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(REVIEW ARTICLE)

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Pharmaceutical packaging innovations: enhancing drug safety, efficacy, and patient compliance: A brief review

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Abstract

In the pharmaceutical sector, packaging plays a significant role in the development of different drug formulations. An essential component that protects the pharmaceutical substance is the packaging. Maintaining the quality of pharmaceuticals during storage, delivery, transit, and sale is dependent on the product's quality. Product containment, ease of use, and compliance during storage, transportation, display, and consumption. the stability of medicine solid, liquid, gel or paste form depend on packing material to prevent drug from chemical degradation. There are three levels of classification for pharmaceutical packaging: primary, secondary, and tertiary. The product is closely protected by the primary packaging. The pharmaceutical formulation has direct control over the primary package. secondary packaging that is used for product display and branding. The tertiary package, which is utilized for transportation, is the outermost package of the secondary packaging. Materials like glass, plastic, rubber metal, etc. are used for packing. By offering display, protection, identification, and information against physical damage, content loss, and undesired environmental elements including oxygen, water vapor, and light, packaging preserves the integrity of the product. The purpose of packaging is to keep a product contained so that it cannot interact with the environment. In order to turn the formulation into a product that is both aesthetically pleasing and commercially viable, pharmaceutical packaging plays a crucial role. The review article focused on type of packaging, packaging material and function of packaging.

Keywords: Pharmaceutical Packaging; Materials; Pharmaceutical Dosage Form; Biodegradable Polymer; Glass; Plastics; Product

1. Introduction

The science, art, and technology of enclosing or safeguarding products for use, sale, storage, and distribution is known as packaging. For the consumer to get the items safely and securely, packaging is crucial. A well-coordinated system called packaging is used to get products ready for handling, distribution, confinement, protection, and sale. Pharmaceutical packaging examines issues such as patient compliance, child safety, product diversion, and manipulation. Packaging offers defence against environmental factors such as chemical, biological, and physical hazards. Pharmaceutical packaging offers medical devices, life-saving medications, blood and blood products, and novel products like nutraceuticals. Packaging is a key component in conveying a company's identity and image. It is completely incorporated into business, government, institutions, industry, and private use in many nations. Clear details about the product, including the manufacturer's name, address, license number, batch number, expiration date, storage conditions, and route of administration, are provided by the packages outside image. Innovative concepts in dynamic packaging, intelligent packaging, and nanotechnology provide arrangements that are essential for enhancing or monitoring food quality (Mohd Sohail Ali).

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1.1. Characteristics of packaging material

- It must not be harmful.
- It must be FDA authorized.
- It must not react with the product.
- The material must shield the preparation from the environment.
- It must not give the product an unpleasant taste or odour.

1.2. Types of packaging

1.2.1. Primary packaging

Direct contact between the package and the product occurs in the primary packing (Praveen Nasa Department of Pharmaceutical Education & Research). It serves as the smallest distribution and use unit. Its primary goals are to inform, contain, and safeguard consumer. Syringe, container, ampoules, vials, closure, strip packaging, and blister packaging are a few examples.

Figure 1 Primary packaging

1.2.2. Secondary packaging

The outer packaging of the primary packaging that groups products together is known as secondary packaging.

Examples: Cartoon, Boxes, Cases, Pallets, Shrink wrap.

Figure 2 Secondary packaging

1.2.3. Tertiary packaging

In addition to the product, primary and secondary packaging are additionally protected by tertiary packaging. It is employed for product delivery, warehouse storage, and bulk handling.

Examples: Containers, Stretch wrap, Shipping Labels.

Figure 3 Tertiary packaging

2. Packaging materials with respect to different dosage forms

2.1. Solid Dosage Forms

2.1.1. Tamper Resistant Packaging:

Strip Packages

One popular type of unit dose packaging for tablets and capsules is the strip package. Two webs of a heat-sealable flexible film are fed through a heated reciprocating plate or crimping roller to create a strip package. Before creating the last set of seals, the product is deposited into the pocket that has been created. Depending on the restrictions of the packing machine, a continuous strip of packets is created, typically several packets wide. The desired number of packets in length is sliced off of the packet strip. According to their qualities, several packaging materials are used for strip packaging in high-barrier applications; a paper/polyethylene/foil/polyethylene lamination is frequently employed (Lachman, 2009).

Figure 4 Strip Package

Blister Package

Heat-softening a thermoplastic resin sheet and vacuum-drawing the melted plastic into a curved Mold creates the blister package. The sheet is taken out of the Mold and sent to the packing machine's filling station once it has cooled. A heat-sealable backing material is used to cover the product-filled, semi-rigid blister that has already formed. Aluminium foil that has been heat-sealed is typically used as the peelable backing material. To provide adequate sealing for product protection and tamper resistance, the foil's coating needs to work with the blister substance. PVC, PVC/polyethylene blends, polystyrene, and polypropylene are often aluminium membrane are utilized in tropical regions to offer better defence against high humidity.

Figure 5 Blister Package

Bubble Pack

Although there are various techniques to create the bubble pack, it is often created by sandwiching the product between a stiff backing material and a thermoformable, extensible, or heat-shrinkable plastic film. Heat-softening the plastic film and vacuum-drawing a pocket into it, much to how a blister forms in a blister packaging, are the usual methods used to achieve this. After the product is dropped into the pocket, it is sealed to a stiff surface, like paperboard coated with heat sealant. When using a material that shrinks when heated, The film contracts into a bubble or skin around the product when the package is passed through a heated tunnel, securely securing it to the backing card (Manukonda Keerthi, 2014).

Figure 6 Bubble Pack

Child Resistant Container

Commonly referred to as CRCs, child-resistant containers are made to keep kids away from potentially dangerous items (Manukonda Keerthi, 2014). Legally speaking, within five minutes of receiving the package, at least 80% of the test panel's 20–42-month-old children are unable to open it. Thus far, all child-resistant compliance testing standards define such a package as immediate packaging that is difficult for young children (less than 52 months old) to open but does not present any challenges for older adults (over 65) to open and, when necessary, re-close correctly (P. D. Bairagi, 2018).

Figure 7 Child Resistant Container

Film Wrapper

A translucent film featuring a unique design is firmly wrapped around a product or product container. To remove the product and open the container, the film needs to be ripped or cut. Options for substrates include voidable films that produce an image when removed and ultra-destructible films. Solvent-sensitive papers, for instance.

Shrink Seals and Bands

Heat or drying causes the bands or wrappers with the unique design to shrink, sealing the cap and container union. To remove the product, the seal needs to be cut or ripped. The shrink band concept uses a stretch-oriented polymer's (often PVC) heat-shrinking properties. The heat-shrinkable polymers are typically made as extruded, orientated tubes that are only a little bit bigger than the bottle's neck ring and cap (Manukonda Keerthi, 2014).

Figure 8 Shrink Seals and Bands

Breakable Caps

When someone tries to open one of these caps, it breaks. In addition to offering exterior tamper evidence, these caps can be used in conjunction with interior seals to give double security (Manukonda Keerthi, 2014).

Sealed tubes

The tube's mouth is sealed, and in order to get the product, the seal must be broken.

Shrink tubing

A packaging design known as a flexible pouch is one that can offer a package that is both tamper-resistant and, with the right material choice, has a high level of environmental protection. During the product filling process, either vertical or horizontal forming, filling, and sealing (f/f/s) machinery is typically used to create a flexible

Figure 9 Shrink Tubing

3. Containers for semi solid and pressurized products

3.1. Collapsible Metal and Plastic Tubes

- Its small opening keeps unused portions of the contents from becoming seriously contaminated.
- Because the patient is less likely to remove too much, waste is decreased.
- Microbial contamination and oxidative or hydrolytic degradation of the remaining contents are decreased because, unlike in conventional containers, when a portion of the preparation is expelled, it is not replaced by an equivalent volume of air.
- Applicators with nozzles can be installed to make it easier to administer medication into bodily cavities like the vagina or nose. Although tin, lead, tin-coated lead, and plastics are also utilized, aluminium makes up the majority of collapsible tubes. Because aluminium tubes have an oxide film on their surface, they are resistant to corrosion.

3.1.1. Glass plastic pots

Good substitutes are cylindrical, wide-mouthed, squat pots made of glass or appropriate polymers with a screw made of plastic (or infrequently metal) or, in the case of plastics, a slip-over top. Glass pots come in a variety of colours, including clear, amber, and opal white. Glass is stable, inert, and hygienic; it also permits transparency and makes the content visible. Compared to plastics, they are more costly unless the patient returns them for reuse (Manukonda Keerthi, 2014).

3.1.2. Aerosols

The product is released through a valve in pressurized packages. When choosing the packaging for any product, the pressure used to force the product out is a crucial factor. Pressurized system packaging of medicinal active substances. Aerosols rely on the force of

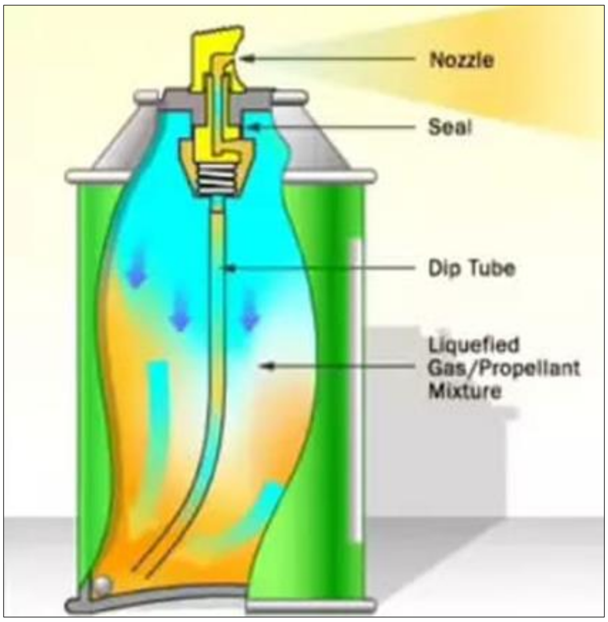

Figure 10 Aerosol

liquid or pressurized gas to force their contents out of containers. It is possible to remove a dose without contaminating the materials. Stability is improved. for these materials negatively impacted by moisture and/or oxygen. Sterility can be preserved throughout the dispensing of a dose when it is a crucial consideration (Manukonda Keerthi, 2014).

3.1.3. Container for liquid /Parenteral

Glass or plastic containers are used to package injectable compositions. Ampoules, syringes, vials, bottles, cartridges, and bags are all part of the container system. All ampoules are made of glass, while all bags are made of plastic. Rubber components for syringe and cartridge seals, rubber plungers, and rubber stoppers for vials and bottles. Glass bottles with screw tops made of aluminium are used to package irrigation solutions. A container that contains a quantity of medication meant for a single dose and that, once opened, cannot be sealed again with guarantee that sterility has been preserved is known as a single-dose container. These containers consist of prefilled syringes and cartridges as well as fusion-sealed ampoules (Manukonda Keerthi, 2014).

3.1.4. Single dose containers

A container that contains a certain amount of the preparation meant to be used all at once or in part.

Figure 11 Single Dose Container

3.1.5. Multi dose containers

This hermetic container allows successive sections of the contents to be withdrawn without compromising the strength, quality, or purity of the remaining pieces (vials). Typically, the tool is a spoon or a 5-milliliter cup.

Figure 12 Multi Dose Container

3.1.6. Well closed containers

Prevent the product from becoming contaminated by undesirable foreign substances and from losing its contents while being used.

3.1.7. Air tight containers:

Are impenetrable to gases, liquids, and solids when used and stored normally the container must stay airtight after reclosing if it will be opened more than once.

3.1.8. Light resistant containers

Light-resistant containers are necessary for a lot of pharmaceutical items. Generally speaking, a container composed of high-quality amber glass or an opaque material that resists light will minimize light transmission enough to safeguard a medication that is sensitive to light. Plastic can be treated with substances known as ultraviolet (UV) absorbers to reduce the transmission of brief UV radiation. The coextruded two-layer, high-density polyethylene bottle, which consists of an outer layer of white polyethylene coextruded with an inner layer of black polyethylene, is a recent development in plastic packaging. The container offers moisture protection and light resistance that surpasses that of amber glass. It is being utilized more and more in pill and capsule packaging to shield the contents from radiation with a wavelength between 290 and 150 nm (Manukonda Keerthi, 2014).

3.2. Closures

3.2.1. Threaded Screw Cap

When used, the screw cap eliminates surface imperfections and protects the enclosed material both chemically and physically. Typically, the screw cap is composed of metal or plastics. Both thermoplastic and thermosetting materials are utilized in plastics, and the metal is typically aluminium or tinplate. The screw cap's thread meshes with matching threads molded into the bottle's neck when it is put on.

Figure 13 Threaded Screw Cap

3.2.2. Lug Cap

The thread cap and the lug cap are comparable. Instead of a continuous thread, the glass finish merely has an interrupted thread. It pulls the cap down to the container's sealing surface by engaging the lug on the cap sidewall. It is utilized in both vacuum and ambient situations.

Figure 14 Lug Cap

3.2.3. Crown Caps

This type of cap has hardly altered in over 50 years and is frequently used as a crimped closure for beverage bottles (Arif sabah, 2014)

Figure 15 Crown Caps

3.2.4. Pilfer proof Closures

With the exception of its longer skirt, the pilfer-proof closure is comparable to the conventional roll-on closure. Below the threaded section, this extra length forms a bank that is secured to the basic cap by a number of thin metals "bridges." The bridges shatter when the pilfer-proof lid is removed, leaving the bank on the container's neck in place. The detachable band shows that the package has been opened, and the closure is readily resealed. In order to remove the cap, torque is required (Lachman, 2009).

3.2.5. Roll-On

The aluminium roll-on cap needs to be properly resealed, opened with ease, and sealed tightly. It is widely used in the packaging of chemicals, pharmaceuticals, food, and beverages. Materials that are easy to shape, like aluminum or other light-gauge metal, are needed for the roll-on closing. For use on glass or plastic bottles and jars, roll-on closures come in three varieties: resealable, non-resealable, and theft-proof.

Figure 16 Roll-on

3.3. Suppositories Package

- These strips come in pouch-style packaging and are made of four layers of material: poly, aluminium, poly, and paper (with the poly inner layer and the paper outermost layer). There are three reasons why strip packs are better than blister packs.
- The suppository can be readily withdrawn without breaking, unlike blister packs, which frequently do.
- Unlike strip packs, blister packs frequently need to be refrigerated to prevent shape deformation.
- Unlike blister packs, which are typically made of pvc, strip packs are made of four layers of material, including aluminium, which has superior moisture barrier qualities and makes the product more stable.

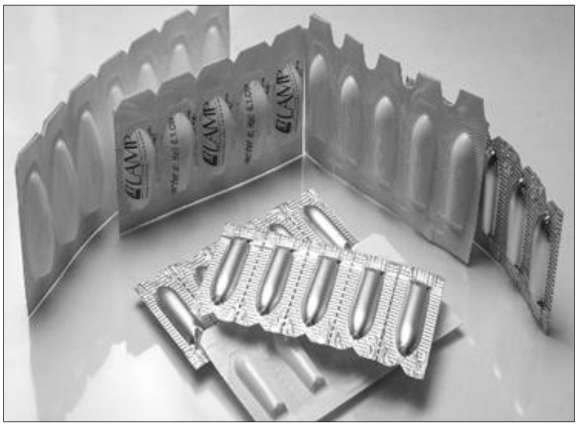

Figure 17 Suppositories

4. Material Type of Packaging

- Glass
- Plastic
- Metal
- Rubber

4.1. Glass

These must be sturdy, stiff, impermeable, and chemically inert in order to receive FDA approval. Glass is a common material for medicine packaging. Glass made of limestone, cullet, soda ash, and sand.

4.1.1. Advantages

- They are transparent.
- Non-reactive.
- Readily labelled.
- Affordable.
- Have excellent protective properties.
- Accessible in a large range of forms and sizes.

4.1.2. Disadvantages

- Glass breaks quickly.
- It weighs a lot.

4.1.3. Types of Glass

Table 1 Types of glass, their composition properties & uses (U.K JAIN, 2009)

Type of glass	Main Constituents	Properties	Uses
Type-1 Borosilicate glass e.g. Pyrex, Borosil	SiO2 B2O3, Al2O3 Na2O+CaO	Has high melting point so can withstand high temperature. Resistant to chemical substances0. Reduced leaching action.	Laboratory glass apparatus. For injections and, for water for injection
Type-II Treated soda-lime glass	Made of soda lime glass. The surface of which is treated with acidic gas like SO_2 (i.e. dealkalised) at elevated temperature(5000 C) and moisture.	The surface of the glass is fairly resistant to attack by water for a period of time. Sulfur treatment neutralizes the alkaline oxides on the surface, thereby rendering the glass more chemically resistant.	Used for alkali sensitive products Infusion fluids, blood & plasma.large volume container
Type-III Regular soda-lime glass	SiO2, Na2O, CaO	It contains high concentration of alkaline oxides and imparts alkalinity to aqueous substances. Flakes separate easily. May crack due to sudden change of temperature.	For all solid dosage forms (e.g. tablets, powders). For oily injections Not to be used for aqueous injection Not to be used for alkalisensitive drugs.
Type NP Non-parenteral glass or General-purpose soda-lime glass.			For oral and Topical purpose Not for ampoules.
Neutral Glass	SiO2, B2O3, Al2O3 Na2, K2	They are softer and can easily be moulded good resistance to autoclaving Resistant to alkali-preparations with pH up to 8) Lower cost than borosilicate	Small vials (<25 ml) Large transfusion bottles
Neutral Tubing for Ampoules	SiO2B2O3 Al2O3 Na2 K2	In comparison to neutral glass its melting point is less. After filling the glass ampoules are sealed by fusion and therefore the glass must be easy to melt	Ampoules for injection.
Coloured glass	Glass + iron oxide	Produce amber colour glass Can resist radiation from 290,400,450nm UV Visible.	For photosensitive products.

- Type I – Borosilicate Glass
- Type II – Treated Soda-lime glass
- Type III – Regular Soda-Lime Glass
- Type NP – General Purpose Soda-Lime Glass.

4.1.4. Type I – Borosilicate Glass

Glass that is extremely durable and chemically inert; glass that substitutes boron, aluminium, and zinc for alkali and earth cations. Because of its high melting point and ability to tolerate high temperatures, it is used to contain strong acids, alkalis, and all kinds of solvents. Main ingredients: SiO2-80%, Al2O3-2%, Na2O, and Cao)6% Pyrex and borosil, for example.

Applications: Glass equipment in laboratories, water injection

4.1.5. Type II – Treated Soda-lime glass

Compared to Type I glass, these are more chemically inert. Soda-lime glass that has been de-alkalized or treated to eliminate surface alkali is used to make Type II containers. "Sulphur treatment" de-alkalizes the glass surface, preventing bottles from blooming or deteriorating (Vikas Pareek)4. As a result, sulphur treatment makes the glass more resistant to chemicals by neutralizing the alkaline oxides on its surface. Applications include high volume containers, blood and plasma, infusion fluids, and alkali-sensitive goods.

4.1.6. Type III – Regular Soda-Lime Glass

Averagely resistant to chemicals, untreated soda lime glass. Its quality is the lowest. Alkali-sensitive products shouldn't be made with this kind of glass. main ingredients: Cao, SiO2, and Na2O. Applications: topical, oral, and not ampoules (puja saha)

4.1.7. Type NP – General Purpose Soda-Lime Glass.

It is composed of soda lime glass and is applied topically and orally. Its hydraulic resistance is the lowest. It works well with solid liquid semisolids but not with parents.

4.1.8. Coloured Glass

Light-sensitive products that don't let UV rays through are made of coloured glass. Parents shouldn't be prepared using coloured glass.

4.2. Plastic

Pharmaceutical products are packaged in plastic. These containers are incredibly resilient to leaks and breaking.

4.2.1. Advantages:

- Inexpensive.
- It cannot be broken.
- It comes in a range of shapes and sizes.
- Its protection power is good.
- Transportation ease.
- It weighs very little.

4.2.2. Disadvantages:

Plastic has low physical stability due to a number of drawbacks, including contact, adsorption, absorption, and lightness.

Table 2 Types of packing (P.D Bairagi, 2017)

Package type	Type of formulation can be packed	Minimum quality of glass that can be used
Ampoule	Aqueous Injectables Of Any Ph Aqueous Injectables Of pH Less Than 7 Non- Aqueous Injectables	Type I Type II Type III
Vial	Aqueous Injectables of Any pH Aqueous Injectables Of pH Less Than 7 Non-Aqueous Injectables Dry Powders for Parenteral Use (Need To Be Reconstituted Before Use)	Type I Type II Type III
Bottles and Jars	Tablets, Capsules, Oral Solids & Other Solids For Reconstitution.	Bottles and Jars
Dropper	Auxiliary Packaging Device with Certain Kind of Products	Type IV
Aerosol Container	Aerosol product (solution, suspension, emulsion or semisolid type)	Type I

4.2.3. Types of Plastics

There are two types plastic material:

- Thermosetting type
- Thermoplastic type
  - **Thermosetting type-:** They do not turn into liquid when heated, but they do become pliable. For instance, phenol formaldehyde, urea formaldehyde, and Melamine formaldehyde.
  - **Thermoplastic type** Heating this plastic will soften it, while cooling will harden it. polystyrene, nylon, PVC, polyethylene, and polypropylene, among others.

4.2.4. Polyethylene

The polymer is polyethylene. It is employed as polyethylene with both high and low densities. Though it offers limited protection from oxygen and other environmental gasses, high density polyethylene offers protection against moisture. Properties: chemical resistance, strength, and stiffness. For squeeze bottles, plastic is preferred over low density polyethylene. Properties include ease of processing, moisture resistance, and flexibility.

Polypropylene (PP)

Polypropylene resists heat sterilizing well. When flexed, it resists cracking well. It has a greater melting point than polyethylene, at 170°C. It works well with things that need to be sanitized and packaging that can be boiled. Polypropylene's brittleness at low temperatures is one of its main drawbacks. It resists strong acids and alkalis very well. It works well with intravenous bottles, tablet containers, and closures.

Polyvinyl Chloride (PVC)

It has a strong oxygen barrier and clarity. Plasticizer can be added to it to make it softer and more flexible. PVC has a melting point of 160°C and very little thermal stability. PVC is used to make bypass sets, blood and blood component containers, etc (Nasa) .

Polystyrene: It is derived from petroleum. solid, non-biodegradable plastic that is crystal transparent. Unsuitable for items that are liquid. In addition to having a high gaseous permeability and water vapor transfer, polystyrene is readily stretchy and breakable. For further strength and quality, polystyrene is mixed with rubber and acrylic compounds. These are divided into three categories according on composition: super impact, high impact, and intermediate impact packing.

4.3. Metals

Containers are constructed from metal. Lead, tin, stainless steel, aluminium, and tin-plated steel are the metals utilized.

Advantages

- Metal holders are solid, usually indestructible, and opaque (puja saha).
- They are resistant to chemical attack.
- Allow labels to be written directly on them.
- They are impervious to gases, light, and moisture. They are powerful

Disadvantages

- Among tin, lead, aluminium, and press, these metals are expensive.
- They combine with specific drugs or substances can create dangerous products.
- They are expensive

4.3.1. Aluminium

Aluminium's low weight makes it a popular material. They have a pleasing appearance. For rigid containers like aerosol cans and tubes for effervescent pills, the thickest metal is utilized. Flexible foil, a component of laminated packaging material, uses the thinnest

Advantages

Because aluminium tubes are lightweight, they reduce the product's shipping costs. They also offer the aesthetic appeal of tin at a slightly lower price.

Disadvantages

H2 may develop as a result of the corrosion process. Any material that reacts with the oxide coating has the potential to produce corrosion. (Lukesh Pegu1, 2019)

Uses: Aluminium ointment tubes, Screw capes.

4.3.2. Iron

Pharmaceutical packaging does not use iron; instead, substantial amounts of tin combine the corrosion resistance of tin with the strength of steel. Use: making drain holders, screw caps, and aerosol cans, as well as milk containers (puja saha)

Advantages

- The least expensive metal for pharmaceutical containers is lead.
- It is a soft substance.

4.3.3. Tin

When compared to other metals, it is the costliest. It is defence against chemical assault. Uses: Tin containers are coated with tin and used for foods like milk powder. Some eye ointment is still available today in tubes made entirely of tin.

4.3.4. Lead

Advantages

- The least expensive metal for pharmaceutical containers is lead.
- It is a soft substance.

Disadvantages

Due to the possibility of lead poisoning, lead should never be used alone for internal consumption.

Use: lead tubes for items like chloride tooth paste are used with internal linings.

4.4. Rubber

Long chain polymers of isoprene units joined together within the cis section make up natural elastic. Its primary source is the Heave Brazilians tree, from which, when shallow cuts are made in the bark, latex—which contains 30 to 40% rubber in colloidal suspension—emerges.

4.4.1. Butyl rubber

These are isobutylene co-polymers with 1-3 percent butadiene (Lukesh Pegu1, 2019).

Advantages

- They are comparatively less expensive than other synthetic rubbers.
- They have extremely little water absorption.
- They are permeable to water vapor.

Disadvantages

- Slow degradation occurs over 130°C
- Poor resilience to solvents and oils.

4.4.2. Nitrile rubber

Advantages

The polar nitrile group makes it oil-resistant.

Disadvantage

Both bactericide absorption and extractive leaching are significant.

4.4.3. Chloroprene rubber

These are 1:4 chloprene polymers.

Advantages

- This rubber can withstand oil.
- Good heat stability.

4.5. Silicon rubbers

Advantages

- Extremely low water absorption and permeability (Lukesh Pegu1, 2019).
- poor tensile strength.
- heat resistance (up to 2500c).

Disadvantage

It is very expensive.

4.6. Function of Packaging

4.6.1. Identification

The printed packaging and its ancillary printed components give both identification and information [19].

4.6.2. Containment

One of the most important ways to ensure that pharmaceuticals are contained is through packaging. The unique needs of the product, together with the production and distribution procedures, must all be considered when designing packaging of the highest calibre. This entails making sure the packaging doesn't leak, stops the product from diffusing or penetrating, and has the strength to sustain normal handling while safely containing its contents.

4.6.3. Protection-

To guarantee the product's purity and efficacy, it must be shielded from harmful external factors such light, moisture, air, biological contamination, mechanical damage, and tampering.

4.6.4. Presentation and Information

In order to provide important information about pharmaceutical medicines, packaging is essential. Labels and packaging inserts are reliable sources of this important information for patients.

5. Conclusion

In the pharmaceutical industry, pharmaceutical packaging is a crucial technology. Pharmaceutical product packaging has a significant impact on the product's stability, patient acceptability, transportation, etc. Packaging gives the patient useful information. Packaging is crucial to the pharmaceutical product's protection. Eco-friendly packaging that is naturally biodegradable is being used these days. This review article concentrated on the types of packaging and the materials used for them.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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