A Comprehensive Review on Selection and Evaluation of Containers for Parenterals

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Abstract

A container is a vessel that mostly stores pharmaceutical medications for Parenteral storage containers come in a variety of shapes and are constructed from a variety of materials. To protect the medicinal components, the containers must have the ideal characteristics. Nowadays, both glass and plastic containers are used for storage; however, the choice for a certain drug relies on a number of circumstances. Numerous assessment procedures must be followed and pass quality control inspection after manufacturing.

Keywords : *Glass, plastic, closures, drug, system, parenter*

Introduction

Drugs as parenteral bypass the enteral barrier by being injected directly into tissue fluids or blood. The most popular parenteral techniques are intramuscular (i.m.), intravenous (i.v.), subcutaneous (s.c.), and intradermal (i.d.). These parenteral drugs need to bedrug-container interactions. A container is a piece of equipment that keeps the drug and could come in contact with it.

Properties of a container:

1.Any container for a parenteral product must maintain the product's integrity as a sterile, pyrogen-free, high purity preparation until the product is used.

2. It needs to be robust enough to withstand processing and shipping and allow the contents to be removed.

3. Dangerous light radiation should be prevented from reaching the content.

4. It must be transparent and colorless. Finally, it shouldn't affect the product in any way. [1]

Some well-known containers for storing parenteral include ampoules, prefilled syringes, vials, cartridges, and infusion solution.

Ampoules

Small, cylindrical bottles made of glass or plastic called ampoules are sealed after a single dose of medicine or liquid is placed inside. The most frequently used term is WFI (water for injection).

Manufacturing of Ampoules

1.Glass Tubing : By pouring molten glass onto a rotating mandrel on a tube drawing machine that is slightly inclined, and then forcing compressed air into the flexible tube that results through a hollow shaft that supports the mandrel, the glass tubing is continually formed. A conveyor is used to pull and transport the tube to a cutting device, where 1.50 m-long tubular portions are cut off and let to roll to the side. Ampoules and vials are made using these tube lengths. Ampoules are frequently produced using carousel machines with the tubes arranged vertically, with the lower end of the tube producing the first ampoule. The entrance is on the top of the ampoule, and the bottom end of the ampoule grows on the lower end of the glass tube. To construct the ampoule spike, the tube is initially softened and stretched out to a place along its vertical height comparable to the ampoule length. At this stage, the tube at the tip of the spike is melted through to form the shoulder and bulb, giving the remaining tube a closed end. [2]

2. The High Speed Automatic Ampoule Filling & Sealing Machine is a small, flexible device for filling and sealing glass ampoules. Empty ampoules that have been cleaned and sterilized are fed into a wire mesh conveyor belt from the machine's left side. A feeding cassette was used to feed eight ampoules to the receiving rack. Eight ampoules are taken from the receiving rack by the horizontally moving moving rack, which then transfers them to the machine in an inclined position going from left to right. Pre-gassing, filling, post-gassing, pre-heating, and sealing stations are used to complete filling and sealing procedures. Ampoules are automatically gathered in an upright position in a stainless steel tray after they have been filled and sealed.[3]

Types of ampoule

Straight-stem, funnel-type, and closed ISO types B, C, and D ampoules are among them. These ampoules have several break mechanisms, including OPC (One Point Cut), CBR (Color Break Ring), and Score Ring .

Pre-filled syringes

Parenteral medication administration can be facilitated by the use of pre-filled syringes. They are reliable when it comes to dispensing a precise dosage of medication and are portable owing to their small size[4]

Major trends

Some of the key market trends for prefilled syringes include the following:

1.COP prefilled needles: Prefilled syringes are kept secure by using a high-performance polymer called cyclic olefin polymer (COP). These are frequently used and have a high level of break resistance in addition to a clarity that is similar to glass.
2.Plazx, a pre-filled syringe without silicone oil It is exclusively produced by Terumo Manufacturing as an empty pre-fillable syringe component, which is then filled in accordance with the customer's specifications by other pharmaceutical businesses. It is constructed of silicone that is oil-free and is autoclave-disinfected. As a result, risks including drug aggregation and oxidation are diminished.
3.Dual Chamber Pre-Filled Syringes: These syringes are used to store significant quantities of active pharmaceutical ingredients that might not be stable for an extended period of time.[5]

Cartridges

Cartridges offer good packaging for both insulin and other drugs. They work with all types of injectors, including those that use a pen or pump, auto injectors, and needle-free injectors. A hand-held device called the magnetic plunger less injection system employs a magnetically driven piston to dispense, transfer, and convey liquid or gas via a cartridge chamber and into a sterile needle for injections. This technology works by sending a magnetic field through the cartridges' glass and plastic walls. A magnet outside the cartridge walls and a ferrous piston inside the cartridge, with the piston replicating the magnet's motions, provide a powerful coupling.Liquids are introduced when the piston moves in one direction, and they are removed when it moves in the other direction.[6]

Infusion solution

Infusion solutions are classified as follows:
For intravenous administration, injectable medications are packaged in LVPs (Large Volume Parenteral Containers). The ASEP-TECH® Blow/fill/seal machine can produce IV bottles from the same mould by modifying the seal mould to produce a variety of top geometries.
There are many applications for SVPs (Small Volume Parenteral Containers), including local anesthesia and immunization. For repeated dosage applications, the 10 to 100 mL range is frequently used. A straightforward twist-off opening feature can be combined with a controlled diameter created in the top to enable spikes without needles. SVPs of a capacity of 2 to 5 mL are most frequently fitted with luer lock or luer slip fittings.[7]

Figure 1: small volume parenteral

Figure 2: large volume parenteral

Vials

A vial, often referred to as a phial or flacon, is a tiny container or bottle made of glass or plastic that is frequently used to store liquid, powder, or capsule pharmaceuticals.

Types of vials

Pharmaceuticals frequently come in single-dose and multi-dose vials, which are available in a variety of sizes and shapes. A multi-dose vial can be used more than once while a single dose vial can only be used once. For multi-dose vials, the Centers for Disease Control and Prevention (CDC) have developed certain requirements.

Manufacturing

The prepared tube is positioned on the production equipment with the film-sealed opening or dot-shaped opening on the bottom. The upper end of the tube is lightly heated. The tube is thermally split at a point above the dot-shaped opening and/or the opening is resealed with a film, creating a closed end on both the lower tube end and the remaining tube, which bursts open again as a result of the accumulating excess pressure. At this time, the mouth for the first vial is built.The tube is thermally split once more at a distance equal to the length of the vial, resulting in the formation of two closed ends—one below for the initial vial and one above—that will both instantaneously burst open again due to the newly developing excess pressure inside. The bottle mouth is shaped here using the aforementioned technique.

Modern trends

Vials made of plastic or glass are frequently used in contemporary containers. There are several options for glass vials, including screw vials (closed with a screw cap or dropper/pipette), lip vials (closed with a cork or plastic stopper), and crimp vials (closed with a rubber stopper and a metal cap).[2] With plastic vials that may be produced, other closure systems, such as "hinge caps," which close when pressure is applied, can be employed. They go by the names flip-tops or snap hats as well.
In contrast to test tubes, which often have rounded bottoms, vials typically have flat bottoms, however this isn't necessarily the case with small hinge-cap or snap-top vials. Bijou or McCartney's bottles are tiny vials in the form of bottles that are frequently used in labs. The bijou bottle is often smaller and has a 10-milliliter capacity [8]. The market for vaccine glass vials is anticipated to reach USD million by 2026, up from USD million in 2020 [9].

Container Material Choices for Parenterals

Glass container

The material of utmost choice for packaging containers is glass. Glass serves as a barrier between new pharmacological and biologic formulations and the outside world (light, moisture, and contamination), extending the shelf life of these products.

To avoid product contact with the glass surface, a thin layer of silicone is placed to the internal surface of the vials and ampoules. Additionally, by using this method, the adsorption of active ingredients from homogenous solutions is reduced, particles from suspensions are not adsorbed, and colloidal preparations are not allowed to aggregate on the glass surface [2].

Manufacturing

Sand, soda ash, limestone, and cullet are some of the constituents in this mixture. Broken glass is combined with sand, soda ash, and limestone to create cullet, which serves as the composition's fusing agent. The most frequent cations found in pharmaceutical glassware are silicon, aluminium, boron, sodium, potassium, calcium, zinc, magnesium, and barium. Only oxygen exists as an anion.

Manufacturing Process: Consists of four major operations-

1.Melting: The components, referred to as batch materials, are combined in the correct ratios and heated to fusion in a furnace. The two most often used furnaces are (i) Pot furnaces and (ii) Tank furnaces.

Clay pots are heated in a pot furnace to fuse the charge. You can close or open the pots. Closed pots are used when the glass needs to be shielded from combustion byproducts. The pots are filled with the ingredients for the batch. They receive heat from burning gas that is produced around them in a furnace. Once the fusing is complete, the pots are removed from the furnace, and the fused plastic mass is removed to be shaped. A pot furnace is used to create premium glass because the charge is shielded from the combustion products.

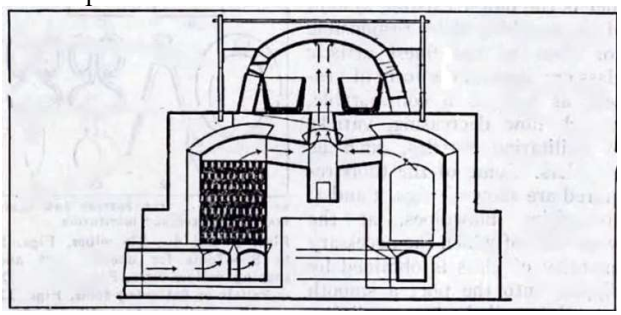

Figure 3: Tank furnace

Tank Furnace: A massive rectangular tank made of fire clay pieces serves as the centrepiece. For 10-12 hours, the batch ingredients were heated to 1400o- 1500oC.

2.Shaping:The necessary goods are then created using the shaped or formed plastic glass that came from the furnace. Both a machine and mouth blowing are acceptable methods. It takes a lot of practice to become an expert glass blower.

Blowing:Compressed air is used to shape the molten glass into a metal mold's hollow. Due of its weight, it extends when hung downward. The long lump is put in a mould, and air is pushed into it through the lips to inflate it. The bottle is taken out of the mould by separating the two pieces after cooling.

3.Annealing:It's a technique for gradually chilling freshly produced things. They become brittle when promptly cooled because of the extreme internal strain. In a lehr, a 50–60 foot long, tunnel-like oven, annealing is carried out. At one end of the oven, the temperature is just below the glass softening point (500°–600°C), and it steadily drops as it moves down the length of the oven. On the other hand, it is very similar to the room's temperature. After shaping, the parts are placed into the lehr from the hotter end and quickly go through a belt that is moving to the cooler end. The products must transit for several hours through the tunnel. Some high-quality glasses require prolonged annealing.

4. Finishing:The items collected from the lehr are processed in order to make them useable, including cleaning, polishing, rounding edges, and other procedures [10].

Advantages:

• Sterilization using heat is easy.

• They won't react with the contents because they are chemically inert.

Water and air cannot be penetrated.

• There are several sizes and forms available.

• Glass that is coloured helps protect contents from harmful light radiation [11].

Disadvantages:

• They might crack if subjected to a sudden rise in temperature.

• More expensive than plastic

• Additional measures and precautions must be taken.

•In some glasses, alkalis are discharged into the liquid[11].

Selection of glass containers*:* Some things to think about while choosing a glass container are:

(i)Hydrolytic resistance (ii) Alkalinity (iii) Calcium and Barium ion sensitivity (iv) Thermal expansion property [11].

Type of Glass Containers

TYPE I: It includes silica (80%), aluminium oxide (q.s.), sodium oxide, and boric oxide (10%). (q.s.). It is chemically inert and extremely hydrolytic resistant thanks to boric oxide. It is resistant to thermal shock and has a low coefficient of expansion. As a result, parenteral nourishment can be stored in Type I glass containers. This container is used to store potent acids and alkalis.

*TYPE II:*It is simply a Type III container modified with an inner surface coated with sulphur. This prevents the container from deteriorating over time. possess a high level of hydrolysis resistance. It is simpler to mould since the melting point is lower than Type I. In this container, both aqueous and acidic preparations can be kept.

TYPE III: Al oxide, aluminium oxide, potassium oxide, magnesium oxide, sodium oxide, silica, and 10% calcium oxide make up its composition. MgO lowers the temperature needed to form the glass. Enhancing chemical resistance is Al2O3. In this container are kept both parenteral and non-parenteral products.

TYPE IV: These low hydrolytic resistance glass containers are used to hold all-purpose soda lime. These are appropriate for things since they will hasten the pace of glass erosion reaction.

Materials used for the manufacture of glass containers

1. *Lime soda glass "Ordinary Glass":* Consists of 75% iO2, 15% Na2O, 10% CaO, and less than 1% each of MgO (lower temperature is necessary during manufacturing), Al2O3, and K2O. (improves mechanical strength and chemical durability).
2. *Borosilicate glass*: By reducing the alkali concentration and adding boric oxide, lime soda glass defects can be minimized. This container is used to hold preparations that are alkali sensitive.
3.*Neutral glass* is composed of 72–75 percent SiO2, 7–10 percent B2O3, 4-6 percent Al2O3, 6–8 percent Na2O, 0.5-2 percent K2O, and 2-4 percent BaO. Neutral glass is a more economical choice for large transfusion bottles.
4.Tubing for ampoules: Because ampoules are sealed by fusion after filling, glass melts easily. As a result, the amount of alkaline and aluminium oxides has grown somewhat, whereas the amount of boric oxide and silica has decreased significantly. These are thermally resistant. These are for injections that are alkali sensitive.
5. Lead free glass: Parenterals like sodium calciumedate and trisodium edate injections would absorb lead from the glass if it weren't lead-free, which is why lead-free glass is necessary because it causes poisoning.
6.*Sulphured container:* A process called as sulphuring is utilized as a surface treatment to provide less expensive containers for large volume injections. The surface of the container is neutralized when it is exposed to wet SO2, and the alkali creates a sulphate layer that may be washed away to reveal a durable, silica-rich surface. It is used to hold fluids for infusions, blood, and plasma.
7.*Silicon treated container*: These are long-chain polymers with variable oxygen and silicone atoms coupled to the latter by an organic group. They are inert chemically and resistant to heat and oxygen. The organic group also provides water resistance qualities [3].

Evaluation of glass containers:

1.Chemical Resistant Test
a)Powdered Glass Test: This test is used to determine how much alkali is present in powdered glass when it is exposed to high temperatures. The leaching of alkali is accelerated by glass powdering, which is visible using 0.02N sulfuric acid and methyl red as an indicator.To prepare the glass specimen is the first stage. The specimen is washed in the next phase. The third step entails mixing 50 millilitres of exceptionally pure water with 10 grams of the specimen or sample. After being autoclaved at 121°C, the solution is decanted into a new flask with 15 mL of water in step four. Utilizing an indicator, titrate the decant solution with 0.02N sulfuric acid and note the volume.

b)Water attack test: This test is for Type II glass. If the alkali leaches from the container's surface is the main concern.The container should first be thoroughly rinsed with high-purity water. 90% of the way full, fill it with water. In step two, autoclave for 30 minutes at 121°C. The liquid is then decanted after cooling. The decanted liquid is titrated with 0.02N sulfuric acid in step three while being monitored by methyl red. Make a calculation of your sulfuric acid consumption and contrast it with the established limitations in step 4.

c)Leakage test: After being filled, the medication container is placed in a container with coloured solution (methylene blue), and it is autoclaved under pressure for 10 minutes at 121°C. After that, the container is examined to see if any colours have gotten inside.

*d)Hydrolytic Resistant Test:*Only newly manufactured glass containers are eligible for this test. The first step is a three-time CO2 free water rinse of the container. Autoclave after filling to a predetermined volume. Step two involves cooking for 10 minutes at 100°C. In 60 minutes, the temperature will increase to 121°C. Reduce the temperature to 100 degrees Celsius. It should be refrigerated. Titrating a specific volume of a liquid solution with 0.01N HCL in step three requires the use of methylred as an indicator. Step 4 entails doing a water blank titration; the difference between the two is used to calculate how much HCL was eaten by the test liquid.

2.*Arsenic test:*
Step 1: Wash the container for 5 minutes on both the interior and outside with D.W.
Step2: Utilize the identical test solution as the hydrolytic resistance test for 50ml
Step 3: Pipette 10 mL of nitric acid and add it to the water bath while maintaining the same temperature.
Step 4: After cooling the residue in the oven for 30 minutes at 130°C, add hydrogen molybdate and reflux for 25 minutes.
Measure the solution's absorbance at 840 nm after it has cooled.

3. *Internal Bursting Pressure Test:*
Step 1: Water should first be added to the test bottle before it is set inside the test chamber.
Step 2: Over a predetermined period of time, the internal pressure is steadily increased.
Step 3: The bottle is subjected to pressure testing at a predetermined level until it ultimately bursts.

4.Thermal Shock Test :
Step 1: Place the sample container upright in the tray and heat the tray in the boiling water for the predetermined amount of time .
Step 2: Put the container in a bath of cold water and regulate the temperature. It's important to check cracks both before and after the test. (There should be a 45°C temperature difference.)
Step 3: A bottle's structural design affects its ability to endure thermal shock. •Pint bottles must be heated to 30 to 40 degrees Celsius, while small bottles must be cooked to 60 to 80 degrees Celsius.[12]

Drug and glass consideration

In comparison to alternative packaging materials, glass has a lot of benefits, but it also has two significant drawbacks: alkali release and the release of insoluble flakes into the liquids contained in the container.

Alkali Release: It has been demonstrated that lowering the soda content or using alternative oxides in place of sodium oxide can prevent the glass from releasing alkali cations into solutions. The surface of the soda lime glass can be treated to create a fine polished silica skin that is more resistant than the interior layer of the glass in order to increase the glass's resistance to alkali discharge. This surface-treated glass is represented by Type II glass. Another choice is to treat the glass surface with sulphur dioxide while it is still wet.

Release Of Insoluble Flakes: Glass containers holding liquids have been found to contain flakes that are insoluble. The type of glass used affects how flakes form. E.g. In non-borosilicate glass, flake production occurs relatively quickly after autoclaving, but only at temperatures higher than those used for borosilicate glass. Flakes can also be found in alkaline, tartrate, citrate, and phosphate solutions. Pre-treating the containers with a weak acid solution caused the creation of flakes to take longer [13].

Plastic container

Plastic packaging systems are a group of packaging items that contain or are intended to contain pharmaceutical formulations and are fully or partially made of plastic. Plastic containers are frequently composed of materials free of any contaminants that might have an impact on the stability or efficacy of pharmaceutical formulations or raise safety concerns because they come into contact with pharmaceutical formulations frequently. Many polymers contain lubricants, plasticizers, antioxidants, antistatic agents, and antistatic agents. The product may absorb these compounds from the plastic. The following characteristics of plastic containers used in the pharmaceutical business should be present:

1. The formulation ingredients in touch with the plastic packaging are neither extensively absorbed into or through the plastic container, nor are they appreciably adsorbed on its surface.

2. The formulation's stability is unaffected by the plastic package due to the release of chemicals (plastic materials leaching) in sufficient quantities into the formulation [2].

Types of plastic container

Thermoplastic: When heated, these become a viscous fluid, and when cooled, they become stiff. The amount of intermolecular interaction and crosslinking affect a material's hardness. Among them are polymers like polyethylene, HDP, PVC, PMMA, polystyrene, polypropylene, polyamide, polycarbonate, and PTFE.

Thermosetting: When heated, these might become malleable but not fluid. At room temperature, they are usually tough and brittle because to the high degree of cross bonding. Some of them are melamine-formaldehyde, urea-formaldehyde, and phenol-formaldehyde.[14]

***Manufacturing* - Thermoplastics processing techniques**

1.*Injection moulding:* This technique uses a long chamber and a reciprocating screw to push melted polymers into a mould cavity. As the plastic cools, it becomes harder, and the finished product pops out of the mould. This method is frequently used for the mass production of plastic items such as syringes, drug inhalation devices, bottle tops and closures. Materials used in this method include polypropylene (PP), nylon, Acrylonitrile-Butadiene-Styrene (ABS), polycarbonate (PC), and polystyrene.

2.Blow moulding: This method is widely employed when creating hollow plastic objects. The three different processes are injection blow moulding, injection-stretch blow moulding, and extrusion blow moulding.

a)Injection blow moulding: In this process, molten plastic is pumped into a mould to create a parison, or plastic tube/core pin. The plastic tube is then formed to fit the inside of the blow mould by blowing compressed air through it. The newly made bottle is then chilled before being discharged. Wide and narrow-mouthed plastic bottles, jars, and tubes can all be produced by injection blow moulding. Among the materials used are polyvinyl chloride (PVC), polypropylene (PP), polyethylene-terephthalate (PET), polyethylene (high density) HDPE, and polyethylene (low density) LDPE (LLDPE).

b)Injection stretch blow moulding:In this process, hot liquid plastic is injected into a mould to produce a preform. The preform is then stretched while being inflated with compressed air to give it the final shape that is required. The newly created transparent bottle is then removed from the mould. Either a one-stage or two-stage approach can be used to finish the earlier stages. A single-stage process is one in which both the preform production and bottle blowing operations are carried out by the same piece of equipment. Before being fed into a reheat stretch blow moulding machine to produce a bottle, preforms are made, packed, stored, and even sold in the two-stage process. The most often utilised material for injection-stretch blow moulding is polyethylene terephthalate (PET). Injection stretch blow moulding is a process used to create high-quality, clear bottles, including those for carbonated and soft drinks, oral hygiene products, cooking oil, agrochemicals, and bathroom and toiletry items.

3.Extrusion Blow Moulding: In this process, the melted polymer is introduced at a right angle into the annular die. A plunger forces the melt into an open mould hole, creating a parison, a hollow (usually round) pipe portion or preform. The mould then closes, creating the bottle neck and sealing the bottom of the parison at the same time. The parison is then pushed with compressed air into the mould, pressing against the interior of the mould. After that, the bottle is allowed to cool before being taken out of the mould. This plastic forming technique is used to create a variety of products, including bottles and containers, venting ducts, watering cans, and boat fenders. Some of the polymeric materials used in extrusion blow moulding include polyvinyl chloride (PVC), polyethylene (PE), polypropylene (PP), and polyethylene-terephthalate (PET) (PVC).

4.*Thermoforming process:* This method of plastic moulding involves horizontally heating thermoplastic sheets or pre-extruded stiff plastic sheets to a pliable forming temperature. The warmed sheet is then shaped by being stretched into or onto a mould, after which it is cooled and finished with trimming. The technique frequently makes use of high-density polyethylene (HDPE), high impact polystyrene (HIPS), glycolized polyethylene terephthalate, polycarbonates, acrylic butadiene styrene (ABS), and other materials. The plastic products made with this technique include trays, blister packages, medical device housing, cups, lids, and plates.

5.Rotational moulding/ Rotamoulding/ Rotomoulding: During this procedure, the raw material-containing mould is rotated within an oven, allowing the powder to melt and bond to the mold's inside. After that, the mould is cooled while still rotating in a biaxial fashion utilising a fan and water sprinklers. The finished item is then removed from the mould. Because no external pressure is applied during the forming process, this approach differs from other plastic forming processes. In this process, polymeric materials like nylon, polyethylene, polypropylene, polycarbonate, and PVC are used. Canoes, tanks, playground slides, and containers are all made using this technology.

6.Profiles Extrusion: The heated rotary screws used in this procedure melt the plastic raw materials and transport them along the conveyor belt. Molten plastic is continuously pressed into a hollow die to produce a specific profile form and thickness. A water bath or spray chamber is used to cool the extruded product after that. The chamber may also apply pressure into a vacuum to help the product pass through at the correct size. The softened plastic is then removed from the die by take-off rollers once the solid product has been transferred to them. Then a cutter or saw is used to make the final product length. Long lengths of plastic tubing, such as catheter and blood drip tubes, rain and gas pipelines, and other medical tubing, are frequently created using this technique. Various common materials are used, including High-Density Polyethylene (HDPE), butyrate, Glycolized Polyethylene Terephthalate, Polycarbonates, and Acrylonitrile Butadiene Styrene (ABS).

7.Blown Film: In the blown extrusion technique, a very small die aperture that is frequently supplied by numerous extruders faces upward in a spherical configuration. With this technique, a massive tin bubble is created, which cools as it rises. Then it is rolled up and folded, or it is made into well-known film items. Polyethylenes are the materials that are used in this process the most frequently (HDPE, LDPE, and LLDPE). Other materials that can be used as mixtures include polypropylene, polyamide, and EVOH (Ethylene Vinyl Alcohol Copolymer). This method is used to create a variety of packaging products, including those for the packaging of industrial items (such as shrink stretch film and container liners), consumer goods (such as packing bags and fill-and-seal packaging film), barrier film, and medical product packaging [15].

Thermoset processing techniques

1.*Compression moulding:* In this method, the raw material is sandwiched between two heated mould halves (granules or a slug of prepared plastic). When pressure is applied to the heated mould, the plastic flows and fills the void. The components are then cooled by air after that. Excess material may leak out of the dividing lines during compression, creating a flash. Commonly used materials include polyester, polyimide (PI), polyamide-imide (PAI), polyphenylene sulphide (PPS), polyetheretherketone (PEEK), fibre reinforced plastics, and others. Using this process, items including electronic device cases, electrical components, flatware, gears, buttons, buckles, and handles can be produced.

2.*Transfer moulding:* In this procedure, a predetermined weight of polymeric raw material is warmed and placed in a holding chamber (pot). Using a hydraulic plunger, the material is then pushed or forced into a heated mould chamber through a channel called a sprue. The material is held in a heated, pressurised environment until it cures and solidifies. Among other things, this technology is used to create dishes, cooking pot handles, rubber components like shoe bottoms, and housing for high-voltage switches. Transfer moulding can use thermoplastics, however most of the materials used in this technique are still thermosets. Some of the common polymers used in transfer moulding include epoxy, silicone rubber, phenol-formaldehyde plastic, and unsaturated polyester.

3.*Pultrusion:* Continuous reinforcements (in the form of rovings or mat/roving shapes) are first pushed or drawn through a resin impregnation mechanism to begin the pultrusion process. To

guarantee that the fibre reinforcement is fully "wetted out," each fibre is coated with a resin that has been specially designed for the job. The extra glue is then scraped off, letting the trapped air escape and the fibres condense.

The coated fibres are routed via preforming guides prior to entering the heated die in order to align reinforcement and preform the object to the desired shape. The final shape and size of the finished product are determined by the die cross section. The temperature of the die is carefully regulated, and heating and cooling zones within the die regulate the rate of reaction to ensure that the composite is fully cured [15].

Advantages

• Plastic storage containers are resistant to breaking.

• They are inexpensive to create

• They are lightweight and water-resistant.

• They give a high level of gloss and may be readily moulded or remoulded.

Plastic containers can be collapsed, are corrosion-resistant, and inert to chemicals.

Disadvantages

• Plastic containers have a low level of physical stability because of adsorption, absorption lightness, and/or interactions between the formulation and the container.

• Because most plastic containers are not as clear as glass, it is difficult to observe the contents.

• They have low heat resistance and are fragile.

Evaluation of plastic containers

1.*Leakage Test:* Ten plastic containers should be filled halfway with water, closed as intended, and inverted for 24 hours at room temperature. If there are no signs of container leaking, the test is deemed successful.

2.*Collapsibility Test:* To find out if containers can be squeezed to release their contents, this test is used. A container that folds inward while being used at room temperature releases at least 90% of its regular content at the required rate of flow.

3.*Clarity Testing:* Parts that are unmarked, unlabeled, and unlaminated are randomly selected from an appropriate container. Then, each of these pieces is cut into a strip with a total surface area of no more than 20 cm2. The strips are shaken in at least two different volumes of distilled water to get rid of extraneous particles. The flask receives 250ml of distilled water before being covered and autoclaved at 121°C for 30 minutes. The extract is given time to cool before inspection. It ought to be clear and devoid of turbidity [13].

Drug plastic consideration

A packing mechanism must safeguard the medication without altering its composition in any way up until the last dose is extracted. It is challenging to choose a suitable package for a drug because a mistake could have disastrous consequences. There are five categories under which medications and polymers have been considered:

1.*Permeation:* The shelf life of a medicine may be shortened if gases, vapours, or liquids pass through plastic packing materials. If the medication is susceptible to these reactions, hydrolysis and oxidation problems result from oxygen and water vapour entering the medication via the plastic wall. For instance, it has been found that the water vapour permeability of penicillin tablets causes them to degrade in polystyrene containers. Temperature and humidity are the primary drivers of O2 and H2O permeability through plastic. As the temperature rises, a gas becomes more permeable. Since molecules cannot flow through the crystalline zone, permeability should decrease as crystallinity increases. While materials like polyethylene are hydrophobic, as opposed to nylon, which is hydrophilic by nature, nylon performs poorly as a water barrier.
2. *Sorption:* This procedure involves the packing material removing components from the drug product, which could lose important components and have significant effects on how medications are made. A typical worry in practise is the loss of preservatives that are used in small dosages. Factors that affect sorption from a product include pH, solvent system, active component concentration, chemical structure, temperature, length of contact, and area of contact.
3.*Chemical reactivity:* One or more medicinal product components may chemically react with a small number of chemicals used in plastic formulation. Sometimes the plastic and the ingredients in the recipe can react. Micro-amounts of chemically incompatible substances can alter how the plastic or medicine product looks.
4.*Modification:* The term "modification" describes the physical and chemical alterations made to the package by the drug product. Examples of phenomena that can alter a plastic's properties and hasten its decomposition include permeation, sorption, and leaching.
Rarely, the drug product may extract plasticizers, antioxidants, or stabilisers, affecting the container's physical and chemical properties as well as the content's and the package's flexibility.
5.*Leaching:* Most plastic containers have one or more compounds added in small amounts to stabilise the plastic or give it a particular quality. These components could leak or move from the container into the drug being taken. Certain colours may migrate into parenteral solution and cause toxicity when colouring chemicals are used in modest amounts during the production of polymers [13].

Glass vs plastic?

Containers made of glass and plastic have several advantages and disadvantages. Glass seems to be the material of choice for containers used to store parenteral pharmaceuticals. Glass is not the only packaging material, though; demand for plastic parenteral vials is predicted to rise 7.7% annually to more than 13.1 billion units by 2021. Glass is difficult to break, which has led to a rise in interest in plastic in recent years. Under specific circumstances, delamination on the glass vial's surface produces glass particles. A number of recalls have been issued by the FDA in recent years because of the possibility that glass fragments could enter a patient through prescription products. Plastic vials are an alternative since the material's nature minimises the chance of breaking and prevents delamination.

Plastic containers have a lot of issues, including scratch sensitivity, a porous barrier to oxygen and water vapour, and a lack of long-term experience. A polymer could be more scratch-sensitive than glass if not handled with extra care.

Understanding the characteristics of the formulation to be contained as well as its particular needs is necessary for the actual container selection. The pharmaceutical business and the packaging supplier choose the ideal packaging material and container closure mechanism [16][17].

Closure system

Rubber is the material of choice for disposable syringe plugs, intravenous fluid bottles, multi-dose vial closures, and ophthalmology pipettes bulbs. Rubber closures make it possible to place a hypodermic syringe needle into a multi-dose vial and then reseal the vial after the needle has been taken out. A band made of aluminium secures the rubber clasp. [4] Leaching and permeation can be reduced by applying a plastic or lacquer coating to the surface of rubber closures in contact with the substance. Another usual concern with rubber closures is the issue of coring [2].

Natural rubber: These closures are made of isoprene, a vulcanizing agent (sulphur), an activator (2-mercaptobenzothiazole), fillers (carbon black or limestone), antioxidants and lubricants, paraffin wax, softeners, and colours. These lack flexibility and are fragile. In a range of solvents, May dissolves [3].

Synthetic rubber:In every aspect, these are better than natural rubber. These can withstand high temperatures better. greater tolerance to substances that speed up ageing (light, Cu, Mg, oxidation). It's hard to understand.

Manufacturing process:

The manufacture of closures includes the processing of raw materials and auxiliary chemicals, weighing and mixing, and vulcanization.

In the chemical process of vulcanization, sulphur (or some analogous curative) is combined with fillers like carbon black or limestone, antioxidants, lubricants, activators like 2-mercaptobenzothiazole, and rubber or related polymers. After vulcanization, moulding and compression take place. The two forms of moulding are compression and injection, with the former being used most frequently.

An initial placement of the preheated moulding material in an exposed, heated mould chamber is known as compression moulding. Pressure is used to press the material into contact with all of the mould surfaces once the mould is closed with a top force or plug part. Heat and pressure are maintained throughout the curing process.

The process of making products out of thermoplastic and thermosetting plastic materials is known as injection moulding. Before being pressed into a mould cavity, material is blended in a heated barrel where it cools and hardens according to the mould cavity's design. Following the moulding process are coating, washing, siliconization (if required, using a specific, high-viscosity silicon oil), and packing [18].

Future aspects

Parenteral medication packaging will soon surpass a line of automacity. This will be more stylish and comforting. The production of infusion pump systems, single-dose vials, and prefilled syringes, whether made of glass or plastic, is at its peak right now. Because they lower the risk of injury from sharp objects, prevent product loss, and provide the right amounts, auto injectors are growing in popularity. Additionally, they permit self-administration, which is advantageous for patients who prefer to remain at home.

Mechanical processes including product preparation, filling, and assessment, as well as packaging, will become more automated as our pharmaceutical businesses grow and more research is done. Along with that, a number of enhancements will be made to the container closure mechanism to increase its quality, lowering the risk of breakage, scratching, and interaction, among other things [19].

Conclusion

Pharmaceutical product storage has been made possible with the availability of containers. These require an additional closure device and might be made of glass or plastic. Glass and plastic containers serve the same purpose, although they differ in some ways.

Plastics are a better option than glass for a number of reasons, including the silicification of glass (some products may form proteins or silicone aggregates), delamination, or interaction with particularly aggressive materials. Plastics are also an alternative to glass because they are less likely to break. And in that case, plastic might be the only choice. There are drawbacks to packaging with plastic containers as well. These need to be handled carefully because getting a scratch is the biggest worry. Some medications may have issues with this barrier protection against oxygen and water vapour permeability. When selecting the container for storing the medicine, important characteristics of the drug, such as its sensitivity or interaction with the material, must be taken into account.

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