

Features of Packaging from Polymers in Pharmaceutics

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Abstract: The article considers various issues related to the peculiarities of using a package of polymers in pharmaceutics. The main types of packaging from polymers for pharmaceutical preparations are analyzed. The main requirements for materials for packaging various drugs are defined. Classification of pharmaceutical preparations by the method of their application and packaging is presented. The classification of pharmaceutical preparations according to the dosage type, the type of treatment, the method of their packaging, and general requirements has been developed. It is shown that the proposed classifications became a prerequisite for the selection of eight basic pharmaceutical preparations types and materials for them. The diagrams of the percentage materials ratio in selected pharmaceutical preparations are constructed. The analysis of the corresponding diagram showed that polypropylene (PP) and polyvinyl chloride (PVC) are most widely used. The most widespread use of materials for packaging pharmaceuticals has been analyzed the main polymers properties have been identified, the presence of which is necessary for the manufacture of packaging.

Keywords: Pharmaceuticals, packaging, preparations, polymers, requirements.

INTRODUCTION

Pharmaceutical packaging is a very complex process that is provided by a separate industry. This is due to the fact that the issues of quality and safety are of paramount importance. The use of advanced technology and high-quality plastic materials for pharmaceutical packaging is one of the fundamental factors for success in the market [1].

For the development of packaging in pharmaceuticals, polymeric materials – of various origins – are actively used. The development of new medical materials intended for contact with pharmaceuticals is a complex task. The polymer should have a certain set of properties and characteristics, but they are not always ideal for packaging. There are several procedures. Apart from that selection of containers and sealing materials. There are selective ranges of materials that are found in the drug industry and when it comes to be used in the drug industry. The range of materials used for packing and sealing are tested for quality control, compatibility and reliability. Sampling for medicinal product retention, homogeneity in quality, etc [2].

According to the "Good Manufacturing Practice" for the drug industry, the high quality packaging method and packaging materials must be used in the following categories [3]:

- Does not allow penetration of the product.

- The packaging material should not react with the medicinal ingredients and should not change the formulation as well.
- The packaging materials should be consistent and strong enough even at severe external influences such as heat, light, moisture, dampness, oxygen, biological or mechanical contamination, etc.

For example, reduced permeability of water vapor can lead to carburization and almost complete loss of the tablets ability to disintegrate, increased permeability of water vapor reduces the tablets strength. If the strength of the packaging is low, then under increased physical stress (impact during fall, compression), it undergoes premature failure, leading to a breakdown in the integrity of the packaging and damage to tablets. Increased oxygen permeability promotes the aerobic microorganisms development of. All this can ensure a rational distribution of the walls thickness along their contour. Increased oxygen permeability promotes the development of aerobic microorganisms.

Proper testing should be done to ensure the compatibility of the packaging ingredients and the pharmaceutical products present inside the container. This, ultimately, determines the need to consider the possibility of using a polymers package in pharmaceuticals as the main objective of this study.

MATERIALS AND METHODS

Related work

In [4] the aim at explaining basics of polymers based materials from different resources and their chemistry along with practical applications which present a future direction in the pharmaceutical industry. The work focuses on polymeric materials in ocular drug delivery systems [4]. describes the historical development of polymers and the basis of their classification. Based on their origin and mode of synthesis, biodegradable polymers are categorized into various classes. The structure, chemistry, biocompatibility, and biodegradability of these biodegradable polymers are discussed and their applications in pharmaceutical and medical fields are summarized.

In [5] presented review of the various packaging elements for pharmaceutical product is aimed at ensuring that medicines arrive safely in the hands of the patients for whom they are prescribed. The paper presents: requirements in the international pharmacopoeia; requirements for dosage form containers; quality assurance aspects of packaging; packaging materials and closures; repacking, relabelling and dispensing.

In [6] reviewing the various aspects of packaging like materials used for packaging, types of packaging as well as recent trends of pharmaceutical packaging in pharmaceutical market. In work, the packaging of pharmaceutical preparations is divided according to dosage forms: solid dosage forms, semisolid, pressurized product and liquid. Types of container used as primary packaging for liquid orals are: single dose containers, multi-dose containers, well-closed containers, airtight containers, light – resistant container. For solid dosage forms: tamper – evident containers, strip packages, blister packages, child

resistant containers. An author also provides the most complete accounting of nano-enabled packaging of pharmaceutical products in various markets around the globe. The main objective of this review is to understand the current state of nano-enabled packaging in the pharmaceutical industry, market opportunities, the companies involved, technologies being pursued and intellectual property (IP) trends.

The materials in manufacturing and packaging systems as sources of elemental impurities in packaged drug products are considered in [7]. This review article contains the information compiled from the available body of literature and considers two questions:

- What elemental entities are present in the relevant polymers and materials and at what levels are they present?
- To what extent are these elemental entities leached from these materials under conditions relevant to the manufacturing and storage/distribution of solution drug products?

In [8] study was a screening study limited to the investigation of the physical stability of a selection of moisture-sensitive repackaged tablets. However, although the physical stability is acceptable, the chemical stability and dissolution rate may be altered. The physical tests outlined are simple but could be suitable for selecting candidates for further chemical stability testing.

In [9] review of packaging of non-injectable liquid pharmaceuticals. In the present review, we focus on the packaging aspects of non-injectable liquid formulations. Different packaging materials, which can be used for packaging of non-injectable liquid formulation, are discussed. Regulatory aspects of Unlisted State Food and Drug Administration (USFDA) and European Medicines Agency (EMA) are also highlighted.

Traditional packaging for pharmaceuticals

The general classification of packaging requirements for polymers is shown in Figure-1 [10].

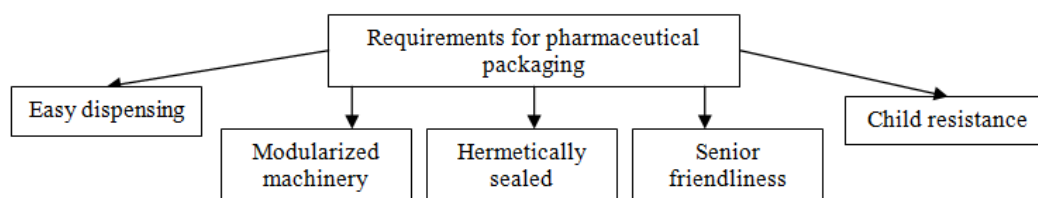


Fig-1: General classification of packaging requirements for polymers

There are two main types of packaging: strip packaging and bottle packaging. Packaging is usually used for packing tablets and capsules. A strip package is formed by feeding two webs of a heat sealable flexible

film through a heated crimping roller. The product is dropped into the pocket formed before forming the final set of seals. A continuous strip of packets is formed which is cut to the desired number of packets in length.

The materials used for strip package are cellophane, polyester, polyethylene, polypropylene, polyvinylchloride (Figure-2(a) [11].

Bottle packaging – made of glass or plastic are used for storing both liquid medications and dry syrup.

The shape of bottles which will be applied for pharmaceutical industry should remain with less marked neck and flat bottom in order to protect medication from external influences. Bottles stay compatible for filling machines as well as capping machines (Figure-2(b) [12, 13].



Fig-2: Main types of packaging (strip and bottle packaging)

Plastics are the most important class of packaging materials [14]. As a result of today multitude of plastic applications there is a corresponding enormous variety of plastic materials. The polymer matrix as well as the incorporated plastic additives can be made to differ in such a variety of ways with respect to their chemical composition and structure that one finds or can develop a tailor made product for every application.

Plastic packaging of pharmaceuticals is becoming quite promising and the latest trends continue to form research and development in this field. As a

consequence, the range of plastics applications for these purposes continues to expand with each passing year.

RESULTS AND DISCUSSION

Investigation of the types and characteristics of polymeric packaging in pharmaceuticals

In order to choose the material for packaging, for example, tablets, it is necessary to analyze the interaction of pharmaceutical preparations and packaging. We propose a classification of pharmaceutical preparations by the method of their application and packaging for them Figure-3.

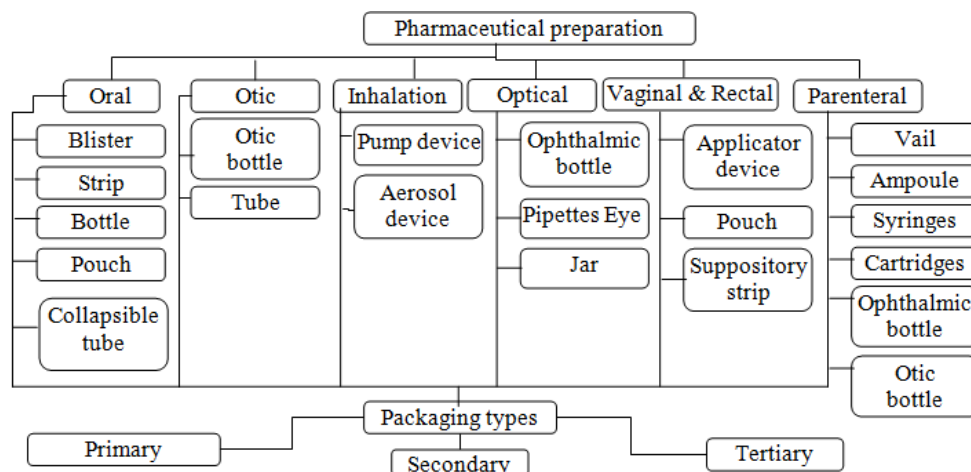


Fig-3: Classification of pharmaceuticals by their use and packaging

Blister packing component. The four basic components of pharmaceutical blister packages are: 1. The forming film (forming films account for approximately 80–85% of the blister package). 2. The lidding material (lidding materials make up 15–20% of the total weight of the package.). 3. Heat seal coating.

Blister packing [15, 16]: 1. Blister packaging is a type of pre-formed plastic packaging used for small consumer goods. 2. The two primary components of a blister pack are the cavity made from either plastic or aluminium - and the lidding, made from, paper, plastic

or aluminium. 3. The cavity contains the product and the lidding seals the product in the package.

Parenteral it is application: intramuscular, intravenous, intradermally, subcutaneously, intra-arterial, in the cavity, intraosseous, in the subarachnoid space. Parenteral preparations. These are usually supplied in glass ampoules, bottles or vials, plastic bottles or bags, and prefilled syringes, which are coloured in the case of light-sensitive substances [5]. Packaging types: 1. Primary packaging – is the materials that first envelops the product and hold it. 2. Secondary packaging is outside the primary packaging – used to group primary packages together (corrugated fibers, box and etc.). 3. Tertiary packaging used for

bulk handling, warehouse storage and transport shipping. The most common form is a palletized unit load that packs tightly into containers. Example: barrel, container, edge protector.

It is determined that polymers are more often used for primary packaging and in some cases for secondary packaging. Types of packaging: strip packaging and bottle packaging (ampoule, bottles, vial).

We propose a classification of pharmaceutical preparations according to the dosage type, the type of treatment, the packaging method and the general requirements for them (Figure-4).

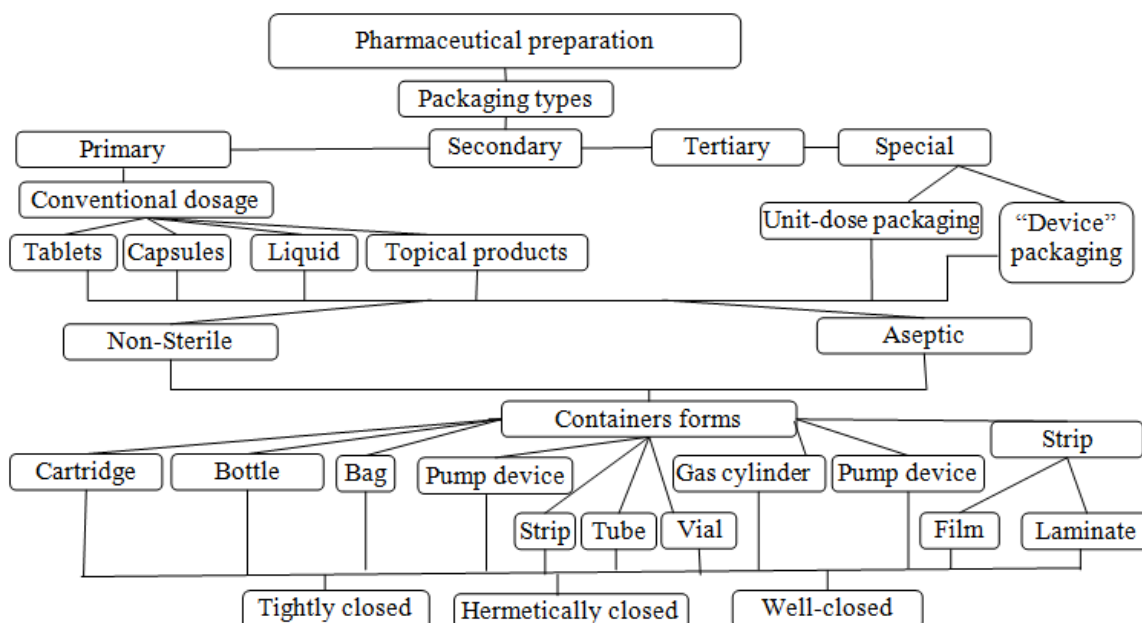


Fig-4: Classification of pharmaceuticals by dosage type, type of treatment, packaging method, and general requirements

Let's special packaging includes: unit-dose packaging and "Device" packaging. Unit-dose packaging. This packaging guarantees safer medication by reducing medication errors; it is also more practical for the patient. It may be very useful in improving compliance with treatment and may also be useful for less stable products [17].

"Device" packaging. Packaging with the aid of an administration device is user-friendly and also improves compliance. This type of packaging permits easier administration by means of devices such as prefilled syringes, droppers, transdermal delivery systems, pumps and aerosol sprays. Such devices ensure that the medicinal product is administered correctly and in the right amount. Semi solid dosage forms like ointments, creams etc. are packed in metallic collapsible tubes [17].

Let's conventional dosage includes: tablets, capsules, liquid, topical products. In topical formulations, including the following:

- A cream formulation combined with tablets for a semi-synthetic pleuromutilin derivative, where we also developed, manufactured and packed both products for clinical trials.
- A thermally-reversible gel for a psoriatic condition, currently in field trials.
- Permeation studies and formulation development for the delivery of poorly-soluble matrix metalloproteinase inhibitors through horse shins.
- A buccal liquid gel formulation to treat xerostomia, currently in Phase II clinical trials.
- A thermally-reversible gel to promote wound healing, currently in pharmacokinetic (PK) studies to investigate the mechanisms of its absorption.
- A vaginal tablet or pessary for HIV treatment that transforms rapidly into to gel after administration.

Selection of materials for polymers packaging in pharmaceuticals

When creating a package for pharmaceuticals, its material must fully meet the specified conditions. Selection of packaging material is product specific and one material cannot be suitable for packaging of all the products.

However, metal containers are used for the packaging of topical aerosols while glass and plastic containers are used for the packaging of oral and ophthalmic liquid formulations. Choice of packaging material depends upon the number of factors including product stability during processing and storage conditions, type of dosage form, route of administration, chemical nature of the drug [9].

Thus, when selecting the material of pharmaceutical preparations, their purpose should be taken into account. And it is important to determine the materials properties in order to perform their functions.

When solving the problem of the polymers choice for pharmaceutical preparations, it is important to analyze the basic properties of various polymers, their advantages and limitations in their application, as well as the classification of polymers for operational purposes, with recommendations for their rational use. Also, when selecting polymers, recommendations for

processing methods, preparation conditions for processing and molding are taken into account.

The basic requirements to the materials are defined:

1. Protection from environmental conditions.
2. Non-reactive with the pharmaceutical product.
3. Non-toxic.
4. Adoptable to commonly employed high speed packaging equipments.
5. Properties of plastic materials:
 - the packaging itself does not have an adverse effect on the product (e.g. through chemical reactions, leaching of packaging materials or absorption);
 - the product does not have an adverse effect on the packaging, changing its properties or affecting its protective function.

The suitability of packaging or packaging material for any particular requirements and conditions can only be ascertained through detailed packaging and stability studies on the product concerned.

The results of the pharmaceutical preparations types analysis and on the basis of the proposed classifications of Figure 3 and Figure 4 are summarized in Table 1.

Table-1: Types of pharmaceutical preparations and their materials

Materials	Type of pharmaceutical preparations							
	Bottles	Jars	Blister	Ampoules	Vials	Tubes	Strip	Cartridges
Polyethylene terephthalate (PET)	+	-	-	-	-	-	-	-
High Density Polyethylene (HDPE)	+	-	-	-	+	+	-	-
Low-density polyethylene (LDPE)	+	-	-	-	+	-	-	-
Linear Low Density Polyethylene (LLDPE)	-	-	-	-	-	+	-	-
Polyvinylidene chloride (PVDC)	-	-	+	-	-	-	-	-
Polypropylene (PP)	+	+	+	+	+	+	+	-
Polyvinyl chloride (PVC)	+	-	+	+	+	-	+	-
Polycarbonate (PC)	+	-	-	-	-	-	-	-
Polystyrene (PS)	-	+	+	-	+	+	-	-
Polyethylene (PE)	-	-	-	+	+	-	-	+
Polyethersulphone (PES)	-	-	-	-	-	-	-	+
Polychlorotrifluoroethylene (PCTFE)/PVC laminates	-	-	+	-	-	-	-	-
Styrene	-	-	-	-	+	-	-	-
Poly(ethylene-vinyl acetate) (PEVA)	-	-	-	-	-	+	-	-
Orientated polyamide (OPA)	-	-	+	-	-	-	-	-

The diagram of the percentage materials ratio in selected pharmaceutical preparations is shown in Figure-5

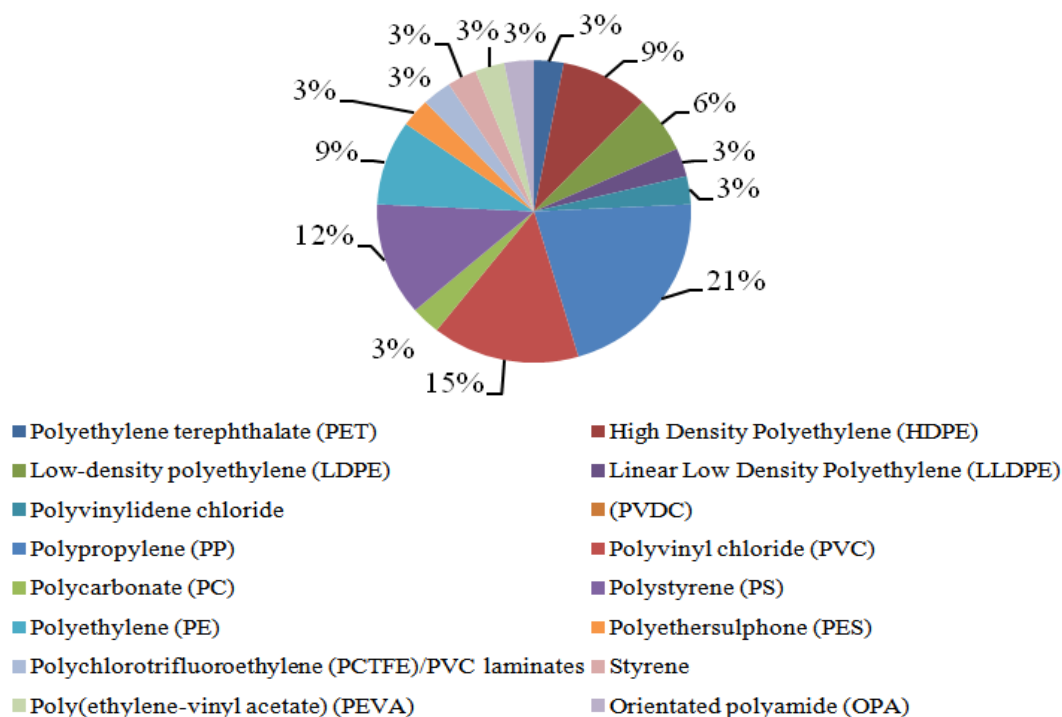


Fig-5: Diagram of the percentage materials ratio in selected pharmaceutical preparations
Packaging recommends presented in Table-2

Table-2: Packaging recommends

Materials	Clarity	MVTR*	O2**	CO2**	Impact Strength	Recycle Code
PET (Oriented or Stretch Blown Polyethylene Terephthalate)	Excellent	2.0	75	540	Good	1
HDPE (High Density Polyethylene)	Poor	0.5	4,000	18,000	Good	2
PVC (Polyvinyl Chloride)	Good	3.0	150	380	Fair	3
PP (Polypropylene)	Poor	0.5	3,500	7,000	Fair	5
PS (Polystyrene)	Excellent	10.0	6,000	18,700	Poor	6

*MVTR stands for Moisture Vapor Transmission Rate in g-mil/100in. 2/24hr. MVTR is a measure of the passage of gaseous H2O through a barrier. The lower the rate, the longer the package protects its contents from moisture and ensures the moisture content of the product remains the same.

**O2 and CO2 stand for Oxygen Transmission Rate (OTR) and Carbon Dioxide Transmission Rate (COTR) in cm³-mil/m²/24hr. OTR and COTR are measures of the amount of gas that passes through a substance over a given period. The lower the readings, the more resistant the plastic is to letting gasses through.

Consider the polymers properties from the view point of the above requirements. Properties of

selected plastic materials for pharmaceutical product in Table-3.

Table-3: Properties of plastic materials for pharmaceutical product

Materials	Properties	Example pharmaceutical product
PET (Oriented or Stretch Blown Polyethylene Terephthalate)	clarity, lightness, strength, toughness, barrier to liquid and gas	
HDPE (High Density Polyethylene)	stiffness, strength, toughness, resistance to moisture, permeability to gas, ease of processing	
PVC (Polyvinyl Chloride)	versatility, ease of blending, strength, toughness, clarity, transparency	
PP (Polypropylene)	strength, toughness, resistance to heat, chemicals, grease and oil, barrier to moisture	
PS (Polystyrene)	versatility, clarity, easily formed	

DISCUSSION OF THE RESULTS

With the proposed classifications of materials for the pharmaceuticals packaging, it is possible to determine the packaging type, the form of the drug and the rational material whose properties are important to take into account, as they affect the quality, compatibility and reliability of the drug.

The proposed classification in Figure 4 differs from existing ones in that it contains special packaging types, which can be unit-dose packaging or "device"

packaging, which allows to expand the range of dosage pharmaceuticals forms.

To conduct research on the characteristics of the polymers packaging in pharmaceuticals, the most widely used types of pharmaceutical preparations are selected and the materials for them are determined. The result was a diagram of the percentage materials ratio in selected pharmaceutical preparations.

As a result, for the selected polymers that are used for packaging most forms of drugs, the table recommends packaging. Data from the table can be used as a guideline when selecting or creating a new material for packaging.

CONCLUSION

As a result of the polymers packaging features studies in pharmaceuticals, the existing range of polymers and dosage forms is disclosed for their application.

The analysis of possible pharmaceutical preparations from polymers is carried out. The main requirements for materials for packaging various drugs are defined.

As a result of the polymers analysis, the following classifications are presented: pharmaceutical preparations by the method of their application and packaging; pharmaceutical preparations by type of dosage, type of treatment, their method and packaging and general requirements. The proposed classifications became a prerequisite for the selection of eight basic types of pharmaceutical preparations and materials for them.

As an analysis consequence of the polymers use for different dosage forms, a percentage chart of the materials in the selected pharmaceutical preparations was constructed. The diagram shows that polypropylene (PP) and polyvinyl chloride (PVC) are most widely used.

Analyzing the most widely used materials for the pharmaceuticals packaging, the following properties of polymers that are necessary are identified: clarity, chemicals, stiffness, strength, toughness, resistance to moisture, permeability to gas, ease of processing, versatility.

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