

**A REVIEW ON PHARMACEUTICAL PACKAGING WITH TAMPER EVIDENT AND  
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**ABSTRACT**

Nowadays, the safety, efficacy and quality of drugs are gradually declining due to the use of counterfeit drugs-both generic as well as branded too. The application of counterfeit drugs results to public health risks. In such conditions, there reflects the needs of tamper evident ideas and anti- counterfeit features which ensure the way to oppose drug counterfeiting. Tamper evident ideas solves use of drugs by its unique features of distinction. The tamper evident features like induction seals and wads, heat shrink bands and film wrappers are discussed in this work. Also the anti-counterfeit ideas like barcodes, security inks, invisible markers and sealing techniques with covert and overt technologies. But to reduce risk of tampering consumer education and updating on packaging must be considered.

**KEYWORDS:** Packaging, Tamper evident packaging, RFID, Anti-counterfeit measures. Etc.**INTRODUCTION**

Packaging is the art of science and technology of product enclosing or protecting for distribution, sales, storage and utilization. It also means for the modeling, assessing and manufacturing process of packages.

Pharmaceutical packaging will ensure and maintain the unity and stability of a product by means of providing security, information, presentation, ease of use, identification and acceptance.<sup>[1]</sup>

**Importance**

- Protect against all adverse external agents that can change the product properties.
- Protect against biological contamination.
- Protect against physical damage.
- For Tamper evident or Child resistance or Anti-counterfeiting.
- Carry the right information and identification of the product.

**Aims of Packaging****Protection**

Packages provide protection against external agents such as temperature, atmosphere changes, vibration and compression etc.

**Assemblage/ agglomeration**

Small dosages are grouped together in one package for reasons of efficient packing.

**Particular transmission**

Packages or label gives information regarding the usage, method of transport, dispose of drugs and product.

**Trading**

Traders uses various packaging and labelling techniques in order to attract and inspire potential buyers for purchase the products.

**Safety**

Detection of tampering done with better tamper evident packages.

**Ease of use and satisfaction**

Features of package with benefit of handling, distributing, displaying, use and reuse.<sup>[2,3]</sup>

**Advantages of Packaging**

- Uniformity
- Integrity
- Purity
- Minimum side effects
- Good stability with a clearly defined Shelf-Life profile.<sup>[4]</sup>

**Types of Packaging****Primary Packaging**

Direct contact with drug and direct effect on shelf life. This is said to be first layer of covering. E.g.: Glass, Bottles, Jars, Blister packs.

**Secondary Packaging**

It is the second layer of covering after warehousing and mechanical protection during transportation and shipment. E.g.: Paper Drums, Boxes.

**Tertiary Packaging**

It is used for bulk transport and shipment. E.g.: Slip Sheet, Edge Protectors Etc.

**Packaging Components****Containers**

The product is enclosed and kept in the container which have direct contact with drug.

**Closures**

Closures are used for tight packaging, for protect against Oxygen, Carbon dioxide, Moisture and Microbes and prevent loss of water and other substances.

**Carton / Outer**

This is the secondary outer covering in order to provide protection from mechanical and environmental hazards and also to display written information. These are made up of Cardboard and expanded Poly-Styrene.

**Box**

The primary protection against external agents and provide shock absorbing features. These are made up of thick card board and woods.<sup>[1]</sup>

**Tamper-Evident Pharmaceutical Packaging**

Tamper Evident Pharmaceutical Packaging can be defined as packaging having indicator to entry which, if broken or missing, can easily be expected to provide audible and visible evidence to the consumers that tampering has been occurred.

**Types of Product Tampering****Criminal Tampering**

By keeping one or more contaminated products on the shelf, so that the consumers may purchase the adulterated product without knowing.

**Staged Tampering**

The final product is purposefully contaminated by an offender in order to say that the manufacturer has been the victim of real tampering. Tampering is also used in suicidal attempts to earn money for their family and hide the true means of death.

**Extortion Tampering**

An offenders claims are not met, they usually endanger to tamper with a product. These claims are always for major amount of money.

**Faked Tampering**

An offender gives alert to media, law enforcement, proper manufacturers, or others of suppositional tampering. Many of the alerts are given for interest.

**Suspected Tampering**

Consumer gives alert to manufacturers when a package has been compromised, when an unusual appearance of a product is detected, or the consumers suffered with certain symptoms after consumption of the product. Rather than tampering consumers complaints are due to compromise in quality, machinery defects and failures.<sup>[5]</sup>

**Tamper Evident Technology**

The primary and secondary packaging used today for pharmaceutical packaging such as bottles for solid dosage forms and liquid dosage forms, tubes for semi-solid dosage forms, vials for parenteral such as powders or liquids are available with special packages in order to prove whether the packaging has been opened before. The technology for packaging explained below meet the requirements for tamper evident packaging which are designed properly. On selecting and developing tamper evident packaging, manufactures are advised to give serious consideration to the needs of arthritic or physically impaired persons.

Knowledge about tampered package is important to consumers too. The main purpose is to lower the risks by eliminating tampering and by detecting already tampered product on the shelf by identification.<sup>[6]</sup>

**Tamper Evident Features****Induction Cup Seals**

Induction Cup Seals creates air tight, water proof containers. On the neck of containers, this seal provides strong, easy to remove and effective tamper evident layer.

Induction sealing is used in almost all type of containers or cap which provide tight pack suitable for foods, beverages, drugs, chemicals and pharmaceuticals.

The process of Induction Cup sealing is based on the principle that a conductive material like aluminum foil are heated on exposure to high frequency magnetic field generated by an induction unit. This is a non-contact procedure without direct heat transfer. Due to this, the sealable closure liner can be placed in the cap by manufacturer before sealing.



**Fig. 1 Induction Cup Sealed Container.**

### Induction Wads

Basically it have four layers,

- Cardboard or Foam Packing
- Wax Layer
- Aluminum Foil
- Sealing Film

The line of force radiates via the foil and induces current flow in it. This enhances the temperature of the foil. Due to this the sealing film melts and clings to the lip of the container. After the seal is broken, the board or foam packing is maintained by the cap.

It helps for tamper proof and protect from leakage, contamination etc.



**Fig. 2: Induction Wads.**

### Blister or Stripe Packs

Individual doses are used to be sealed in plastic or foil. The individual seals of the pack must be broken to get access to the product and the blister or stripe pack materials cannot be separated or replaced without leaving evidence of opening.



**Fig. 3: Blister Pack.**

### Bubble Packs

Using a plastic bubble, the product and container are sealed and are mounted in or on a display card. This plastic or card must be broken to enter to the product directly. This cannot be achieved by without leaving visible evidence of entry. Bubble pack seals are intact and are completely sealed.



**Fig. 4: Bubble Pack.**

### Heat Shrink Bands or Wrappers

Heat Shrink bands is the concept based on the heat-shrinking stretch oriented polymer usually PVC. The polymer is produced as an extruded, oriented tube in a diameter greater than the neck ring bottle and the cap to be sealed. Bands or wrappers with distinctive design (E.g. Name, Logo or Pictures) are shrunk by heat to seal the fusion of the cap and the container. For the removal of the product the seal must be cut or torn. Perforated tear stripe enhances the tamper evidence.



**Fig. 5: Heat Shrink Band.**

### Breakable Caps

Breakable closures are seen in various designs. The roll on cap design uses an aluminum sheet, which are kept over the bottle neck during capping operation. The cap blank is carry on the bottle under pressure while rollers press together and shape the bottle tread into the cap blank. The bottom section of the cap is rolled around and below the locking ring on the bottle neck finish. When the cap is unscrewed, the perforated lower portion of the cap blank is breaks away, which provide the signs of prior opening. The plastic or metal sealed cap that either breaks away when removed from the container or remains on the neck of the container as an attachment.



**Fig. 6: Heavy screw cap with tear-off locking flange.**

### Bottle Mouth Inner Seals

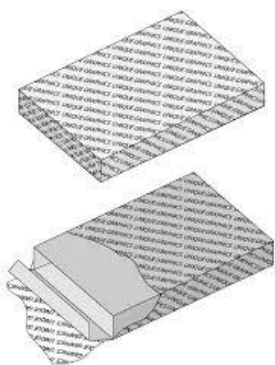
A bottle is made tamper resistant by providing inner seal to the rim of bottle in such a way that the access to product is only possible after destroying the seal. Heat induction is applied to the seals of containers to offer high degree of tamper resistance than those depend on adhesive to create bond. Printing and decorating the inner seals by unique designs will meet the tamper resistance criteria.



**Fig. 7: Bottle Mouth Inner Seal.**

### Transparent Film Wrappers

The entire product is sealed by a transparent film with distinctive design to ensure the complete sealing and secure tight fit. To get access to the product the wrapper must be ripped or broken.



**Fig. 8: Film Wrappers.**

### Types of Film Wrappers

- End – folded Wrapper
- Fin Seal Wrapper
- Shrink Wrapper

#### a. End - Folded Wrappers:

The product is pushed into sheet of overlapping film, which leads to form the film around the product and fold the edges in gift wrap fashion. Heat sealable films must be used on both surfaces. Cellophane and Polypropylene are the commonly used materials for this applications.

The overwrap must be sealed well, printed or uniquely decorated to exclude the substitution of an alternate overwrap in its place. The printed surface of wrapped carton is coated with heat sensitive varnish, which makes permanent bonding of overwrap to the paper board carton during sealing. The removal of overwrap from carton makes the carton unsuitable for reuse.

#### b. Fin Seal Wrapper

The two inside surfaces of the film were crimped together and sealed together to produce a “fin” seal. By tearing the wrapper, the overwrap can be removed.

### c. Shrink Wrapper

Product is packed in a thermoplastic film that has been stretched and oriented during its manufacture and has the property to revert back to its non-stretched dimensions as the film unwinds on the overwrapping machine, a pocket is formed in the fold of the sheet, into which the product is kept. The loosely wrapped product shrinks while passing through heated tunnel causing a tightly wrapped unit.<sup>[7]</sup>

### Paper, Plastic or Foil Pouches

The product is kept in an individual pouch or sachet that must be ripped, peeled open or broken to access to the product. The pouch or sachet have various designs. Seals cannot be separated without showing visible evidence of entry.<sup>[5]</sup>

### Tamper Evident Stickers

The cellulose acetate film have adequate strength to undergo change into label stocks in roll form. The stickers can be impulsively dispensed on automatic label dispensers and when tried to be removed these break up into very compact pieces.<sup>[8]</sup>



**Fig. 9: Tamper evident stickers.**

### Anti-Counterfeit Packaging

Counterfeiting is high extend, high profit business which causes the contravention of intellectual property rights, medicine rulings, and other features of criminal law.<sup>[9]</sup> Counterfeiting and piracy are same since they are both duplication of genuine product. Life style drugs are the most common counterfeit drugs in developed countries. The internet and unlicensed pharmacies are the source of these drugs.<sup>[10]</sup> Counterfeit drugs are the major reasons for mortality, morbidity, loss if connection in the health care system.<sup>[11]</sup> In India, the use of counterfeit and pirated products through reuse, repair and refill methods are reported. In Europe and Unites States, re-packaging is one of the source of counterfeit drugs.<sup>[12,13]</sup>

### Anti- Counterfeit Measures

#### ➤ Overt (Visible) Features

Overt features assisted to ensure the authenticity of a pack. Such features are visible and are expensive to manufacture.

#### Overt features like

- Holograms
- Watermarkers
- Optically variable devices (OVD)
- Sequential product numbering

- Colour shifting security inks and Films.<sup>[14]</sup>

### Holograms

Holography technology is the recently emerged technology which provide the consumers a simple way to infer the authenticity of the drug. These are seems to be resistive to tampering. Ideally, security holograms provide three levels of authentication, overt for identification, overt and covert for authentication and forensic to seize counterfeits. Holograms are designed to be simply recognizable to the public and hard to replicate by counterfeiters.<sup>[15]</sup>

### Watermarkers

Watermarkers are images or patterns that are placed into packaging design and are visible when package is hold upto light. Watermarkers are often incorporated into packaging to conflict counterfeit products. Visual water markers are affordable, but business or consumer end-users must be alert to the watermark and must know how to check that the product is genuine.<sup>[16]</sup>

### Colour-Shifting Security Inks

Colour shift inks appear as two or more distinct colours when viewed from the similar angles. Such features are visible when the product containing the colour shift are tilted at different angles. Colour shifting security techniques are limited due to the highly specialised colour-shift pigment production and requirement of technical knowledge. Supply of colour-shift inks is strictly controlled in order to ensure its use under genuine circumstances.<sup>[7]</sup>

### Covert (Hidden) Features

Covert features enable to identify the counterfeit products.

Covert features like:-

- Laser coding
- Invisible printing
- Embedded printing
- Anti-Copy and Anti-Scan design
- Hidden marks and printing.<sup>[14]</sup>

### Laser Coding

The application of batch variable details by lasers coding requires special and expensive equipment, and results in detectable artifacts which may difficult to simulate. Laser codes can be applied to cartons and labels, and plastic and metal portions.

### Invisible Printing

Invisible markings can be printed using special inks, and which only appear under IR/UV illumination. They give distinct colour with illumination at different wavelengths.

### Embedded Printing

An invisible image can be embedded within the pack graphics which can only be viewed using a special filter,

and cannot be replicated by normal scanning means. The effects can be entirely dramatic, and yet well hidden.

### Anti-Copy or Anti-Scan Design

Fine line background patterns appear as uniform tones, but when scanned or copied give out a latent image which was not previously visible. Commonly used on secured documents to block photocopying, they may be applied to product packaging as a background tint.

### Hidden Marks and Printing

Special marks and prints are applied in such a way that clear off attention and are difficult to copy. Their efficacy relies on a union of secrecy and subtlety.<sup>[17]</sup>

### Track and trace technologies

- Barcodes
- Radio frequency identification (RFID).<sup>[18]</sup>

### Barcodes

Barcodes are two-dimensional codes integrated on to the product package, which are scanned and send to central data base. These codes are printed by online methods for digital printing.<sup>[19]</sup> High quality images and two dimensional barcodes can formed by laser technology. Sufficient print contrast between light and dark bars must ensure the production of legible representation.<sup>[20]</sup>



Fig. 10: Barcodes.

### RFID

RFID tags can help to verify the products and support data collection for history records. The equipment that encoding and printing the tag-equipped labels confirms the tag before and after encoding. Good label are encoded and re-examined. If tags read perfectly, labels are printed and their barcodes are verified. If the barcode doesn't read properly, the unit pulls the label back in, marks it with a checker board design, expel it, and encode then print a new label.<sup>[8]</sup>

RFID tags contain more data than a barcode since, every product holds a unique tag, RFID act as a precious technique in detecting counterfeit drugs.<sup>[15]</sup>

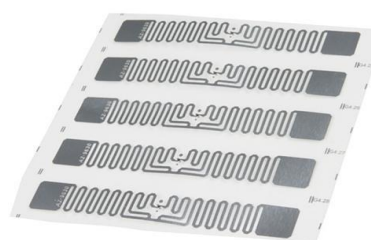


Fig. 11: RFID Tag.

### Future of Pharmaceutical Packaging

Patient compliance, novel drugs and environmental ethics demands significant development on packaging and delivery systems in pharmaceutical industry. The timely used old glass and elastomeric closure systems may not yield the effective barrier properties much needed for high value, lifesaving remedies. Packaging R&D provided us with new materials and technologies that secure prolonged drug-product shelf life. Lyophilisation had led to the formulation of liposome's and then the pro-liposome's, the therapies which are not stable in liquid form are lyophilized or converted to dry powder dosage forms. Lyophilized drugs need special care for storage and administration for the optimal performance by products. Lyophilisation chambers with actual, non-sticky stoppers are used for dose accuracy.

Development of packaging technologies influences on the advanced research of pharmaceuticals. Quality of packaging provide assurance during storage, shipment and delivery of pharmaceuticals. Efficient pharmaceutical packages using 3D design software and their evaluation with software like Finite Element Analysis (FEA) need to be promoted in pharmaceutical packaging. This approach of virtual to real packaging can make product right from scratch using software to create their models and then testing them with certain parameters virtually based on the data only the prototypes are created. This terminates the need for the customer to set up costly and time consuming production runs at their sites for testing at all stages of development.

Packaging system is required to ensure that the strength of the drug must be preserved and it should promote acceptance with a dosage regimen, ensuring dosing accuracy, be safe, easy to use and painless as possible for patients. Delivery systems that simplify drug re-constitution before use are provided by manufacturers involved in packaging for the self-drug administration.<sup>[8]</sup>

### Smart Phone Technology in Packaging

The coding on the package helps the consumers to connect via smart phone to product content, drug label and inserts. This helps to increase patient compliance and establishes authenticity of products. The emergence of self-verification enables the patients to authenticate their own medicine through a smart phone, helps to protect poorer populations from falsified and counterfeit medicines and other products. Technology can be used in the way to ensure time release mechanisms that could dispense only the specific amount at a predetermined time of day.<sup>[21]</sup>



**Fig. 12: Smartphone Technology in Brand Identification.**

### CONCLUSION

On these days, the main challenge for the pharmaceutical packaging industry is that ensure the product authenticity, internal standards and quality. These are possible only by cost effective anti-counterfeit and tamper evident packaging technologies. Here arises the importance of mandatory incorporation of scientific methods in pharmaceutical packaging. The innovative techniques provides security, patient convenience and brand identity. The precautions followed on designing and manufacturing can be reduce the risk of counterfeiting.

Nevertheless, the true manufacturers fails to compete with counterfeiters because they tries to develop newer methods of counterfeiting to cheat the consumers. Although, the better way to resist counterfeit drugs are to provide new updating on packaging and educating the consumers about product identification techniques on tampering. Public awareness regarding the importance of tamper evident package and anti-counterfeit measures will influence safer use of medicines.

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