Transparent Plastic Envelope for Dispensing Antibiotics - The Best Option in the Market?

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Abstract

Different antibiotics have different characteristics but the aspect of antibiotic stability is the main concern of the pharmacist when dispensing the drug. The stability of drug such as chemical stability, physical stability, microbiological stability, therapeutic stability and toxicological stability will ensure its therapeutic effect. There are some factors that may affect antibiotics' effectiveness like, hydrolysis, oxidation, epimerization, photolysis, temperature and microbial contamination. These factors are avoidable by dispensing antibiotics with a proper container. Transparent plastic envelope is the major method in dispensing drugs, but it was not fully secure the stability of drug. Some other alternatives such as, blister packaging, strip packaging and plastic bottle are more preferred compared to transparent plastic envelope.

Introduction

Antibiotics are of the oldest discovered drugs that combat specific microorganisms like bacteria and fungi. Although there are several classification schemes for antibiotics, based on bacterial spectrum (broad versus narrow) or route of administration (injectable versus oral versus topical), or type of activity (bactericidal vs. bacteriostatic), the most useful is based on chemical structure. Antibiotics within a structural class will generally show similar patterns of effectiveness, toxicity, and allergic potential.

The first class is penicillins. The penicillins are the oldest class of antibiotics, and have a common chemical structure which they share with the cephalosporins. Penicillin is a group of antibiotics derived from Penicillium fungi[1]. Penicillin antibiotics are historically significant because they are the first effective antibiotics against diseases like syphilis and staphylococcus infections[1]. The natural penicillins are based on the original penicillin G structure; penicillinase-resistant penicillins, notably methicillin and oxacillin, are active even in the presence of the bacterial enzyme that inactivates most natural penicillins[2]. Aminopenicillins such as ampicillin and amoxicillin have an extended spectrum of action compared with the natural penicillins; extended spectrum penicillins are effective against a wider range of bacteria. All penicillins are beta-lactam antibiotics and are used in treating bacterial infections that are caused by Gram-positive organisms. It also kills bacteria by inhibiting the final step in cell wall biosynthesis[2]. Like all other beta lactam antibiotics, it works by inhibiting the formation of peptidoglycan cross-links in the bacterial wall.

The second group is cephalosporins. They are a class of beta-lactam antibiotics, where they are originally derived from Penicillium fungi. Like most beta-lactam antibiotics, they work to disrupt the cell wall of bacteria this will cause the cells to die[1,2,3]. Cephalosporins are bactericidal agents like penicillin. Cephalosporins are indicated for the treatment of bacterial infections that are gram-positive, however later generation have increased activity against gram-negative. It is facilitated by Penicillin binding proteins (PBPs). Beta-lactam antibiotics mimic this site and inhibit PBP crosslinking of the peptidoglycan. The “cepha” drugs are among the most diverse classes of antibiotics, and are themselves sub-grouped into 1st, 2nd and 3rd generations. Each generation has a broader spectrum of activity than the one before. In addition, cefoxitin, a cephamycin, is highly active against anaerobic bacteria, which offers utility in treatment of abdominal infections. The 3rd generation drugs, cefotaxime, ceftriaxone and others, cross the blood-brain barrier and may be used to treat meningitis and encephalitis[1,2].

The next group is fluoroquinolones. Fluoroquinolones are part of a family of synthetic broad-spectrum antibiotics[2,4]. The quinolones, were not well absorbed, and could be used only to treat urinary tract infections. The fluoroquinolones are broad-spectrum bacteriocidal drug. They are well distributed into bone tissue, and so well absorbed that in general they are as effective by the oral route as by intravenous infusion. Quinolones are able to erradicte by interfering with bacterial DNA replication[1].

Macrolides are another group. The macrolide antibiotics are derived from Streptomyces bacteria form the macrolide ring, a large macrocyclic lactone ring to which one or more deoxy sugars, usually cladinose and desosamine, may attached. These rings are usually 14, 15, 16 membered. They are protein synthesis inhibitors. The mechanism of action of macrolides is inhibition of bacterial protein synthesis.
biosynthesis. Erythromycin, the prototype of this class, has a spectrum and use similar to penicillin. Newer members of the group, azithromycin and clarithromycin, are particularly useful for their high level of lung penetration[5].

The next group is tetracyclines. They are derived from a species of Streptomyces bacteria. Tetracyclines penetrate into most body tissue and fluids. Tetracyclines are effective against: rickettsiae, spirochetes, helicobacter pylori, Vibrio sp, Yersinapstis, Francisellatularensis Brucellesp, Bacillus antracis, Plasmodium vivax, mycoplasma sp, Chlamydia and Chlamydophila sp[1].

Different antibiotics have different characteristics but the aspect of antibiotic stability is the main concern of the pharmacist when dispensing the drug. The stability of drug will ensure its therapeutic effect. There are five types of stability. First is the chemical stability. Only for a specific limit, active ingredient of each antibiotic can maintain its chemical integrity and potency. The second is the physical stability. This stability will ensure the original physical properties such as solubility and suspendability to be retained. The next one is microbiological stability. This stability is crucial as it keeps the drug’s sterility and resistancy towards microbial growth. Therapeutic stability will maintain its effectiveness. The last one is toxicological stability. This will prevent any toxic effect of antibiotics. Some of the important factors that can alter the stabilities are discussed in the following part[6,7].

Factors That May Affect The Effectiveness Of Antibiotics

Although antibiotics were very effective against various types of infection and disease, but many problems are facing by antibiotics in term of stability. The effectiveness of antibiotics and its stability were significant associated. Factors that affect the stability of antibiotics are shown at below:

1. Hydrolysis
Some of the antibiotics groups are composed or chemically structured by amide and beta-lactam rings, examples, penicillin, cephalosporin and more. However, esters and beta-lactam rings are easily to hydrolyse in the presence of water or at a high humidity or moisture environment. The hydrolysis rate may dramatically increases with the high water vapour pressure in environment[6].

2. Epimerization
Epimerization is mostly occurs on tetracycline. The causes of this reaction are due to the presence of water or tetracycline exposed to a pH range at which the pH was higher than 3. This will leads to rearrangement of the dimethylamino group in the tetracycline and produce epimer of tetracycline which do not have any antibacterial function[6,8].

3. Auto-oxidation/ Oxidation
Oxidation is a common factor that causes decomposition of drugs, without exception antibiotics are also one of the “victims”. The present of oxygen in air was the main reactant of this process. Products of oxidation usually lack of therapeutic effects and the significant detection of oxidation is the colour changes of the drug.[6]

4. Photolysis
Photolysis usually occurred when antibiotics are exposure to sunlight. When the energy from the sunlight is absorbed by the antibiotics and triggers the antibiotics to the excited state. When the reaction was returns to the ground or stable state, the energy released either by emitting light or decomposition. Photolysis will results in the scission of covalent bonds in the antibiotics.[6] All antibiotics should be protected from direct sunlight. Rifampicin and amphotericin B are very sensitive to light and should be stored in the dark.

5. Temperature
Temperature can significantly affect the stability of antibiotics. When the temperature of the environment increases, this will fulfil other degradation reaction like oxidation by increase the energy of the antibiotics to achieve the activation energy of the reaction. Besides, the temperature also affects the shelf life of drug. Antibiotics may store longer if under a cool condition[6]. In general, antibiotics require storage in a freezer. Aminoglycosides (e.g. kanamycin) are hygroscopic and should be stored in a desiccator. Storage of many powdered antibiotics at -20 °C is not recommended and increases the risk of water condensation.

6. Contamination by microbial
Even though antibiotics functions as antibacterial due to different groups of antibiotics with its own specificity towards different bacteria and this may causes some bacteria remain unaffected and stick on the antibiotics due to personnel hygiene habits.

Since there are various types of challenge toward antibiotics, the dispensing of antibiotics must able to protect them from the degradation. Nowadays, most of the hospitals and clinics are using transparent plastic envelope for dispensing antibiotics.

Transparent Plastic Envelope For Dispensing

Nowadays, transparent envelope is major form of
pharmaceutical packaging material used in clinical and hospital settings. The usage of transparent plastic envelopes has displaced other options like glass, metal, rubber, paper and so forth. Drugs in the form of capsules and tablets are normally packaged with transparent envelopes like antibiotics. Common diseases such as fever, running nose, coughing, infections and sore throat need antibiotic as these diseases generally caused by bacteria. Apart from common diseases, some serious infections need antibiotics as well. For instance, diseases include meningitis, pneumonia, and tuberculosis. Thus, antibiotics are dispensed in a high frequency as compared to other drugs. The plastic envelope used for packaging the antibiotic is a great concern since years back. None of the pharmaceutical packaging material is perfect without any flaws. Plastic envelope is no exception. It has its advantages plus some disadvantages. This is crucial as drug in vitro interaction with the plastic can change drug stability and so the therapeutic effects altered.

Advantages Of Transparent Plastic Envelope For Dispensing

Transparent plastic envelope allows easy detection of the type of drug that it carries. Since it is transparent, it provides convenient to the patients to recognize the drugs easily. In terms of economics, it is cheaper than any other containers such as glass containers. Hence, pharmacies and hospitals will not have to spend a big capital on the containers as they can use it for better purpose such as buying other drugs. Transparent plastic materials are also biodegradable. Plastics that are naturally produced such as polyhydroxyalkanoates (PHAs) like the poly-3-hydroxybutyrate (PHB), polyhydroxyvalerate (PHV), plastics that are produced from renewable resources such as polylactic acid (PLA) and most of the starch derivatives are biodegradable which means that the plastics will decompose in natural aerobic (composting) and anaerobic (landfill) environments[9]. Furthermore, biodegradable plastics from natural materials, such as vegetable crop derivatives or animal products, sequester carbon dioxide during the phase when they're growing, only to release carbon dioxide when they're decomposing, so there is no net gain in carbon dioxide emissions leading to less harm to environment. Biodegradable plastics reduce dependence on foreign oil. The use of biodegradable plastics will decrease the country’s dependence on other countries for fossil fuels. The majority of the oil that is needed to make regular plastic comes from the Middle East, which has not always been friendly toward the U.S. Biodegradable plastics are created from domestic biomass materials, so it reduces the dependence on foreign oil, providing a domestic solution instead[9]. Other than that, it is also very convenient for patients to carry those plastics to anywhere. They are neither bulky nor heavy; hence patients can carry it with them when they are out for vacations or to other places. In terms of drug stability, transparent plastic materials will maintain the drugs stability as there is no adverse reactions of those plastics with the drug. Hence, the effectiveness of drugs is guaranteed as well. It is also a safer method of dispensing drug as transparent plastics are not easily damaged compared to other containers that maybe broken if they are handled carelessly. Transparent plastic materials are also recyclable. The used transparent plastic envelope can be recycled back into the same type or into different materials. This will ensure the continuous supply of the plastic which will not be depleted easily. Hence, it can be used as a source of container for a long period and the recycling property saves cost as well. Transparent plastic envelope allows easy detection of the type of drug that it carries. Since it is transparent, it provides convenient to the patients to recognize the drugs easily. In terms of economics, it is cheaper than any other containers such as glass containers. Hence, pharmacies and hospitals will not have to spend a big capital on the containers as they can use it for better purpose such as buying other drugs. Transparent plastic materials are also biodegradable. Plastics that are naturally produced such as polyhydroxyalkanoates (PHAs) like the poly-3-hydroxybutyrate (PHB), polyhydroxyvalerate (PHV), plastics that are produced from renewable resources such as polylactic acid (PLA) and most of the starch derivatives are biodegradable which means that the plastics will decompose in natural aerobic (composting) and anaerobic (landfill) environments[9]. Furthermore, biodegradable plastics from natural materials, such as vegetable crop derivatives or animal products, sequester carbon dioxide during the phase when they're growing, only to release carbon dioxide when they're decomposing, so there is no net gain in carbon dioxide emissions leading to less harm to environment. Biodegradable plastics reduce dependence on foreign oil. The use of biodegradable plastics will decrease the country’s dependence on other countries for fossil fuels. The majority of the oil that is needed to make...
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Disadvantages Of Transparent Plastic Envelope For Dispensing

Transparent plastic envelope is neither water resistant nor tear-resistant. It is easily damaged when there is a friction applied on it accidentally. Water and water vapour are able to diffuse inside and have direct contact with the antibiotics that lead to the hydrolysis of antibiotics. Hence, transparent plastic envelope is unable to protect the drugs in any circumstances such as high humidity environment which can cause hydrolysis. This followed by the alteration of the pH of antibiotics. So, the problem of epimerization might be arose especially tetracycline. The seal off part in the transparent plastic envelope increases the probability of auto-oxidation on the antibiotics by promoting the air-flow. The occurrence of hydrolysis and oxidation are unavoidable due to the frequent opening and closing of the transparent plastic envelope that causes damages to the zip fastener. Due to the transparency of plastic envelope, sunlight is able to penetrate inside and promote photolysis of antibiotics. Photolysis may make changes on the chemical structures of the antibiotics and reduces its pharmacological effect and thus therapeutic failure plus toxic effects[10]. Plastic cannot protect antibiotics from high temperature. This will lead to unwanted reactions on the antibiotics such as auto-oxidation. Sorption is another process that might occur when antibiotic is stored in the transparent plastic envelope. Sorption includes both the absorption and adsorption. It is a term to describe the binding of molecules from drug to the plastics[11]. The particles and molecules are normally refers to preservative. This causes the drug loses an amount of its preservative and reduces the stability of the drugs towards microbial contamination. The package of antibiotic which is in the form of tablet and capsule into the transparent plastic envelope may cause difficulty of accessing to the drugs. The width and length of a typical transparent plastic envelope is approximately 7 and 10 cm respectively. Since transparent plastic envelope is normally not meant for single-dose, the patient needs to open and close the sealed off parts for several times a day. Unless the tablets and capsules are packed individually in the blister packs and sealed with aluminium foil, otherwise the free tables or capsules will concentrate at the bottom part of the plastic envelope. Thus, the patient will either insert his finger inside the plastic envelope to get the medicine or trying to pour the medicine out by inverting the envelope. Both of the ways to get the drugs mentioned above will introduce microorganisms to the drugs. The former one is because the patient’s finger might not be cleaned and completely free from microorganisms. While the latter will causes the medicine exposed to the microorganisms on the palms or surroundings. Thought antibiotic is used to kill or delay the multiplication of microorganisms, it may only have activity towards a certain types of microorganisms. The way to solve the problem is to add preservative as one of its excipients. By using transparent plastic envelope to pack the antibiotics may cause mechanical damage to the tablets or capsules. Transparent plastic envelope is not hard and flexible. It does not produce a fully protection to the medicine. If the patient is going to take the medicine to travel, the transparent plastic envelope might not be able to withstand the weight of stuff placed on it. This causes the tablets or capsules to change their original shape after undergoing cracking. This alters the amount of active ingredient and excipients in the drug. Consequently, the desired pharmacological effect of the drug is affected.

Solutions to enhance the maintenance of effectiveness for antibiotics
The white colour appearance of plastic envelope reduces the amount of sunlight reaching the antibiotics. Plus the protection of antibiotics in the blister packs, sunlight can barely penetrate into the antibiotic and photolysis can be prevented[12]. By packing antibiotic individually into the blister packs sealed off with aluminium foil, water and air are hindered in contact with the antibiotics. Blister packs are drugs in the form of tablets and capsules pack individually into the pockets of the PVC foil which is transparent and sealed with aluminium foil. The prevention to hydrolysis can be further enhanced[13]. In addition, since it is almost the same as a single dose drug, the contamination of the antibiotics is avoided. Besides, it helps patients to recognise their medication in terms of shape, colour and size.

The second solution is by placing the strip packs inside a transparent plastic envelope. Strip packs are drugs in the form of tablets and capsules pack individually into the pockets of the aluminium foil and sealed with aluminium foil. So, strip packs are non-transparent. This hinders the photolysis of antibiotics by further blocking of the penetration of sunlight into the medicine.

Both of the solutions mentioned above are able to forbid the antibiotics in contact with moisture and air. To put it in simple words, hydrolysis and auto-oxidation of the antibiotics are shielded[14]. Apart from that, the packaging of antibiotics into the blister packs or strip packs can lower down the probability of microbial contamination. Since the medicine are pack individually, patient can puncture the necessary dose without contaminate the others. Antibiotic pack in the blister packs or strip packs are relatively better protection from mechanical damage than those without packs.

In order to have a greater protection against this mechanical stress, plastic bottle is one of the alternative solutions. The preferable appearance of the plastic bottle is white colour which is poor in absorption of heat. So, the plastic bottle may protect the medicine from excess heat. The non-transparent plastic bottle does not allow the permeation of sunlight and therefore no photolysis of antibiotics. Compared to blister packs and strip packs, plastic bottle has a weaker protection of drugs from auto-oxidation and hydrolysis. However, the addition of silica gel inside the bottle can absorb moisture for better protection against hydrolysis. In addition, the selection of plastic bottle must fulfil some criteria such as reduction in adsorption of drugs onto the container and plastic material should not release substances sufficient enough to cause toxic effects[15].

**Conclusion**

Transparent plastic envelope is not the best option in the market for dispensing antibiotics. The better choices are blister packs or strip packs inside a white plastic envelope and non-transparent plastic bottle. Manufacturers are encouraged to pack antibiotics in blister pack, strip pack or plastic bottle. The three solutions mentioned have advantages over transparent plastic envelope in terms of stability of drug. In terms of cost, plastic bottle is the best choice for packaging antibiotics as it provides enough volume to fill in all tablets or capsules. But blister packs or strip packs only able to fill in a certain number of antibiotics. However, blister packs and strip packs are better than plastic bottle in terms of stability. In terms of environmental friendly, plastic bottle is the right choice since it can be recycled. In terms of convenient, blister packs and strip packs are the ones. The choice of appropriate packaging material is important as not to affect the pharmacological effect of the antibiotics.

After considering all the factors, the best option for packaging antibiotic is strip pack and the only disadvantage is the problem of identification of antibiotics by patients, physicians and pharmacists.

**References**

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Illustrations

Illustration 1

Transparent plastic envelope

Illustration 2

Zip fastener of the envelope
Illustration 3

Zip fastener of the envelope

Illustration 4

Zip fastener of the envelope
Illustration 5

Blister pack (top view)

Illustration 6

Blister pack (bottom view)
Illustration 7

Strip pack (top view)

Illustration 8

Strip pack (bottom view)
Illustration 9

Screw-cap white plastic bottle

Illustration 10

White plastic bottle with silica gel
Illustration 11

Screw-cap white plastic bottle (inside view)

Illustration 12

White plastic bottle (top view)
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