Review Article

Anticounterfeit packaging technologies

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Abstract

Packaging is the coordinated system that encloses and protects the dosage form. Counterfeit drugs are the major cause of morbidity, mortality, and failure of public interest in the healthcare system. High price and well-known brands make the pharma market most vulnerable, which accounts for top priority cardiovascular, obesity, and antihyperlipidemic drugs and drugs like sildenafil. Packaging includes overt and covert technologies like barcodes, holograms, sealing tapes, and radio frequency identification devices to preserve the integrity of the pharmaceutical product. But till date all the available techniques are synthetic and although provide considerable protection against counterfeiting, have certain limitations which can be overcome by the application of natural approaches and utilization of the principles of nanotechnology.

Key words: Counterfeit drugs, covert, overt, packaging

INTRODUCTION

Packaging is a link connecting production with marketing whereby the goods reach from the production center to the consumers in a safe and sound condition with a minimum overall cost.[1] Packaging can also be defined as the coordinated system which can enclose or protect the products for distribution, storage, preservation, transportation, information, and sales.[2] The pharmaceutical brands are most vulnerable due to their higher market share, ease of production, and greater profit margins.[3] Counterfeit is a problem of product security. Products sidetracked from their proper distribution channel, or sold past their expiry date, or by modification of the package are associated with the problem of counterfeiting.[4,5]

Counterfeits are unauthorized reproductions of a trademarked brand, which are closely similar or identical to genuine articles.[6,7] The first international meeting on counterfeit medicines was held during April 1–3, 1992, at World Health Organization (WHO) in Geneva and the following definition was accepted: "A counterfeit medicine is one which is purposely and falsely mislabeled in accordance to identity and/or source. Counterfeiting can pertain mutually to both branded as well as generic products comprising of either correct or incorrect ingredients, lacking active ingredients, or with forged packaging."[8] Later on, the concept was modified by the Nigerian National Agency for Food and Drug Administration and Control (NAFDAC) as "those medicines with the same quantity of active ingredient as that of genuine brand, insufficient or no active ingredients, medicines which are post expiry date, herbal preparations that are toxic or ineffective and medicines which do not bear the name and address of the manufacturer are counterfeit."[9]

Counterfeiting is a high-volume, high-profit business which causes the infringement of intellectual property rights, medicine legislations, and other aspects of criminal law.[10] Counterfeiting and piracy are in term the same since they are both the reproduction of identical copies of the genuine product.[7,11] The most common counterfeit drugs in industrialized or developed countries are so-called lifestyle drugs. The individuals often buy these drugs from the internet or unlicensed pharmacies.[12] Counterfeit drugs are the major cause of morbidity, mortality, and loss of confidence in the healthcare system.[13] In India, the consumers reported a wider use of counterfeit and pirated products through reuse, repair, and refill of products.[14] Repackaging is one of the sources of fake drugs in Europe and the United States.[15] Estimates put the total loss of life to counterfeit pharmaceuticals between 500,000 and 1,000,000 people per year.[16]

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MARKET SCENARIO AND DRUG PERSPECTIVES

According to the BCC research report, the anticounterfeit packaging technology in the United States increased to approximately $34.2 billion in 2006. Sales are likely to reach $43 billion in 2012, viewing a compound annual growth rate (CAGR) of 3.2% over the tenure of 5 years from 2007 to 2012,[17] while as per the statement released by the Organization for Economic Co-operation and Development (OECD), three-fourths of forged drugs supplied world over have some origin in India, followed by 7% and 6% from Egypt and China, respectively.[18] As of 2005, OECD estimates the international trade of counterfeit goods to be $200 billion per year.[19] China ranks first for the counterfeit products, the United States is at the second and India at the fourth rank globally.[20] WHO estimates that up to 1% of medicines available in the developed world are likely to be counterfeits. This figure rises to 10% globally, although in some developing countries the estimation is about one-third for the counterfeit medicines.[21]

Medicines have been the center of attraction for the counterfeiters due to the number of reasons listed in Table 1,[8,22] and the factors responsible for the counterfeiting are shown in Figure 1.[19,23] Maximum counterfeit reports are related to antibiotics, antiprotozoals, hormones, and steroids.[22] The medicines counterfeited worldwide with their outcomes are mentioned in the Table 2.[24-32]

AUTHENTICATION TECHNIQUES

Authentication is the act of establishing or conforming something as genuine. Authentication is of utmost importance because the use of counterfeit medicines can be harmful to the health and wellbeing of the patients. Their use may result in treatment failure or even death.[22,33] Authentication is generally done through the overt or covert features upon the product.

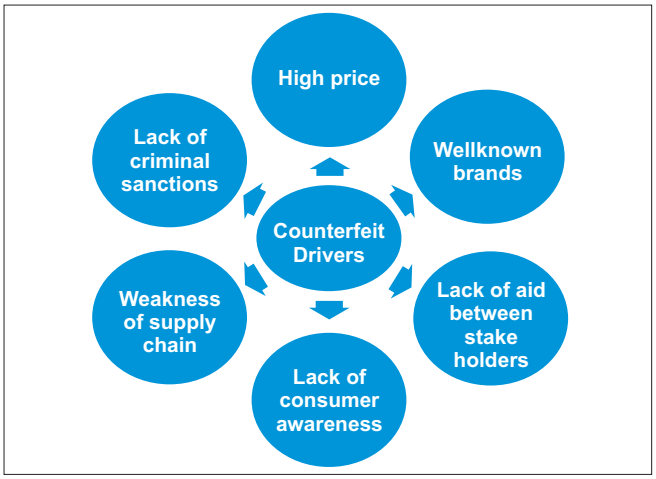

Figure 1: Drivers of counterfeiting

Overt (Visible) Features

Overt features are expected to assist the users to confirm the genuineness of a pack. Such features will be significantly visible, and complex or expensive to reproduce.[4] They include optical variable coatings with changing colors, thermochromic inks, and watermarks.[34] Inkjet is commonly used for printing variable text on packaging. The process

Table 1: Medicine as a target for counterfeiting

Reasons for attraction toward medicine
Absence of or weak National Medicines Regulatory Authorities (NMRAs)
High prices of medicines
Lack of control over export medicines
Trade through several intermediaries
Lack of prosecution and penalties

Table 2: Counterfeit medicines globally

Year	Country	Outcome
1990	Nigeria	A cough mixture diluted with a poisonous solvent. Over 100 children died
1996	Haiti	At least 59 children died after taking a counterfeit syrup used to treat fever
1998	Brazil	Ineffective contraceptive pills resulted in unwanted pregnancies
1998	India	Diethylene glycol poisoning killed at least 30 children
2000	Cambodia	At least 30 deaths resulted from counterfeit malaria drugs
2001	China	The Shenzhen evening news reports that more than 100,000 people died of fake drugs in 2001
2002	USA	The FDA reported three lots of counterfeit Combivir
2003	USA	Recall of 200,000 bottles of the anticholesterol drug, Lipitor
2005	UK	A counterfeit Viagra factory was discovered in north London
2007	UK	A counterfeit antipsychotic drug Zyprexia was noticed by a repackager which resulted in batch recall
2009	Ghana	A counterfeit antimalarial drug of Novartis was brought to inspection by a citizen
2009	Europe	More than 2 million counterfeit insulin needles were found in established European distribution channels
2009	Kenya	Counterfeit antihypertensive and antidiabetic drugs were seized by Kenyan officials
2009	China	An antidiabetic traditional medicine contained six times the normal dose of glibenclamide; two people died and nine were hospitalized
2010	Bangladesh	Testing of 5000 samples revealed that 300 were either counterfeit or of substandard quality
2010	China	A hospital has paid compensation to patients who suffered adverse effects after being treated with a counterfeit drug of Roche

can be untidy and does not always provide the print quality necessary for creating small codes, which must stay clear for weeks or months.[35] This requirement for quality codes led to the development of the barcodes.

Barcodes are high-density linear or two-dimensional codes incorporated onto the product package, which are scanned and sent to the central database as shown in Figure 2. These codes are printable by online methods accounting for inkjet or digital printing.[4] Laser technology can produce high-quality small images and two-dimensional barcodes. Users must make sure that there is a sufficient print contrast between light and dark bars to produce a legible representation.[35] But still today even the high-quality barcodes are easy to replicate.

Holography is well known for its capacity to produce striking three-dimensional images, which are difficult to get through with the conventional photography. A major benefit of this process is that they can be reformed under white light.[36] Holograms are generated from the interference patterns obtained through the contact of laser beams by either angular image or laser technology. Such high-definition holograms are used as a security feature on the product bottle as shown in Figure 3. The complexity of the hologram varies from the traditional three-dimensional images to computer-generated two-dimensional diffraction patterns. Holograms are now widely available in variety of formats such as holographic shrink sleeves, blister packaging aluminum foil, holographic induction cap seals, polyester-based tamper evident labels, and holographic hot stamping foil. But still it is reported that more than half the sales of the artesunate drug in South East Asia is forged, despite the presence of the hologram.[4,25,37-39] The overall advantages and disadvantages of overt technologies are described in Table 3.[4]

Covert (Hidden) Features

The rationale of a covert feature is to aid the brand owner to recognize a counterfeited product. The general public will not be aware of its presence nor will have the resources to confirm it. A covert feature should be difficult to sense or copy without the specialist knowledge.[4] Covert features include microscopic particles of specific colors and labels printed with color combinations.[34]

The highly appreciated though expensive technology used presently is the radio frequency identification device (RFID). The RFID tag comprises an antenna with a microchip at its center. Unlike barcodes, RFID includes batch information which can be interrogated at a distance without requiring the line of sight. The RFID allows the recognition of objects through wireless communications in a set frequency band. Three vital components in any RFID system are the tag, the reader, and the software. The tag is an integrated circuit containing an exclusive tracking verifier, called an electronic product code (EPC), which is transmitted via electromagnetic waves in the radio spectrum. The reader captures the transmitted signal and provides the network connectivity. For their track and trace usage, the diverse RFID tags that are used are active, passive, and semiactive.[4,40] The high cost of a RFID tag (20–50 cents as opposed to a 2 cent barcode) might forbid the companies from implementing it.[35,41,42]

The biometric fingerprints introduced by the Bayer group utilize 1-MW diode lasers to analyze the innate surface makeup of each item. Microscopic irregularities which are caused by the setting of paper fibers or plastic result in spreading of the laser beam by a laser speckle event. By measuring the dispersal of the light at various angles, surface uniqueness is recorded. Laser surface authentication combined with RFID

Figure 2: Package showing two-dimensional barcodes, scanned and sent to the central database

Figure 3: Bottle with a hologram as a security feature

Table 3: Advantages and disadvantages of overt and covert technologies

Technique	Advantages	Disadvantages
Overt	User verifiable	Require user education
	Can add decorative appeal	May add to a cost
	Can be a deterrent to counterfeiters	May rely on covert features for authentication
Covert	Can be simple and low cost to implement	Need strict secrecy
	Needs no regulatory approval	If widely known or used, may be easy to copy
	Can be easily added to or modified	More secure options add complexity and cost

tags could provide an overall anticounterfeit solution.[43] The overall advantages and disadvantages of covert technologies are described in Table 3.[4]

SECURITY-ENFORCING PACKAGE COMPONENTS

Authentication in packaging utilizes mainly the concept of sealing which has been significantly demonstrated by American Bank Note Holographics. HoloSeal™ is a patented pressure-sensitive, tamper apparent holographic security label that features a customized tamper apparent fracture pattern, black light verification system, and machine-readable entrenched code. For the tracking purpose, HoloSeal can be numbered or personalized to give an account of region, plant, or product. HoloCap™ comprises several different heat-sealable films which are attached directly to the containers using the induction seal technology. These different films unite to form a single holographic inner seal that provides a higher level of defense to containers or bottles.[28,44] Such a sealing tape securely covered around the package is shown in Figure 4.[4]

The trend of utilizing sealing in packaging for the development of anticounterfeiting techniques changes with the upcoming concept of lasers and forensic approaches. Holospot® is a discrete forgery-proof information carrier that can be attached to any product. It uses laser encryption of computer-generated lithograms into small polymeric data carriers and offers multiple overt and covert security features, whereas on the other hand Ident Seal® is a visible text or high-contrast barcode inscribed by lasers. It offers overt protection, identification, and a successful tamper evident feature.[45] The anticounterfeit label Forge Guard of Fujifilm Corporation can visualize full color images or text clearly with a special viewer. This label regulates light wavelengths on the nano-optic level, so those with the viewer can see hidden full color images. This requirement of the viewer makes the label difficult to forge.[46] Still the need was for the invisible substrates to enhance the security and the research led to the development of forensic markers. These forensic markers include physical, chemical, and biological taggants.[25,47] A Merck product, ESAN features numerous hidden and forensic security features on the pack from its Securalic product line. The security features are built into the ivy leaf design element printed on the folded box. These Securalic products are also used for two-color blisters in UV flexoprinting.[45]

Other systems include a tamper evident packaging system, film wrappers, and breakable caps. The tamper evident feature helps to maintain the integrity of the drug product by preventing the profit of counterfeiters by either repacking or reselling of the pharmaceutical products[48] as shown in Figure 5.[4] A film wrapper is a transparent film with a characteristic design covered securely around a product or product container. The film must be cut or torn to open the container and remove the product. Substrate options include ultradestructible films, solvent-sensitive papers, and voidable films that provide images when removed as shown in Figure 6. Breakable caps, as the name suggests, break when an effort to open is made. These caps provide external tamper evidence and can also be combined with the internal seals, thereby assisting with double security. The overall choice of anticounterfeit techniques at various levels of packaging has been described in Table 4.[4]

CONCLUSION

Medicines save lives and prevent diseases and epidemics only if they are safe, efficacious, of good quality, and are rationally used. The use of unsafe, substandard, ineffective, and counterfeit medicines can be harmful to the health and wellbeing of the patients. Governments must establish the National Medicine Regulatory Authority (NMRA) to monitor the quality of medicines in the market to detect and prevent any substandard and counterfeit medicines from reaching

Figure 4: Package sealing tapes

Figure 5: External and internal tamper evident feature

Table 4: Choice of anticounterfeit solutions at different packaging levels

Anticounterfeiting technologies	Primary sales pack	Secondary group pack	Transport pack
Packaging design	Yes	No	No
Printing and graphics	Yes	Yes	No
Labels	Yes	No	Yes
Tamper evidence	Yes	Yes	Yes
Forensic markers	Yes	No	No
RFID	Yes	Yes	Yes

Figure 6: Label that leaves a void mark on tampering

the public, by working closely with national law enforcement agencies such as the police and custom officers. The NMRA must ensure that all medicine manufacturing, import, export, and distribution activities are carried out in premises approved by the NMRA, and that individuals and companies engaged must have licenses to operate such activities.

The Counterfeit Pharmaceuticals Initiative (CPI) was launched by the ICC in 2003 for

i. the creation of a counterfeit pharmaceutical database with online search facility;
ii. construction of a dedicated CPI website;
iii. liaising with regulators;
iv. providing assistance to members by lobbying and investigation;
v. special projects and surveys, e.g., internet pharmacies; and
vi. the implementation of anticounterfeiting technologies.

The implementation of overt and covert techniques by the industries can raise the bar for the counterfeiters, but the final awareness must be at the consumer level. The consumers should buy medicines only from licensed pharmacies and medicine outlets, be suspicious of heavily discounted medicines, and check if the packaging indicates the batch number, manufacturing date, expiry date, and the manufacturer's name. Counterfeit drugs not only affect the sick and innocent consumers but also the general public, and deserve more attention.

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