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Review Article

A REVIEW ON GLASS: PACKING COMPONENT

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ABSTRACT

Pharmaceutical packaging material plays a vital role in the stability of the pharmaceutical dosage form. Packaging should be such that it should maintain the integrity of the dosage form, should be inert in nature, should not be fragile, should have good mechanical strength. The glass is most widely used packaging material. The selection of packaging material is very important parameter during the study of stability testing of the dosage form. Present review has been extensively reviewed about glass as packing components which play the role in many aspects of life one particularly important area is pharmaceutical.

KEYWORDS: Packaging material, Pharmaceutical dosage form, glass, packaging, product etc

INTRODUCTION

It is inorganic product; non-crystalline, amorphous solid of fusion which has been cooled at rigid condition without crystallization. Glass will transmit, reflect and refract light. These qualities can be making enhanced by cutting and polishing to make optical lenses, prisms. Glass play the role in many aspects of life one particularly important area is pharmaceutical.

Advantages:

- Glass is physiochemical inert, hard but brittle, Non-crystalline, Non-corrosive.
- Glass does not conduct electricity or heat.
- Glass is visible and transparent to light.
- Glass is not permeable to gas and liquid (fluid).
- It is versatile, attractive and can be reused and it is hygienic and suitable for sterilization also it is used for primary sterilization.
- Glass is softened by heat and easily remoulded into another shape. It can be moulded into many sizes, shapes and colours of containers.

Disadvantages:

- It is fragile, heavy. Hence, it is difficult in transport.
- It is harder to dispose and expensive in nature.

General Chemical Composition

Glass starts his life from sand, which is in its pure form called "Quartz". It is principally composed of fused silica, silicon dioxide and alkaline earth metals in the form of oxides (Ca, Na, and K etc.). The most common cations found in the pharmaceutical glassware's are silicon, aluminium, boron, sodium, potassium, calcium, magnesium, zinc, barium. The only anion of consequence is O_2.Many useful properties of glass are affected by the kind of elements it contains. The principle ingredient of glass is silica. It is derived from sand, flint or quartz which can be melted at very high temperature -1723° C.It is mixture of silicon and oxygen surrounded by four oxygen atom and forming tetrahydron.Overall glass chemical structure having perfect symmetry in a crystal form. Glass is amorphous structure which changes from his crystalline form to the amorphous form.

Table: 1 Composition of various types of Glass

Sr.No	Glass Type	SiO_2	Na_2O	K_2O	CaO	MgO	B_2O_3	Al_2O_3	PbO	Material or Product
1	Soda silicate (Water glass)	(Composition varies widely with SiO_2: Na_2O ratios from 1.6 to 3.7)								Detergent and cardboard adhesive
2	Soda lime silicate	72.1 72.1 63.7	21.1 14.0 20.6	- - 0.5	2.8 9.9 9.1	2.0 3.2 5.2	- - -	2.0 0.3 1.0	- - -	Light bulb Windows Egyptian glass
3	Borosilicate	81.0	4.5	-	-	-	12.5	2.0	-	Laboratory glass
4	Aluminium silicate	54.5 59.0 65.8	- 11.0 3.8	- 0.5 -	17.5 16.0 10.4	4.5 5.5 -	10.0 3.5 -	14.0 4.5 6.6	- - -	Fiber glass Glass fiber insulation Tableware
5	Lead silicate	56.0 3 5	2.6 - -	13.6 -	- - -	- - -	- 11 10	- 11 3	29 75 82	Radiation shielding windows
6	High silica	96.9 99.9	- -	- -	- -	- -	2.9 -	0.4 -	- -	Fused quartz or fused silica

There are some ingredients which are added to the glass to give certain physical property.

1) Lead: Due to addition of lead in to glass results to softness of the glass.
2) Alumina: Due to addition of alumina increases hardness and durability.

3) Boron: Addition of 6% boron to the borosilicate glass reduces leaching of sodium which is loosely combined with silicon.

Effect of alkali and acid attack on the glass:

1) Alkaline attack: If an alkaline attack on the glass then it slowly destroys the silica network then releases other glass components called etching.
2) Acid attack: If acid attacks on the glass hydrogen ions exchange for alkali or other positively charged mobile ions.

Types of Glass

There are mainly following two types of glass as per USP.

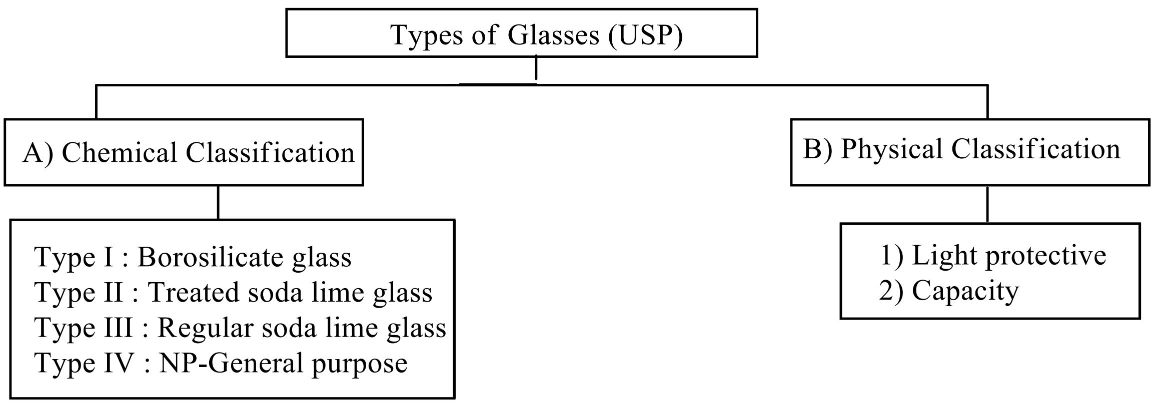


Fig.: Types of Glasses

A) Chemical Classification

1) Type I : Borosilicate glass

This type of glass is highly resistant glass and more chemically inert than soda-lime glass. It has superior resistance to alkaline product. This type of glass is used for strong alkalis as well as all types of solvents. The addition of 6% boron in this type of glass leads to reduce the leaching action.

It is used for buffered and non-buffered solution and also it is only glass used for alkaline products. This type of glass is also used when high thermal shock is required.

2) Type II : Treated soda lime glass

These types of containers are made up of commercial soda lime that has been de-alkalized or treated to surface alkali.

The de-alkalizing process is known as “Sulfur treatment” which prevents “Weathering or Blooming”.

When glassware of these types are stored for several months especially in a damp atmosphere or with extreme temperature variations which leads to the wetting of the glass surface due to condensed moisture (Condensation) results in salts being dissolved out of the glass. This is called “Weathering or Blooming”. It gives appearance of fine crystals on the glass.

Exposure of this glass surface to the atmosphere containing water vapour and acidic gases particularly SO_2 at an elevated temperature this results in reaction between gases and some of the surface alkali. The alkali removed from the surface as a sulphate bloom. Sulfur treatment neutralizes the alkaline oxides on the surface rendering the glass more chemically resistant.

This type of glass used for Buffered solution up to pH of 7, large volume parenteral,irrigating solutions and also for blood components.

3) Type III : Soda-lime glass

These containers are untreated and made up of commercial soda-lime glass. This type of glass having least uses like this containers used in oleagenous products, powder solutions, non-aqueous parenteral products.

4) Type IV : Non-Parenteral glass

This type of glass is also called general glass. These type of containers made up of soda lime which are supplied for non-parenteral products like for oral and topical use.

B) Physical Classification

1) Colored glass

The amber coloration results from the addition of *iron oxide* to the glass.

For decorative purposes, special colors such as blue, emerald green and red may be obtained from the glass manufacturer.

Colored glasses are effective in protecting the content from the effect of sunlight by screening them.

Types of Glass Container

1) Bottles
2) Containers for solid preparation
3) Containers for tablet and capsules
4) Ear and nasal dropper bottles
5) Jars
6) Glass vials
7) Glass ampoules

Types of glass on the basis of manufacturing process

There are following types of glasses on the basis of manufacturing process.

1) Molded glass
2) Tubular glass

Molded glass	**Tubular glass**
1. It is hot formed by injecting a 'gob' of molten glass into a mould, this gob is the preformed then blown out with compressed air to fill the mould when cooled the mould is opened and the vial or bottle is removed.	1. Long sections of glass called tube or cane. Machinery used to cut this cane into shorter lengths and then manipulates glass into vials or glass dropper pipettes.

	
2.Heavier and more durable	2.Lighter to store
3. Available in both clear & amber neutral Type II glass.	3. Available in both clear & amber neutral Type I glass.
4. High tolerance to thermal shocks & low extractable.	4. High tolerance to thermal shocks & low extractable.
5. It is economical for producing large size container	5. It is economical for producing small size container
6. It is economical for production of large quantities of same shape	6. It is economical for production of small lots of containers
7.Less flexibility for changes	7. High flexibility for changes
8. Changes are expensive and need long time	8. Changes are cheap and need short time
9. It is thick and not having consistent uniformity	9. It is having uniform body diameter and wall thickness
10.Possible problems for lyophilization	10. No problems for lyophilized products
11. Problems with particulate examination	11.Problem free particulate examination
12.Strenous optical control due to low degree of clarity	12. User friendly optical control due to high degree of clarity and transparency
13. It is inconsistent in productivity	13. It is consistent in productivity
14. Low yield at consumers end	14. High yield at consumers end

Manufacturing of glass:

1) Blowing:

It uses compressed air to form the molten glass in the cavity of metal mould. Most commercial bottles and jars or produced on automatic equipment by this method.

Fig.1: Blowing

2) Drawing:

Molten glass is pulled through the dies or rollers that shape the soft glass, tubes and sheets.

Fig 2.: Drawing

3) Pressing:

Mechanical force is used to press the molten glass against the side of mold.

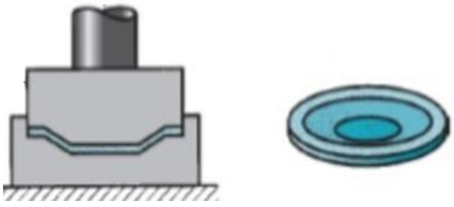


Fig.3: Pressing

4) Casting:

This uses gravity or centrifugal force to cause molten glass to form the cavity of the mold.

Fig 4.: Casting

Sterilization methods for glass:

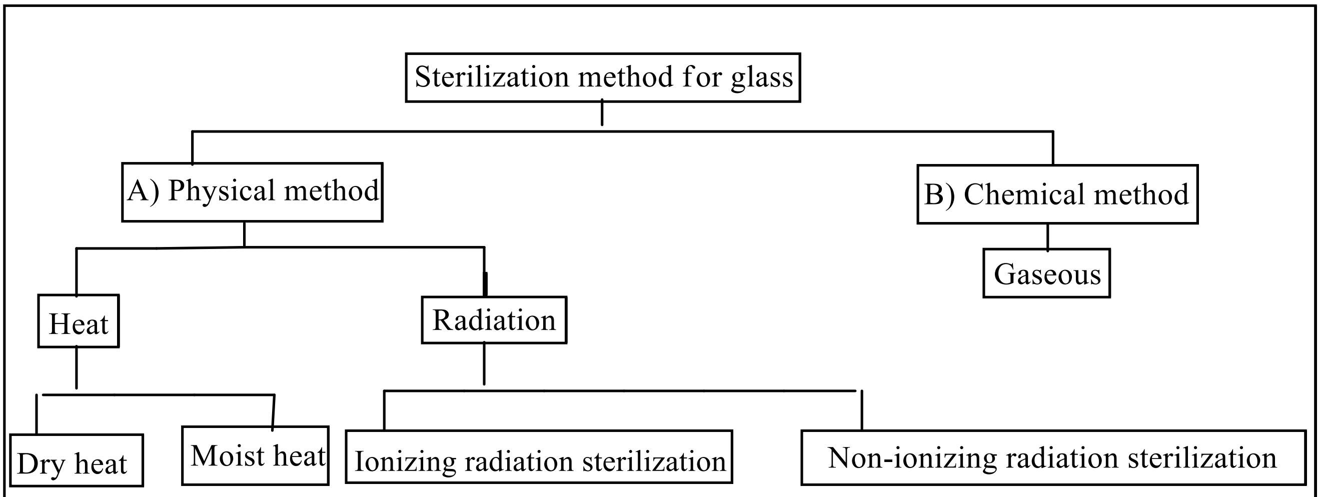
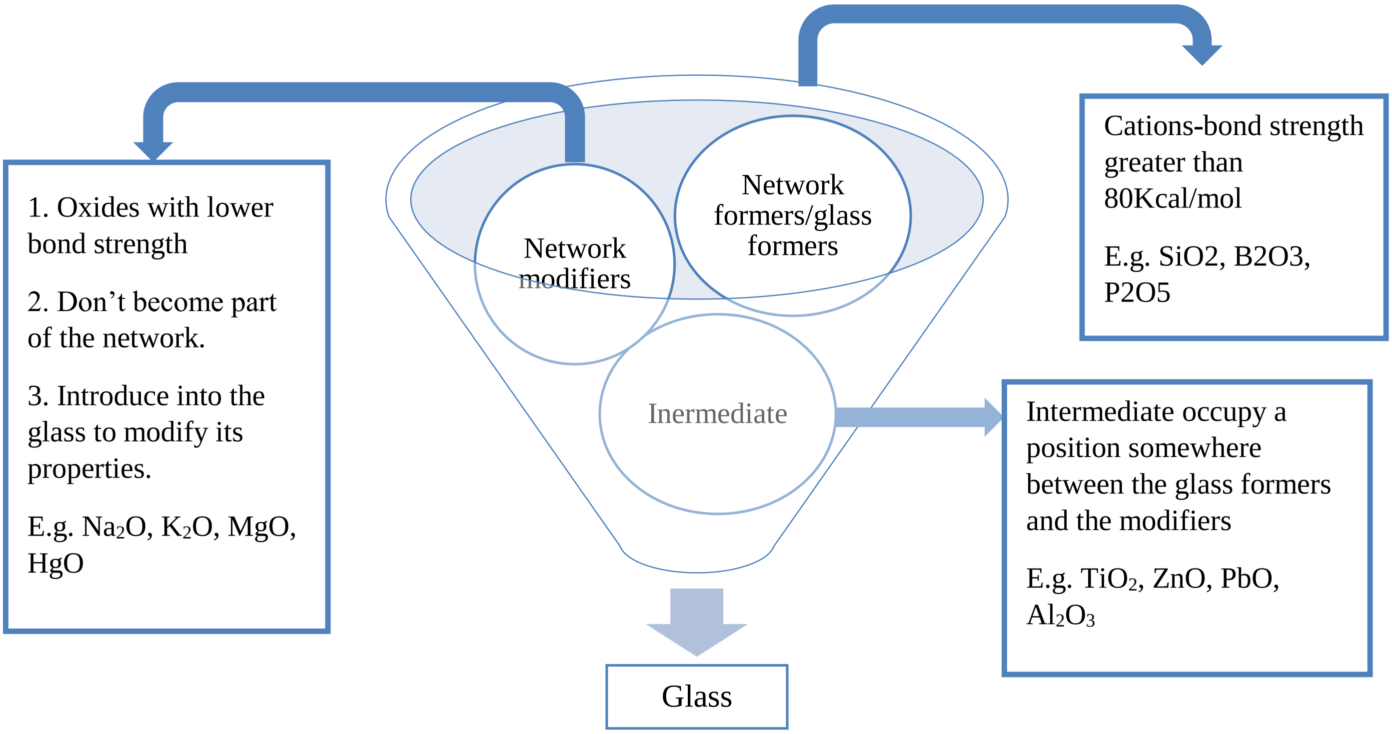


Fig.:

Glass chemistry:



The basic network building block for silicate glasses is a tetrahedral form of silica, (SiO4).

Ideally, each silicon atom has shared bonds with four oxygen atoms and each oxygen atom has shared bonds with two silicon atoms.

This configuration leads to a cross-linked, 3-D network of shared covalent bonds.

The spatial interaction of these bonds causes viscosity to increase rapidly with decreasing temperature and inhibits the molecular reordering needed for the material to make the transition from a randomly ordered structure of the liquid state to the regular, long-range order of a crystalline solid. As a result, the network cools to rigidity in the glassy state. When processed under the appropriate conditions silica will crystallize as quartz.

Hydrolysis of Glass Surface:

$$\boldsymbol{R - O - R_1 + H_2O \rightarrow R - OH + H - O - R_1}$$

Where, R and R_1 are cations that may or may not be linked to the glass network.

- Break one or more oxygen bonds such that component species become solvated and released into solution or the bonding scheme is altered in glass.
- While the strain energy of a bond in a glass will affect some reactions, it can be assumed that the strain is removed as neighboring bonds are broken.
- **Alkali Release-** The reaction to release alkali metal ions from a non-bridging oxygen can be written as

$$\equiv \boldsymbol{SiO - M + H_2O \rightarrow \equiv SiOH + M^+ + OH^-}$$

Where,

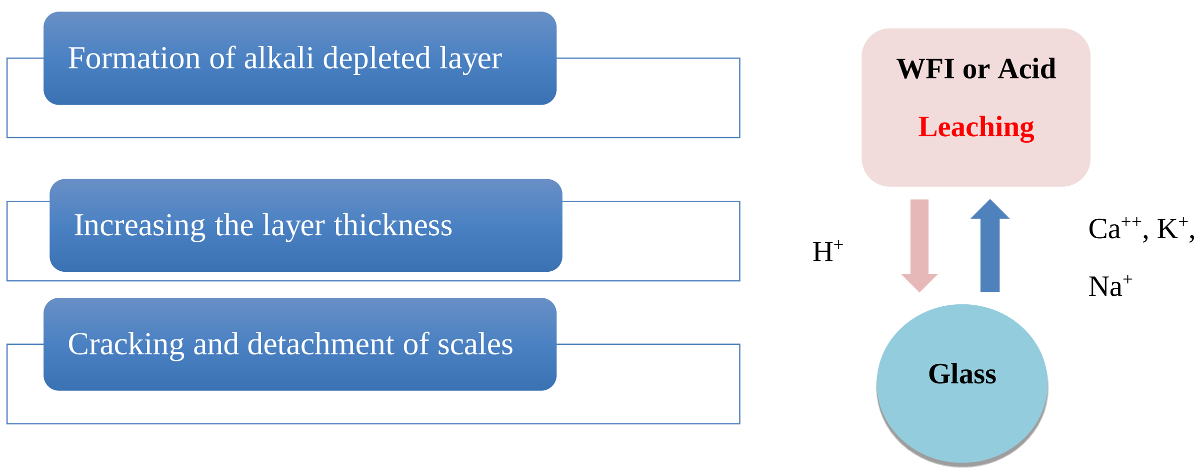
SiOH represents a silanol group andM+ is an alkali metal ion.

- Hydrolysis reaction is the replacement of an alkali atom in the glass by a proton from solution.
- Alkali release is often written as an ion exchange, since the reaction can also be written as,

$$\equiv \boldsymbol{SiO - M + H^+ \rightarrow \equiv SiO - H + M^+}$$
$$\equiv \boldsymbol{SiO - M + H_3O^+ \rightarrow \equiv SiO - H + M^+ + H_2O}$$

Mechanism of Interaction of Glass with Product

A. Ion exchange



Ion exchange is the interaction between glass surfaces with glass content which will prone to glass delamination.

B. Attack on glass by reactive groups

Alkaline hydroxyl group is present in the product which may attack to the glass surface and breaks Si-O bonds. It is also depends on various factors like pH, ingredient of product. E.g., Chelating agents pull various metal ions out of the surface.

C. Additional mechanisms

1) Glass delamination

It is defined as degradation of glass surface. The surface of glass vial will produces glass flakes.

Glass delamination occurs when top layer of glass surface flakes off, due to breakdown of the glass surface.

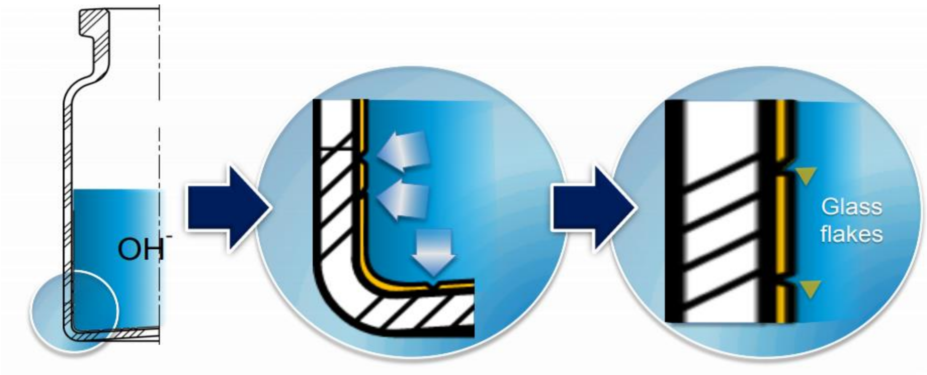


Fig. 5. Schematic representation of glass flakes

There are following two main mechanisms which may cause for the glass delamination.

A) During manufacturing vials are fused at neck or base

B) Chemical reaction of glass with vial content

The oxide which leaches out from the glass surface which creates a less resistant layer. Formation of flakes, which slough off into solution.If any manufacturing defects is observed then it can also be the catalyst for glass delamination.

Factors contributing to glass delamination

External factors

- Time exposed to the solution
- Temperature fluctuaions- Autoclaving/Sterilizaton
- Fluctuations over time/sorage conditions
- Chemistry of solution
- pH
- Ionic strength

Nature of vials

- Process of vial manufacturing (Annealing condition, Adjustment of burners)
- Chemistry of glass/Composition of glass
- Surface treatments- Sulfur treatment, Siliconization, coaing

Factors related to drug product which influence the inner durability of glass

Drug product

- Nature of drug substance
- Additives like Acetate, Citrate, Phosphate buffers
- Sodium salts of organic acids e.g., Gluconate,Malate,Succinate,Tartrate
- High ionic strength e.g., > 0.1M of alkaline salts
- Complexing agents e.g., EDTA
- High pH content e.g., > 8.0
- Shelf life

Analytical methods for screening studies

Sr.No.	Parameter	Test	Analytical methods
1)	Glass surface	Degree of surface pitting	DIC microscopy
		Chemical composition as a function of depth	SIMS (Secondary ion mass spectroscopy)
2)	Extracted elements in solution	SiO_2 Concentration	Conductivity/ pH meter
		SiO_2/B_2O_3 or Si/Al ratio	IC-MS or ICP-OES
		Individual and total extractable	
3)		Particle number and size	Particle size analyser

	Visible and sub visible glass particle	Particle morphology and compound	SEM- EDX

2) Metal ions interaction

A) Aluminium

B) Barium

C) Iron

D) Silicates

Various metal oxides are added in glass during manufacturing process to impact physical and chemical properties. The metal ions listed above like Aluminium, Barium etc. have tendancy to leach out and attack the product.

3) Interaction with buffers

4) Adsorption of drug(s) or formulation components on glass surfaces

Quality control tests for Glasses

1) Chemical Resistant of Glass Containers:

A) Powdered glass test:

It is done to estimate the amount of alkali leached from the powdered glass which usually happens at elevated temperatures.

If glass is powdered → Leaching of alkali increases

It has two following steps:

Step 1: Preparation glass specimen

↓

Container rinsed with H_2O

↓

Dry and grind in mortar to fine powder

↓

Pass through sieve no. 20 and 50

Step 2: Washing he specimen

↓

Take 10 gm of this specimen in 250 mL conical flask

↓

Wash with 30 mL acetone

↓

Repeat the washing, decant acetone and dry which is to be use within 48 hrs

Procedure:

10gm of sample + 50ml of highly purified H_2O in 250ml flask

↓

Place in an autoclave at 121◦C ± 2◦C for 30 minute

↓

Cool it under running water. Decant the solution into another flask

↓

Wash again with 15ml of high purity water and again decant

↓

Titrate immediately with 0.02N H_2SO_4 acid using methyl red as an indicator and record the volume.

B) Water attack test:

This is only for treated soda lime glass containers under the controlled humidity conditions which neutralize the surface alkali and glass will become chemically more resistant.

Principle:involved is whether the alkali leached or not from the surface of the container.

Procedure:

3container filled 90% overflow capacity high purity water

↓

Autoclaving at 121° C for 30 min

↓

100 mL of combined extract titrate with 0.02N H_2SO_4 acidusing methyl red as an indicator

2) Hydrolytic resistance of glass containers:

Rinse each container at least 3 times with CO_2free water and fill with the same to their filling volume

↓

Heat to 100° C for 10 min in autoclave. Rise he temperature from 100ºC to 121º C over 20min.

↓

Maintain the temp at 121ºC to 122ºC for 60min.Lower the temp from 121ºC to 100°C over 40min venting to prevent vacuum

↓

Remove the container from autoclave, cool and combine the liquids being examined. Titrate with 0.01M HCl using methyl red as an indicator. Perform blank with water and the difference between the titration represents the volume of HCl consumed by the test solution.

Nominal capacity of container (ml)	Number of containers to be used	Volume of test solution to be used for titration (ml)
5 or less	At least 10	50.0
6 to 30	At least 5	50.0
More than 30	At least 3	100.0

Type of Glass	**General description of glass**	**Type of test**	**Limit size, mL**	**Limits (mL of 0.02 N acid)**
I	Highly resistant borosilicate glass	Powdered glass	All	1.0
II	Treated soda- lime glass	Water attack	100 or over less 100	0.7 0.2
III	Soda- lime glass	Powdered glass	All	8.5
IV	General purpose soda-lime glass	Powdered glass	All	15

3) Arsenic test:

This test is for glass containers intended for aqueous parenteral.

Wash the inner and outer surface of container with fresh distilled water for 5min.

↓

Prep test as described in the test for hydrolytic resistance for an adequate no.of samples to produce 50ml.Pipette out 10ml solution from combined contents of all ampoules to the flask

↓

Add 10 mL of HNO3 to dryness on the water bath, dry the residue in an oven at 130° C for 30 min cool and add 10 mL hydrogen molybdate reagent

↓

Swirl to dissolve and heat under water bath and reflux for 25min. Cool to room temp and determine the absorbance at 840nm.Do the blank with 10ml hydrogen molybdate

- The absorbance of the test solution should not exceed the absorbance obtained by repeating the determination using 0.1ml of arsenic standard solution (10ppm) in place of test solution.

4) Thermal shock test:

Place the samples in upright position in a tray. Immerse the tray into a hot water for a given time and transfers to cold water bath, temp of both are closely controlled. Examine cracks or breaks before and after the test. The amount of thermal shock a bottle can withstand depends on its size, design and glass distribution. Small bottles withstand a temp differential of 60 to 80ºC and 1 pint bottle 30 to 40ºC.Atypical test uses 45C temp difference between hot and cold water.

5) Internal bursting pressure test:

The most common instrument used is *American glass research increment pressure tester* .The test bottle is filled with water and placed inside the test chamber. A scaling head is applied and the internal pressure automatically raised by a series of increments each of which is held for a set of time. The bottle can be checked to a preselected pressure level and the test continues until the container finally bursts.

6) Leakage test:

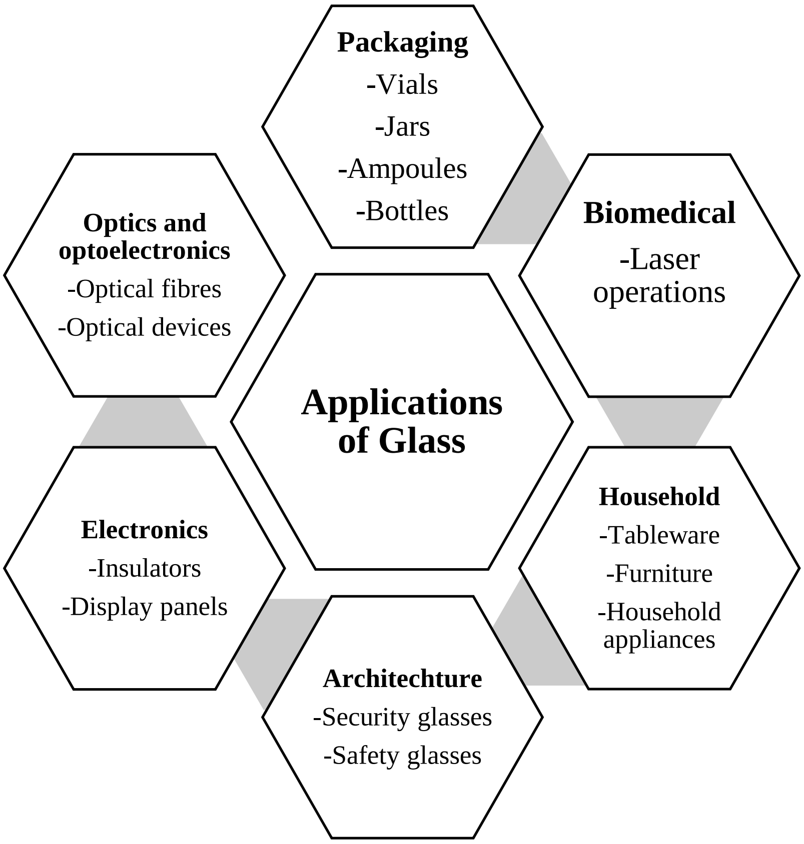
Drug filled container is placed in a container filled with coloured solution (due to the addition of dye)which is at high pressure compared to the pressure inside the glass container so that the coloured solution enters the container if any cracks or any breakage is present.

Pharmacopoeial status of quality test for glass container

Container Type	**General description**	**EP test**	**USP test current**	**USP test proposed**
Type I	Borosillicate glass	Glass grain	Powdered glass (Surface glass)	Glass grains
		Surface glass	Water attack at 121° C (Surface glass)	Surface glass

		Surface etching	-	Surface etching
Type II	Treated soda-lime	Glass grains	Water attack at 121◦C (Surface glass)	Glass grains
		Surface glass	-	Surface glass
		Surface etching	-	Surface etching
Type III	Soda-lime glass	Glass grains	-	-
		Surface glass	-	-

Other applications



Abbreviations: DIC-Differential interference contrast, SIMS-Secondary ion mass spectroscopy, SEM-EDX- Secondary electron microscopy energy disperse X-ray spectroscopy ,ICP-OES- Inductively coupled plasma-optical emission spectrometry, IC-MS- Inductively coupled plasma mass spectroscopy

CONFLICT OF INTEREST:

The authors declare that there is no conflict of interest in publication of this paper.

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