount of SiO₂ extracted in a delamination resistance test was 2.89 µg/cm² or less.

For the measurement of strain point Ps, the temperature at which the viscosity of the glass was 10^{14.5} dPa·s was determined by Fiber Elongation method in accordance with ASTM C336.

15 For the measurement of annealing point Ta, the temperature at which the viscosity of the glass was 10^{13.0} dPa·s was determined by Fiber Elongation method in accordance with ASTM C336.

For the measurement of softening point Ts, the temperature at which the viscosity of the glass was 10^{7.6} dPa·s was determined by Fiber Elongation method in
20 accordance with ASTM C338.

For the measurement of working point, the temperature at which the viscosity of the glass was 10^{4.0} dPa·s was determined by a platinum ball pulling up method.

The hydrolytic resistance test was performed in accordance with the European pharmacopoeia. The detailed test procedure is as follows. A glass sample was ground
25 in an alumina mortar and classified into 300 to 425 µm through a sieve. The obtained powder was washed with distilled water and ethanol and dried in an oven at 140°C. 10 g of the dried powder sample was placed in a quartz flask, further 50 mL of distilled water was added, and the flask was capped. The quartz flask containing the sample was placed in an autoclave and treated. The treatment conditions were as follows: the
30 temperature was raised from 100°C to 121°C at 1°C/min, then maintained at 121°C for 30 minutes, and lowered to 100°C at 0.5°C/min. The solution in the quartz flask was transferred to another beaker. Further, the inside of the quartz flask was washed three times with 15 mL of distilled water, and the washing water was also added to the

beaker. A methyl red indicator was added to the beaker, followed by titration with a 0.02 mol/L hydrochloric acid solution. With 1 mL of the 0.02 mol/L hydrochloric acid solution equivalent to 620 μg of Na_2O , the amount of alkali extracted was calculated.

The alkali resistance test was performed in accordance with ISO 695. The detailed test procedure is as follows. A 15 cm^2 glass sample piece with an entirely mirror finished surface was prepared. First, as a pretreatment, the sample was immersed in a solution containing fluoric acid (40 wt%) and hydrochloric acid (2 mol/L) mixed in a volume ratio of 1:9, followed by stirring for 10 minutes with a magnetic stirrer. The sample was then taken out, ultrasonically cleaned for 2 minutes with ultrapure water three times, and then ultrasonically cleaned for 1 minute with ethanol twice. Subsequently, the sample was dried in an oven at 110°C for 1 hour and allowed to cool for 30 minutes in a desiccator. The mass of sample m1 was measured to an accuracy of ± 0.1 mg and recorded. A 800 mL solution containing an aqueous sodium hydroxide solution (1 mol/L) and an aqueous sodium carbonate solution (0.5 mol/L) mixed in a volume ratio of 1:1 was placed in a stainless steel container and heated to boiling using a mantle heater. After boiling, the sample suspended on a platinum wire was placed therein and maintained boiling for 3 hours. The sample was taken out, ultrasonically cleaned for 2 minutes with ultrapure water three times, and then ultrasonically cleaned for 1 minute with ethanol twice. Subsequently, the sample was dried in an oven at 110°C for 1 hour and allowed to cool for 30 minutes in a desiccator. The mass of sample m2 was measured to an accuracy of ± 0.1 mg and recorded. From the masses of sample before and after placed in the boiling alkaline solution, m1 and m2 (mg), and the total surface area of sample A (cm^2), the mass loss per unit area was calculated by the following equation as a measurement value of the alkali resistance test.

$$(\text{Mass loss per unit area}) = 100 \times (m1 - m2)/A$$

The delamination resistance test was performed in accordance with the method described in NPTL 1. However, because there are differences in the sample from, or the like, the method described in NPTL 1 was used with some modifications. The detailed procedure is as follows. A glass piece with an entirely mirror finished surface having a surface area of about 13 cm^2 was prepared and, in order to replicate thermal processing for the production of a container, heated for 20 seconds at the softening point of each sample. Subsequently, a Teflon (registered trademark) container was filled with a 0.9% aqueous NaCl solution adjusted to pH 8.0 with an aqueous Na_2HPO_4 solution. The

sample was immersed therein, and the container was capped. The Teflon container containing the sample was placed in an autoclave and treated. The treatment conditions were as follows: the temperature was raised from 100°C to 121°C at 1°C/min, maintained at 121°C for 1 hour, and lowered to 100°C at 0.5°C/min. Using ICP-OES (Inductively Coupled Plasma Optical Emission Spectrometry), the amount of SiO₂ that had been extracted into the solution through the treatment was determined as the amount of extractable relative to the surface area of the sample (μg/cm²). The amount of SiO₂ extracted is used as an index of delamination resistance. The smaller the amount of SiO₂ extracted is, the higher delamination resistance such a glass is considered to have.

While the present invention has been described in detail and with reference to specific embodiments thereof, it will be apparent to one skill in the art that various changes and modifications can be made therein without departing from the spirit and scope thereof. All references cited herein are incorporated in their entirety. This application is based on Japanese patent application No. 2013-119894 filed on June 6, 2013, the entire contents of which are incorporated hereinto by reference.

CLAIMS

1. A glass for pharmaceutical containers comprising, in mol% on an oxide basis, 69 to 81% of SiO₂, 4 to 12% of Al₂O₃, 0 to 5% of B₂O₃, 5 to 20% of Li₂O + Na₂O +
5 K₂O, 0.1 to 12% of Li₂O, and 0 to 10% of MgO + CaO + SrO + BaO.
2. The glass for pharmaceutical containers according to claim 1, comprising, in mol% on an oxide basis, 0 to 4% of B₂O₃.
- 10 3. The glass for pharmaceutical containers according to claim 1 or 2, comprising, in mol% on an oxide basis, 0 to 11% of Na₂O and 0 to 5% of K₂O.
4. The glass for pharmaceutical containers according to any one of claims 1 to 3, comprising, in mol% on an oxide basis, 0 to 9% of MgO, 0 to 4% of CaO, 0 to 4% of
15 SrO, and 0 to 4% of BaO.
5. The glass for pharmaceutical containers according to any one of claims 1 to 4, further comprising 0 to 2 mol% of ZrO₂.
- 20 6. The glass for pharmaceutical containers according to any one of claims 1 to 5, having a hydrolytic resistance of Class 1 in a test in accordance with the European pharmacopoeia.
7. The glass for pharmaceutical containers according to any one of claims 1 to 6,
25 having an alkali resistance of at least Class 2 in a test in accordance with ISO 695.
8. The glass for pharmaceutical containers according to any one of claims 1 to 7, having a working point of 1260°C or less.
- 30 9. A glass for pharmaceutical containers comprising, in mol% on an oxide basis, 69 to 81% of SiO₂, 4 to 12% of Al₂O₃, 0 to 5% of B₂O₃, 5 to 20% of Li₂O + Na₂O + K₂O, 0.1 to 12% of Li₂O, 0 to 11% of Na₂O, 0 to 5% of K₂O, and 0 to 10% of MgO + CaO + SrO + BaO, wherein the Li₂O content is higher than the K₂O content.

10. A glass tube for pharmaceutical containers, made of the glass for pharmaceutical containers of any one of claims 1 to 9.

INTERNATIONAL SEARCH REPORT

International application No
PCT/JP2014/065394

A. CLASSIFICATION OF SUBJECT MATTER
 INV. C03C4/20 A61J1/06 C03C3/087 C03C3/091 C03C3/093
 ADD.
 According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
 Minimum documentation searched (classification system followed by classification symbols)
 C03C A61J
 Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

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

C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2013/101853 A1 (DRAKE MELINDA ANN [US] ET AL) 25 April 2013 (2013-04-25) the whole document especially examples DD and EE in table 6 -----	1-10
X	US 2012/183812 A1 (KAJITA HIROSHI [JP]) 19 July 2012 (2012-07-19) abstract examples 43-55 -----	1-10
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Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance	"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"E" earlier application or patent but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"O" document referring to an oral disclosure, use, exhibition or other means	"&" document member of the same patent family
"P" document published prior to the international filing date but later than the priority date claimed	

Date of the actual completion of the international search 28 August 2014	Date of mailing of the international search report 04/09/2014
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Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Heer, Stephan
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INTERNATIONAL SEARCH REPORT

International application No
PCT/JP2014/065394

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2013/101596 A1 (DEMARTINO STEVEN EDWARD [US] ET AL) 25 April 2013 (2013-04-25) the whole document	1-10
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Information on patent family members

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