Pharmaceutical Packaging Material: A Review

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Abstract- *In the pharmaceutical sector, packaging is a key component in the production of various medication formulations. A pharmaceutical package is an essential component that protects the pharmaceutical substance. The quality of the packaging material assures the safety of pharmaceuticals quality during storage, shipping, delivery, and sale. To protect the medicine against chemical degradation, the stability of the drug in solid, liquid, gel, or paste form is dependent on the packing material.The primary package has direct control over the product, while the secondary package is the packaging that surrounds the primary package. Tertiary packages are used for transporting. The pharmaceutical packaging has a hermetic seal that prevents contamination of the pharmaceutical substance. Glass, plastic, metal, and rubber are significant components in container closure systems. Containers and closures are made from several types of glass, plastic, and metal. The materials used are determined by the items that will be stored in the container. Closure is an important aspect of pharmaceutical packaging since it has direct contact with the medicinal preparation. As a result, the container and closing materials should be carefully chosen so that they do not interfere with the therapeutic efficacy of the goods.*

Keywords- Pharmaceutical Material, Glass, Metal, Plastic, Closure.

I. INTRODUCTION

Packaging may be defined as the collection of different components (e.g., bottles, vials, closures, ampoules) that enclose pharmaceutical products from the time of production until they are consumed (1). Pharmaceutical packaging is the method used to provide safeguarding, presentation, recognition, details, and comfort to encourage compliance with a course of remedy. It aids to prevent damage during delivery, provides the information needed to reach its intended destination, and even focuses on keeping the handlers and consumers safe (2). Packaging must be affordable and provide protection against environmental conditions such as physical, chemical, and biological endangerments (3). Packaging plays a vital role in carrying the image and recognition of a company. The package's exterior picture provides clear information about the product, such as route of administration, storage condition, expiry date, batch number, manufacturer name, license number, and new concepts in dynamic packaging, intelligent packaging, and nanotechnology (4). The worldwide pharmaceutical packaging market was valued at $ 117.2 billion in 2021 and is anticipated to extend at a growth rate (CAGR) of 9.5% over the forecast period (2021–2030)(5).

Ideal Characteristics of Pharmaceutical Packaging Materials

- It must safeguard the composition against environmental factors.
- It must not interact with the products.
- It must be non-noxious.
- It must be FDA authorized.
- It must have a reasonable price in relation to the product.
- It must not contribute to the odor or taste of the product(6).

Types of pharmaceutical packaging.

Packaging is done by three types.

1.PRIMARY PACKAGING

Primary packages are those that come into direct touch with the pharmaceutical formulation. The primary package's primary goal is to protect the formulation against environmental, chemical, mechanical, and/or other risk. Glass, ampoules, syringes, vials, closures are some examples

2.SECONDARY PACKAGING

Secondary package refers to the package that is not part of primary package. This package provides additional protection during storage and also contain information on the drug product such as leaflets.

3.TERTIARY PACKAGING

It is utilized in warehouse storage and shipping. Example; barrel, crate, container, slip sheet (7).

Types of containers used for primary packaging are:
For liquid orals:

Well-closed container:

These containers safeguard the product against shock, foreign particle and loss during transit, distribution and sale, etc.

Air tight container:

During typical storage and usage, airtight containers remain impenetrable to solids, liquids, and gases. If the container will be opened more than once, it must stay airtight after re-closing.

Single dose container:

Single dose containers hold single use products E.g: glass, ampoule.

Multidose container:

This type of container stores many dosages and its content are removed at different interval.
E. g: vials.

Light resistance glass:

Some materials are sensitive to light. They lost the characteristic on exposure to sun-light. Such materials are stored in light-resistance container (3,8).

For solid dosage forms:

Strip package:

Strips are commonly used to store tablets and capsules.The contents are enclosed in a package.The package is comprised of two layers of film. A strip packagewith severalpockets and each holding a single dose of medicament.
e. g: polyethylene, poly vinyl chloride, cellophane.

Blister package:

It is composed of base layer with cavities which enclose the medication. They are morestiff than strip packages and are not suitable powder and semi-solids. Cavity composed of plastic and aluminum as well as a cover made of aluminum and paper foil.
E. g: polyvinyl chloride, polypropylene, polyethylene.

Child resistance package:

Child-resistant packaging, sometimes known as CR packaging, is a type of packaging designed to limit the danger of hazardous compounds being consumed by children. This is frequently achieved by employing a specific safety cap.

For semi-solid dosage form:

Creams, pastes, and ointments are examples of semi-solid dosage forms. Containers for semi-solid dosage forms include collapsible tubes, among other things. Plastic containers are very widely used these days (4,8).

PACKAGING MATERIALS:

1. Glass
2. Plastic
3. Metal
4. Rubber

GLASS:

Glass is often used in pharmaceutical packaging because it has great protective capabilities, looks elegant, and is accessible in a wide range of sizes and shapes. It is chemically inert, impermeable, robust, and stiff, and has FDA approval. Glass does not degrade with age, and when properly sealed, it provides an effective barrier against almost every element except light.When necessary, tinted glass, particularly amber, can provide light shielding.

Glass material is made up of Sand, Soda ash, Lime stone and cullet. Cullet is broken glass that acts as a fusion agent for the entire mixture (9).

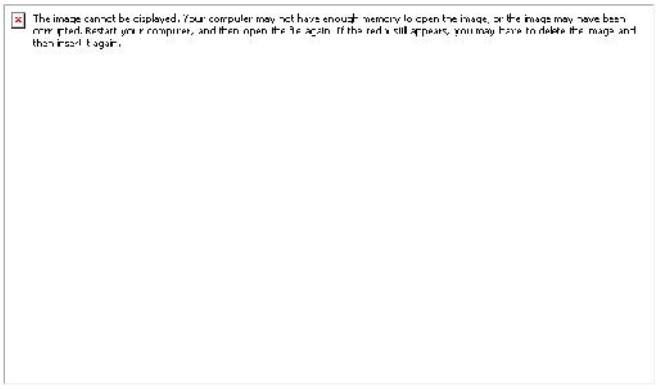
Advantages:

- They are impenetrable to water vapors, air, etc.
- They are translucent, allowing the contents to be viewed from the outside, like in the case of parental preparations.
- By combining glass with metal oxides, they can be transformed into light-resistant glass.
- They are more attractive than plastic containers.
- They can endure high temperatures and pressures during sterilization.
- They are easy to label.
- Easy to clean and readily available.
- It can be recycled and reused.

Disadvantage:

- They are bulky, which raises the expense of transportation.
- They are easily breakable.
- If they are not adequately handled with chemicals, they can readily leach alkali into aqueous solutions(7).

Table(1): Packaging types:(10)



Glass Types:

- Type I – Borosilicate Glass
- Type II – Treated Soda-lime Glass
- Type III – Regular Soda-Lime Glass
- Type -NonParenteral.

Type - Borosilicate Glass:

- Glass that is extremely resistant.
- Boron and/or Aluminum and zinc replace a significant portion of the alkali and earth cations.
- It has a higher chemical inertness than soda-lime glass (which contains none or only a little quantity of these cations).
- It is used to hold strong acids and alkalis, as well as other solvents.
- Adding approximately 6% boron to type I glass minimizes leaching activity.
- Sio2-80%, Al2o3-2%, Na2o, Cao-6% are the main elements.

E. g: Pyrex, Borosil.

Type – Treated Soda-Lime Glass:

- Highly chemical resistance but not much as type .
- Type containers are composed of commercial soda-lime glass that has been de-alkalized or treated to remove surface alkali.
- The de-alkalizing technique is called as Sulphur treatment, and it essentially prevent weathering/blooming of empty bottle.
- Thus, Sulphur treatment neutralizes the alkaline oxides on the surface, making the glass more chemically resistant.
- Some manufactures subject the glass to an environment including water vapor and acidic gases. This causes a reaction between gases and surface alkali, making it resistant to water assault (11).

Type – Regular Soda-Lime Gas:

This glass comprises metal oxides, sodium oxides, aluminum oxides, earth oxides, particularly calcium oxides.The biggest drawback is that it might leach alkali during the preparation process. As a result, it is utilized to preserve non-alkali sensitive liquid formulations. It's also utilized to keep all kinds of solid dosage forms safe.

Type – non-Parenteral:

This type of glass, as the name implies, it is used to hold non-parenteral compositions when heat shock is not an issue. These formulations are used to keep capsules, tablets, and topical medications safe. This glass is not utilized in autoclaved items because autoclaving speeds up the glass erosion process (7).

PLASTIC:

According to the British Standards Institute, plastics are "a wide spectrum of solid composite materials that are essentially organic, generally based on synthetic resins or modified polymers of natural origin, and exhibiting substantial mechanical strength. Most plastics may be cast, molded, or polymerized straight into form at an appropriate point in their manufacture (2).

Advantages:

- Plastics are indestructible.
- They are lighter than glass and hence have a lower transportation cost.
- They are available in a variety of sizes and forms.
- They have a higher range of resistance to chemical danger.
- They do not leach alkali like glass container.
- They also have ability to suck back.

Disadvantage:

- Permeation is the biggest drawback. Gases, vapors, liquid from surrounding environment can easily travel inside aplastic container.
- Permeation creates oxidation and/or hydrolysis problems and can destroy the products that are sensitive to oxidation and/or hydrolysis.
- Another issue is sorption, which is the process by which one or more elements of the product are removed by packaging material. This may have an impact on the product's medicinal effectiveness.
- The container material might also absorb the preservative. This may impact the container's flexibility (12,13).

PLASTIC TYPES

Plastics are classified into two types

1.Thermoplastic
2.Thermosetting

Thermoplastic

Capable of being molded after initial heating and hardening by cooling.Resistant to breakage and inexpensive to manufacture, the correct polymers will offer the essential protection of the product in beautiful containers.

E. g: Polyethylene, Polystyrene, Poly vinylidene chloride, Polypropylene, Nylon

Thermosetting:

They require heat to be processed into a permanent form. Such materials establish permanent cross-links between the linear chains upon heating, resulting in solidification and loss of plastic flow.

E. g: Phenol formaldehyde, urea formaldehyde (4).

Materials used in the manufacturing plastic containers:
Polyethylene:

Provides an excellent moisture barrier but a weak one against oxygen and other gases. High density polyethylene is employed, with densities ranging from 0.91-0.96, resulting in four main container characteristics: (1) stiffness, (2) moisture-vapor transfer, (3) stress cracking, and (4) clarity or translucency depending on the polymer density used.

Polypropylene:

Polypropylene has the same properties as polyethylene, except it does not stress-crack under any circumstances. The packaging is softened using hot aromatic or halogenated solvents. It has a high melting point, making it useful for boilable packaging and sterilizable items. Brittleness at low temperatures is one of its key drawbacks.

Poly-vinylidene Chloride:

Outstanding barrier characteristics against moisture, water vapor, UV radiation, scent, inorganic acids, alkalis, aqueous salt solutions, organic water-soluble acids, aliphatic hydrocarbons, esters of long chain fatty acids, detergent base materials, emulsifying agents, and wetting agents.PVDC is particularly cost-effective since coating weight may be modified based on barrier property needs.Non-toxic and of medical quality.High degrees of transparency, which improves product attractiveness.

Nylon(polyamide):

Many di-basic acids and amines mix to form a different type of nylon. Nylon is a very robust material that is difficult to damage mechanically. Nylon is resistant to a wide variety of acids and alkalis. Its sole downside is that it is permeable to water vapor to some extent; however, this can be mitigated by covering the container with PE.Products should not be stored for an extended period of time (14).

METAL:

Metal containers are only used for non-parenteral delivery of medications. Tubes, foil or blister packets, cans, and aerosol and gas cylinders are some examples. Aluminum and stainless steel are the metals of choice for both primary and secondary pharmaceutical packaging. They have several benefits and make good tamper-evident containers. Metal is the best packing material for pressurized containers since it is robust, impermeable to gases, and shatterproof (15).

Advantages:

- They are less heavy than glass.
- Metal containers are sturdy and generally indestructible.
- Chemical resistant.
- Quickly coats a variety of metals.
- Labels do not need to be placed because they may be printed right on the surface.

Disadvantage:

- Metal particles may be leached into the product.
- They may react with certain medications or substances, resulting in the production of a hazardous compound.
- They are more expensive than plastic.

ALUMINIUM:

Aluminum is an excellent recycling material. It has a high intrinsic value and hence a high scrap value. As a result, there is a strong incentive to recover metal from packaging trash. In general, the economics of collecting and recycling aluminium for packaging purposes are advantageous. Because recycling does not damage metal, fresh aluminium may be created from 100% recycled material (16).

Advantages:

- Because aluminium is a light metal, the product's shipping costs are lower**.**
- The surface of aluminium interacts with ambient oxygen to generate an atomic-thin, robust, coherent, transparent oxide covering that shields the metal from further oxidation**.**

Disadvantages:

- Any material that interacts with the oxide layer might produce corrosion, for example, goods with high or low pH, certain complexing agents, and so on.
- H2 may emerge as a result of the corrosion process (17).

Use:

- Ointment tubes made of aluminium.
- Screw covers.
- Aluminium strips for tablet and pill strip packing Internally lacquered aluminium containers are sometimes used to halt the reaction with the substance.

IRON:

Advantages:

- Large quantities of tin-coated steel, generally known as tin, combine the strength of steel with the corrosion resistance of tin and are utilized for pharmaceutical packaging.

Disadvantages:

- If an aqueous liquid can penetrate a pinhole or other flaw in the tin layer, a short-circuited galvanic cell is formed, and the powerful chemical reaction that occurs causes fast corrosion of the underlying steel. The tin surface is also coated as an extra precaution.

LEAD:

Advantages:

- The least expensive of all metals used in pharmaceutical containers.
- Metal that is soft.

Disadvantages:

- When lead is consumed internally, there is a danger of lead poisoning. As a result, lead containers and tubes should always have an inert metal or polymer lining on the inside.

Use:

Lead tubes with linings are utilized for products such as fluoride tooth paste (2).

CLOSURES:

Pharmaceutical closures, often known as stoppers or bungs, are an essential component of the final packing of pharmaceutical preparations, especially those designed to be sterile. The elastomeric closure is the most prevalent form of stopper. An elastomer is any substance that, when a deforming force is withdrawn, returns to its original shape, a property known as viscoelasticity. The elastomer used in the manufacture of closures can be either natural or synthetic, such as butyl rubber or chloro-butyl rubber. The benefit of synthetic rubbers is that they are very resistant to oxygen or water vapor penetration (18).

Rubbers:

This is mostly utilized in the production of closures, filters, caps, and droppers (pediatric purpose). Rubber prevents leaks and prevent from the surrounding environment. Rubber comes in two varieties.

- Natural rubber,
- Synthetic rubber

Natural rubber:

Natural rubber is mostly derived from the Malabar plantation in Kerala. Hevea brazilensis is the botanical name of the plant. From the stem, it excaudates delicious sticky substance to manufacture rubber. It is vulnerable to microbial contamination. If any additives are used. They are incompatible and cannot reach the necessary forms, strength, and capacity.

Synthetic rubber:

It is largely utilized in the pharmaceutical industry. It comprises isoprene derivatives such as neoprene butylated rubber and other additives that are used to create synthetic rubber with the necessary form, strength, capacity, and elasticity.

Benefits of rubber as closure:

- It has a very good anti-aging action (long shelf life).
- It has adequate flexibility (it can compress or extend to fit inside any sort of container).
- It will not allow air (or) moisture to pass through it.
- They come in a variety of sizes and forms, allowing them to fit into the necks of various types of containers.
- They are not brittle (if a rubber closure is used for multi-vials, little fragments of rubber can enter the medicine if it is delicate).
- They are inexpensive.

Drawbacks of rubber as closure:

- It goes through the leaching process.
- It may be affected by the sorption process.
- It is unable to withstand high temperatures (19).

Threaded Screw Cap:

When used, the screw cap overcomes imperfections in the sealing surface and offers physical and chemical protection to the content being sealed. Screw caps are generally composed of metal or plastic. The metal is often tinplate or aluminum, while thermoplastic and thermosetting materials are employed in plastics.

Figure 1: Threated screw cap

Lug Cap:

The lug cap works on the same basis as the threaded screw cap. Instead of a continuous thread, it's only an interrupted thread on the glass finish. It engages a lug on the cap sidewall and draws the cap down to the container's sealing surface. In contrast to the threaded closure, it just takes a quarter turn. The lug cap is used for both atmospheric and vacuum pressure closure.

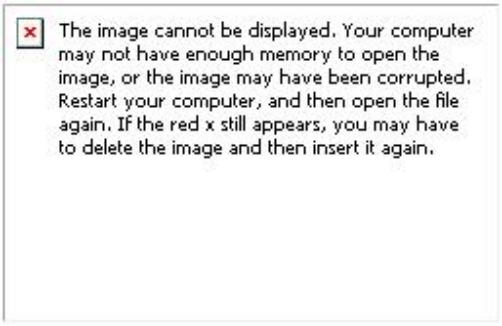


Figure 2: Lug cap

Crown Cap:

This form of cap is often used as a crimped closure for beverage bottles and has remained virtually unaltered for more than 50 years.

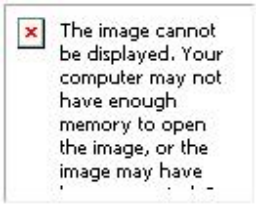


Figure 3: Crown cap

Roll On Closure:

The metal roll-on cap may be securely closed, readily opened, and efficiently resealed. It is widely used in the packaging of food, drinks, chemicals, and medicines. The roll-on closure requires a material that is easy to shape, such as aluminium or other light-gauge metal. The roll-on closure is available in resealable, non-resealable, and pilfer proof varieties for use on glass or plastic bottles and jars.

Figure 4: Roll on Closure

Pilfer proof closure:

The pilfer proof closure is identical to the normal roll-on closure but has a longer skirt. This extra length continues below the threaded part to form a bank that is held to the basic cap by a series of small metal "bridges." When the pilfer proof closure is removed, the bridges break and the bank remains on the container's neck. The closure is readily resealable, and the separated band shows that the package has been opened. Torque is required to remove the cap (15).

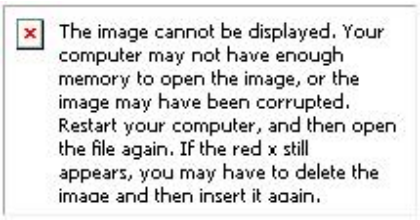


Figure 5: Pilfer proof closure

II. CONCLUSION

Pharmaceutical packaging is an essential technology in the pharmaceutical industry.In recent years, the pharmaceutical packaging industry has grown at a rate of at least 9.5 percent every year.Pharmaceutical packaging is necessary for product stability, patient acceptability, transportation, etc. Packaging provides crucial information to the patient. Packaging is vital for pharmaceutical product protection. This review focus on pharmaceutical packaging material, advantages and disadvantages of packaging.

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