Recent Advancements in Pharmaceutical Packaging

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Submission: 2 June 2017
Accepted: 10 June 2017
Published: 25 June 2017

Keywords: pharmaceutical packaging, compliance, storage, stability, packaging materials, recent advancement.

ABSTRACT

The pharmaceutical packaging market is constantly advancing and has experienced annual growth of at least five percent per annum in the past few years. Packaging is both art and science of enclosing or protecting the products. The main role of pharmacist is to maintain quality of pharmaceutical products during storage, transportation, delivery, sale and use. Containment, convenience and compliance for a product during storage, carriage, display and until the product is consumed. Pharmaceutical packaging is a multiphase broad process which is classified into primary, secondary and tertiary level. Presently, numerous advancements and changes are taken into consideration for product safety, stability and patient’s compliances. Therefore in the present review various aspects of conventional pharmaceutical packaging and recent advancement have been delineated.
INTRODUCTION

Packaging denotes an amassment of different packaging materials which encase the pharmaceutical product from the time of manufacturing to the cessation of the utilizer. Encasing of drugs is consequential for life-preserving drugs, medical treatments, medical contrivances and incipient products like medical nutritionalis. Pharmaceutical packaging productis a broad process and a multifaceted task. It is responsible for providing lifesaving drugs, medicinal treatments and new products like medicinal nutritionalis in every dosage form. Packaging must provide protection against environmental condition such as physical, chemical and biological hazards and it must be economical. The external image of the package should provide clear and concise product identification. Package should provide adequate information regarding route of administration storage, condition, batch number, expiry date, manufacturer’s name, and address and product license number. It should be in acceptable design and should assist in patient compliance.

Nowadays numerous changes are occurring in the pharmaceutical industry. Manufacturers of drugs face pressure to reduce cost from government and patients. The shift in growth from initial phase to mature phase in the market due to the demand for low cost drugs is predominant. This leads to the reduction of price. Poor patient adherence is a further problem contributing to rising health care cost meanwhile manufacturers and investors want to see much lower failure rates and a higher return on drugs in response. The drug development cycle which involves various aspects such as compliance and easy to use techniques helps to determine ways to success earlier. The industry adopted a more patient centric focus, paying close attention to the drug development preferred by patients intended by their doctors. Dosing regimens, methods of delivery and product packaging are now considered much earlier in development of drugs cycle.

New ideas of dynamic packaging, intelligent packaging and nanotechnology offers arrangements which play a vital part to improve or observing food quality and security and amplifying time span of usability.

SELECTION OF PACKAGING

The packaging materials used should possess the ideal characteristics such as

1. Protection from environmental conditions such as humidity, temperature etc.
2. The product packed in the container must be non-reactive to the container enclosing it.

3. The odor and the taste of the product must not be altered.

4. The packaging material must be non-toxic.

5. FDA approved packaging materials must be used.

6. Requirements such as tamper-resistance must be maintained and

7. The packaging material to be used should be easily adaptable to high speed packaging equipment.\textsuperscript{11}

**ADVANTAGES OF PACKAGING**

1. The product uniformity is maintained during packaging.

2. The integrity of dosage form is maintained.

3. The side effects are minimized and the inert environment is maintained and protected from contamination.

4. Packaging enhances the shelf life of the product preventing deterioration of the product, thus enhancing better stability.

5. Minimizes the side effects.\textsuperscript{12}

**OBJECTIVE OF PACKAGED PACKAGING**

Packaging and package labeling have several objectives:

- Package should provide adequate information regarding the contents, route of administration, batch number, expiry date, storage condition and manufacturer name and address.

- Package should have acceptable design and assist patient compliance.

- The primary packaging consists of packaging components which have direct contact with the product such as container, cap, label etc. The primary function of these packages is to restrict chemical, biological and climatic hazards which may lead to product decomposition.
The packaging external to primary package is called as secondary packaging. This packaging mainly provides physical protection which is necessary to ensure the safe warehousing and for refilling packaging.3

PHYSICAL PROTECTION

The drugs which are enclosed in the package requires protection from shocks, temperatures, vibrations, compression which are generally caused by improper transportation and handling. So it is necessary to have a package that can resist these problems.

BARRIERS PROTECTION

A barrier from atmosphere is often required in order to prevent from environmental hazards which may be caused by oxygen, water vapour, dust etc. Package permeability is crucial in design, some packages contain oxygen absorbers in order to prevent a drug from oxidation and it helps in extension of drugs shelf life.

INFORMATION TRANSMISSION:

Labels and packages help to provide adequate information related to the drugs and communicate how to use, transport, dispose and recycle of the product. For pharmaceuticals, medical, chemical and food products, some types of information are required by governments.

CONTAINMENT

Small particles or objects are typically grouped together in one objects are efficiency.

Forexample: (a single box of thousands of containers requires less physical handling than thousands of single containers). Dosage form such as liquids, powders need containment.

CONVENIENCE

Packages can have features that add convenience in handling, distribution, opening, closing use and reuse.
MARKETING

Package has been an important factor for several years. It helps to encourage potential buyers to the purchase of product. Graphic design and marketing communication are applied to the surface of package and the point of sale display.⁷

TYPES OF PHARMACEUTICAL PACKAGING

Pharmaceutical packaging is classified into three different types: they are

1. Primary packaging system
2. Secondary packaging system
3. Tertiary packaging system

The primary packaging system contains the product and holds it that those package components actually come in contact with the product or those components that may have direct effect on the product shelf life. Example: ampules, IV containers etc.⁸

Secondary packaging system is outside the primary packaging which stores pharmaceutical packaging in it for their grouping. Example: cartons box etc.

Tertiary packaging system is used for bulk handling shifting of pharmaceutical packages from one place to another. Example: containers, barrels etc.⁹

TYPES OF PRIMARY AND SECONDARY PACKAGING MATERIAL: ¹⁰

Table-1. Types of Primary and Secondary Packaging Material.

<table>
<thead>
<tr>
<th>Material</th>
<th>Type</th>
<th>Example of use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glass</td>
<td>Primary</td>
<td>Ampules or vial</td>
</tr>
<tr>
<td>Plastic</td>
<td>Primary</td>
<td>Ampules, vial and dropper bottle</td>
</tr>
<tr>
<td></td>
<td>Secondary</td>
<td>Wrapper to contain primary pack</td>
</tr>
<tr>
<td>Cardboard</td>
<td>Secondary</td>
<td>Carton box</td>
</tr>
<tr>
<td>Paper</td>
<td>Secondary</td>
<td>Labels, patients information leaflet</td>
</tr>
</tbody>
</table>
Types of containers which are used as primary packaging are as follows:

Primary package for liquid orals is

- **Well closed containers:**

These types of containers provide the protection from shocks, foreign particles and loss during transportation, distribution, sale etc.

![Well Closed Containers](image1.png)

**Fig.1: Well Closed Containers**

- **Air tight containers:**

These types of containers protect the drugs from environmental, physical and chemical hazards. If these containers are intended to be opened on more than one occasions then they remain airtight after reclosed.

![Air Tight Containers](image2.png)

**Fig.2: Air Tight Containers.**
• **Single dose containers:**

This type of container contains a single dose of drug. For e.g. vials or ampoules

![Image of Single Dose Containers](image1)

**Fig.3: Single Dose Containers**

• **Multi dose containers:**

This type of container holds multiple doses and their contents are withdrawn at various intervals e.g.: vials

![Image of Multi Dose Containers](image2)

**Fig.4: Multi Dose Containers**
• **Light resistant containers:**

These containers protect the contents from light. These are made up of the material which does not allow the light to pass through them. E.g.: Amber coloured glass containers.

![Light Resistant Containers](image)

**Fig.5: Light Resistant Containers**

**PRIMARY PACKAGE FOR SOLID DOSAGE FORMS:**

• **Strip package:**

The package is made up of two layers of film. A strip package contains many pockets and each pocket contains single dose of drug.

![Strip Package](image)

**Fig.6: Strip Package**

• **Blister package:**

It is made up of base layer (polyvinylchloride layer) with cavities which contain pharmaceutical product. It provides greater protection than strip package. It contains a lid which is made up of aluminum and paper foil.
Primary package for semi solid dosage forms:

Semi solid dosage forms include ointments, creams and pastes. The containers used for semi solid dosage forms include tubes and plastic containers. Other type of products is also available in market for e.g. Pressurized products. For these types of products the package made up of stainless steel. The package used must be strong enough to control pressure built up in the container.  

Fig.7: Blister Package

Fig.8: Collapsible Tubes
TYPES OF GLASS USED IN PHARMACEUTICAL PACKAGING:

- **BOROSILICATE GLASS/ TYPE 1 GLASS:**

These are used to contain strong acids and alkalis. They are highly resistant and chemically inert glasses, and the alkalis and earth cations of glass are replaced by boron and zinc.

![Borosilicate Glass](image)

**Fig.9: Borosilicate Glass**

- **TREATED SODA LIME GLASS/ TYPE 2 GLASS:**

These are chemically more inert than type 1 glass (Borosilicate). The glass surface is dealkalized by sulpha treatment which prevents blooming from bottles.

![De Alkalized Soda lime Glass](image)

**Fig.10: De Alkalized Soda lime Glass**

- **REGULAR SODA LIME GLASS/ TYPE 3 GLASS**

It is relatively inexpensive, chemically stable, and reasonably hard.30
ADVANCES IN PHARMACEUTICAL PACKAGING: ¹³

- CYPAK’S ADVANCED MEDICATION MONITORING AND REPORT CARD SYSTEMS:

This is an advanced packaging technology can enable patients to communicate with healthcare professionals through printed technology. This record the time and data that a pill was taken based on when it is removed from its blister pack. This allows the patients to log their feedback on side-effects and treatment efficacy and upload it. ¹⁴

This technology holds significant potential for new levels of patient-doctor interface to workout best treatment plan. Sensor-based packaging concepts are best applied in clinical trials. This helps in drug development to establish whether a drug is ineffective or simply not being taken properly.

Cypak’s advanced medication technology is used in targeting clinical trials market, as poor date resulting from non-compliance can be financially devastating in this context. ¹⁵
• **BURGOPAK’S SLIDING CR BLISTER PACK:**

Burgopak healthcare and technology – won the award for the ‘Most Innovative Child Resistant Packaging Design’ at the Pharmapack Paris exhibition. The Burgopak’s sliding CR blister pack can only be opened by applying force at two different points on the packaging. The blister pack and leaflets are coordinated with the outer box, which insures the product is never separated from its packaging.  

![Burgopak’s Sliding CR Blister Pack](image1)

**Fig -13: Burgopak’s sliding CR Blister Pack**

• **PHARMA SMALL HANDS RESISTANT (SHR): A RE-CLOSABLE AND TEAR-RESISTANT CARTON:**

A reclosable and tear-resistant carton is ideal for highly toxic drugs. Stora Enso and Bosch launched Pharma small hands resistant (SHR). Stora Enso Pharma SHR is a child resistant reclosable carton. It is ideal for highly toxic drugs and it is easy to use for senior adults.

It is tested with the highest F=1 rating in the US. It is an innovative paperboard package system it only requires simple squeeze and pull manoeuvre.  

![Stora Enso Pharma SHR](image2)

**Fig -14: Stora Enso Pharma SHR**
**ECOSLIDE –RX SUSTAINABLE COMPLIANCE PACKAGING:**

The pack is made from 100% recycled material using unbleached paperboard and clay coated surface designed to house blister packaging with a low of unsustainable film and foil.

The slide package is very useful and it meets modern expectations for child-resistance and accessibility for seniors. It doesn’t require heat sealing in the manufacturing process that reduces both cost and energy usage.\(^\text{18}\)

![Fig-15: Ecoslide –RX Sustainable Compliance Packaging.](image)

**PREFILLED SYRINGES:**

**SYREEN PREFILLED SYRINGE DESIGN**

Environmental awareness is even starting to extend to the syringe market. It replaces glass with cyclic olefin polymer (COP). This material has allowed secondary packaging altogether as the COP design forms its own outer shell. The ability of packed syringes to clip into place eliminates the need for packing materials like cardboard.\(^\text{19}\)

![Fig-16: Syreen Prefilled Syringes](image)
Advantages of prefilled syringes: Prefilled syringe cartridges are designed to fit into specialized syringes, which are habituated to administer sundry fluid medications. These are utilized in the position of standard syringes, which practitioners must fill manually afore each dose is administered. The first prefilled syringe cartridges were composed of polypropylene. The advantages of prefilled syringe cartridges are their accuracy, safety, sterility, convenience and affordability.

- **Accuracy**

Prefilled syringe cartridges assure that patients receive precise dosages. This is particularly worthwhile for patients who need to self-infuse medicine but have no medical training. As indicated by boschpackaging.com, with standard syringes it is conceivable to stuff (or under fill) the barrel, which could contrarily affect the viability of the treatment.

- **Safety**

Prefilled syringe have a high caliber of precision, which makes them safer to utilize. Some cartridges are designed to fit into self-aspirating syringes, which essentially perforate the skin and inject medications without having to push on a plunger. This ascertains that injections reach the opportune depth and that dosages are administered smoothly.

- **Sterility**

Once a standard syringe is loaded with a drug, it will remain ideally compelling, or sterile, for around 12 hours. In examination, a solution put away within a prefilled syringe cartridge will stay sterile for roughly a few years (this is withal referred to as a “shelf life” of two to three years).

- **Convenience**

During an emergency (an allergic reaction), filling of standard syringes can be a time-consuming and perplexed process, so that requires an expeditious injection syringes. Prefilled syringe cartridges can preserve time, and sequentially preserve lives. Prefilled cartridges sanction injections to be administered more expeditiously especially in a diligent hospital. They can lessen stuffing in emergency rooms and other treatment regions.
• Affordability

Standard syringes highlight tube shaped glass barrels and firmly fitting glass poles, which are a great deal more costly to produce in contrast with plastic based prefilled cartridges and their relating syringes. Moreover, prefilled cartridges are a great deal less inclined to split or break in contrast with their standard, glass partners.\textsuperscript{22, 23}

• Manufacturing advantages

Another key advantage is that prefills require less overfill. For example, for a 0.5 ml vial, the USP recommends 20-25\% overfill. In contrast, for a 0.5 ml, required overfills is less than 2\%. As a result, potentially 18-23\% more doses can be engendered. Simple and flexible processing formats make prefills more facile to incorporate into a pharmaceutical company manufacturing line.

• Medical advantages

Healthcare professionals benefit from precise, pre-quantified doses, reduced dosing and medication errors, and reduced risk of microbial contamination. Prefills are convenient for emergency use and have potential for duplicate peel-off labels, which facilitate patient charting. Single-use prefilled syringes typically do not require preservatives. In fact, in studies conducted recently, nine out of ten healthcare professionals preferred prefills to conventional needles and syringes.

• Marketing advantages

Not only do healthcare providers prefer prefills, but healthcare products are withal accepted and prominent ecumenically. Products can be found in virtually every hospital in the US and overseas. This authentic-time exposure gives us a unique opportunity to develop products for customers that will be well accepted by their ultimate recipients – end-users, medics, and other healthcare professionals.\textsuperscript{22}

PACKAGING AGAINST COUNTERFEITING:

As per FDA – counterfeit drugs account for 10\% of all medication in the US. Latest developments are fluorescent labels, packaging with laser surface authentication that can be recognised by a linear code.\textsuperscript{26}
In India for instance, drug companies have been sending their medicines to overseas markets including an obligatory sport barcode on their outermost packaging, this was started in October 2011.

These are different aspects to deciphering and de-complexifying the counterfeit pharmaceutical supply chain. These technologies include bar codes, Tamper-evident packaging and the more recent RFID.

The problem with these security devices is that packaging components provide no assurance as to authenticity of the contents, which may have been adulterated.

Security devices alone do not reduce counterfeits but are designed to make them easier to detect.

CLASSIFICATION OF ANTI-COUNTERFEIT TECHNOLOGIES:

- **Overt (Visible) Features**

  Overt features are intended to enable end users to verify authenticity of a pack. Such features will normally be prominently visible, and expensive to reproduce.

  The list of overt feature includes:

  1. Security Graphics
  2. Holograms
  3. On-product Marketing
  4. Sequential Product Numbering
  5. Optically Variable Devices (OVD)
  6. Colour Shifting Security Inks and Films
Fig-17: Overt (visible) Features

- **Covert (hidden) features:**

  The purpose of a covert (hidden) feature is to enable the brand owner to identify counterfeited product. The general public may not be aware of its presence nor have the means to verify it. If publicized, more covert features will lose some security value.

  The list of covert features is given below:

  1. Laser coding
  2. Substrates
  3. Embedded Printing
  4. Invisible Printing
  5. Odour
  6. Digital Watermarks
  7. Anti-copy and Anti-scan design
  8. Hidden marks and printing
Forensic markers:

There is a vast range of high technology solutions which requires laboratory testing. Some of them may also require dedicated file test kits to prove authenticity of the products.

The list includes:

1. Isotope ratios
2. Micro-taggants
3. Chemical Taggants
4. Biological Taggants
5. DNA Taggants

Track And Trace Technologies:

A number of Track and Trace applications are under development for the pharmaceutical sector. It involves assigning a unique identity to each stock unit during manufacture, which helps to remain the drug with the supply chain until its consumption.
* **The Talking Packaging**

There are two development in talking packaging they are

The “TalkPack” can be invisibly integrated into packaging material which needs a special scanning pen.

![Fig no-22: Talk Pack](image)
VVT Technical Research centre using tags with NFC based technology enables mobile phones to download audio, text, web page and product information. By using a special pen-shaped reader information can be retrieved and stored and it can replay as audio files, music, etc to obtain the information on the manufacturer, shelf life, brand.\textsuperscript{28}

\begin{figure}
\centering
\includegraphics[width=0.5\textwidth]{talk_pack.png}
\caption{Talk Pack}
\end{figure}

Using a special varnish a dot code is printed on the top of the images and text. This technology can be used with all package types and printing technologies.

**DISPENSING CAPS:**

Dispensing caps store liquid and dry supplements separately from the water released by the consumer they form an energy or sometimes a medical drink. Everything from nutraceuticals to pharmaceuticals can be packed and properly dosed by a dispensed cap.\textsuperscript{28}
Robotics in Pharmaceutical Packaging:

In many instances, robotics are utilized to automate the subsisting manual process such as loading cartons, horizontal form fill seal machines or blister machines. In these cases, the advantages include incremented celerity, efficiency and an increase to overall equipment efficacy (OEE), other advantages may lead to reduced cost, reduced injury and eliminating rework. Robots prodigiously precise and repeatable. They operate 24/7 and, with options like vision and line tracking, can verify placement of product and track kineticism of perpetual kineticism machines to keep up with engenderment celerity.

Robotic cells typically offer a minutely diminutive foot print compared with other type of packaging equipment. Concurrently, these cells offer a benevolent work envelope, sanctioning the installed equipment to handle multiple packaging lines. A typical robotic loading assembly, or collating system utilizes a foot print less than 3’ x 3’. Even a dual cell palletizer, typically an immensely colossal robotic packaging machine, only occupies less
than 12’x 10’ of floor space. In integration to minute footprint, robotic packaging lines can preserve space by utilizing a single robotic cell for multiple functions, eliminating the desideratum for adscititious equipment. For example, a robotic case packing and palletizing cell can be engendered that both loads products into cases but additionally places the filled cases on a pallet, reducing the equipment and space required.13

**Robotic dispensing:**

Robotic dispensing machines have been accessible for over 10 years as an option stockpiling framework to routine haul out drawers in group drug stores. This framework is an electronically controlled computerized stockpiling framework that offers the limit of an unmistakably bigger, routine stockpiling, while taking up just at least space.

Robotic dispensing is the only solution that brings the benefits of consummate prescription fulfillment. The latest generation of robotic prescription dispensing systems transcends pristine counting to introduce consummate prescription processing, from vial cull and labeling to counting, capping and sorting, alleviating the desideratum for direct human intervention with every prescription.30

**CONCLUSION**

As the packaging of the pharmaceutical products is very important with regard to its stability, acceptance to patient, transport, etc. There is always scope for advancement and improvement of the pharmaceutical packaging. Therefore, new techniques like Cypak advance medication, Syreen prefilled syringe design, etc. seems to be promising in pharmaceutical products packaging.

**ACKNOWLEDGEMENT**

Most importantly I am thankful to the Almighty, who is the creator and director of all that initial and final modes to destiny. I take this opportunity to express my deep sense of gratitude, respect to Prof. Dr. Abdul Mannan, Associate Professor, Department of Pharmaceutics Deccan School of Pharmacy, Hyderabad, for encouraging me during this work.
CONFLICT OF INTEREST

Authors state that there is no conflict of interest.

REFERENCES

6. Patel R P et al., outline of pharmaceutical packaging technology. Inter Res J of Pharmacy I (1) 2010 105-112
22. EMEA Note for Guidance on Quality of Water for Pharmaceutical Use. 2002
