CHILD-RESISTANT FEATURES OF PHARMACEUTICAL PACKAGING IN THE EGYPTIAN AND GLOBAL MARKET; A COMPARATIVE STUDY

Mai Ahmed S. Hussein [1], Mohamed Attia [2], Noha Mohamed [2]
[1] Higher Institute of Applied Arts, Printing, Publishing & Packaging, New Cairo, Egypt
[2] Helwan University, Faculty of Applied Arts, Printing, Publishing & Packaging, Helwan, Egypt

Abstract: *Child-Resistant packaging is substantial requirement especially when it is related to pharmaceuticals. Children under five years old are the most groups in risk of drug poisoning, as a result of their constant passion and attracting their attention to medicines, especially the distinctive color and small size. Due to the presence of medicines for adults, especially chronic diseases that require the presence of the drug always at home with exciting properties for the passion of a young child who is affected by colors and the small size which they can insert easily into their mouths.*
The child-resistant features attached to packages may present a problem (e.g., how to open the package) to its potential user (child or adult). Many of these features are used with the primary packaging and less for the secondary ones. Are these features efficient with available cost or not. Evaluation of each one might be varied according to package structure, level and child behavior.
Therefore, the importance of adding some features in the pharmaceutical packaging Child-Resistant, in order to achieve the safety of children with a targeted age (children under 5 years old).
By adding these special properties to the pharmaceutical packaging it will affect the design of the pharmaceutical packaging.
Finally, this paper aimed to review and evaluate the child resistant features & securing methods that are used with pharmaceutical products in the Egyptian market, with which are available globally, then make a comparison between them by description and analysis.

Keywords: Blister Packaging, Strip packaging, Child-Resistant C.R, bills, Seal. OTC

1. INTRODUCTION

Packaging can be defined as an economical means of providing presentation, protection, identification information, containment, convenience and compliance for a product during storage, carriage, display and until the product is consumed. Packaging must provide protection against climatic conditions biological, physical and chemical hazards and must be economical. The package must ensure adequate stability of the product throughout the shelf life (Shete et al, 2020).
Pharmaceutical packaging firms are some of the industry's leading innovators evident by the recent advancement in technology. The current trends are result of continuous series of challenges faced by industry. Packaging is a science which is continuously evolving and is a major success contributor for pharmaceutical industries (Nasa, 2014). According to Poison Prevention Packaging Act (PPPA), the child resistant packaging should be designed or constructed so as to be significantly difficult for children under five years of age to open within a reasonable time, so as to get a toxic effect of substance contained and also not difficult for normal adults to use properly (Sangeeta and Gupta 2015).
As regards *socio-demographic data,* the highest percentage of children admitted to the poison center (44.8%) was in the age group of 3-5 years. At this age, children usually gain motor independence and they go around actively exploring their environment. Therefore, children become highly mobile and able to get into dangerous situations quickly. Additionally, children at that age have well developed skills to locate and ingest liquids and solids, but are unable to discriminate rapidly between edible liquids and solids from toxic ones. It`s reported that the peak of accidental poisoning was seen in children between 2-5 years, (Maklad et al, 2012).
Through this research Child-resistant features at different types of pharmaceutical packages used in the Egyptian and Global market will be evaluated and compared.

1.1 Types of package

There are three level/ types of packaging; they can be described as the following (Kulkarni and Agrawal, 2015; Nasa, 2014):

• **Primary packaging :** is the material that first envelops the product and holds it i.e., those package components and subcomponents that actually come in contact with the product, or those that may have a direct effect on the product shelf life e.g., ampoules and vials, prefilled syringes, IV containers, etc. (Kulkarni and Agrawal, 2015).
The main aim of primary package is to protect the formulation from environmental, chemical, mechanical and/or other hazards (Nasa, 2014).
• **Secondary packaging** : The package external to Primary package is known as secondary package. This package provides additional protection during warehousing and also provides information about drug product for e.g. Leaflets (Nasa, 2014).
• **Tertiary packaging:** is used for bulk handling and shipping e.g., barrel, container, edge protectors, etc. (Kulkarni and Agrawal, 2015). The most common form is a palletized unit load that packs tightly into the container (Nasa, 2014).
This paper will focus on studying the primary packaging of solid forms of packaging, as it is considered the first risk to the child as a result of the granular shape of tablets and colored pills that are similar to their colored candies in both size and color

2. CHILD-RESISTANT PACKAGING

2.1 Child-resistant packaging definition :

Child-resistant packaging (CRP) or C-R packaging is special packaging used to reduce the risk of children ingesting dangerous items. The CRP containers defy penetration by children but can be opened by adults. This is often accomplished by the use of a special safety cap with locking mechanism. In developed countries like UK, it has been made compulsory to pack drugs like Aspirin, Paracetamol, Elemental iron, Contraceptives and many other drugs to be packed in CRP (Zadbuke and Shahi, 2013).

2.2 Importance of using Child-resistant features at pharmaceutical packaging:

Medications are high on the list of pediatric toxins and are to blame for hundreds of thousands of incidents each year. Part of the problem is that parents may not be aware that child-resistant packaging isn't childproof, and that even young children have the dexterity to eventually open these containers. There are certain common medications and substances that may place a child at greater risk for fatality, such as antidepressants, prenatal iron supplements, and salicylates, all of which have been reported to cause severe toxicity in toddlers (Maklad et al, 2012).
Further compounding the aforementioned problems are two other phenomena that cannot be ignored (Chen, 2015):
• Children are becoming increasingly skillful at younger and younger ages. Tablets, smartphones and gaming systems, many of which contain software applications and games intended for toddlers and preschoolers, have improved children's fine motor skills and made it easier for them to interpret symbols.
• Children are around more medicine than ever before. The "typical" household is changing; increasing numbers of grandparents reside in homes with small children.

2.3 General Classification of packaging requirements for polymers:

Child-resistant is one of the five basic requirements for pharmaceutical packaging which can be classified as shown in Figure 1 (Lyashenko et al, 2018):

- Senior friendliness.
- Hermetically sealed.
- Modularized machinery.
- Easy dispensing.
- Child-resistant.

Figure 1: General classification of Packaging requirements for polymers

2.4 Factors affecting Child-resistant:

Child resistance is a factor of the packaging system and containers and closures must be tested together. Should aspects of the packaging system change it may be necessary to vary the marketing authorization and include additional evidence that the new packaging system has been shown to comply with the relevant international standard. Factors which may affect the child resistant properties of a container-closure system include (but are not restricted to) (Malhotra et al, 2013):

- Change in foil material.
- Change in blister material.
- Change in adhesive.
- Different orientation of blister pockets.
- Different wadding materials in closures.
- Inclusion of a liquid medicine in a container-closure system previously used for solid dosage forms.

2.5 Pharmaceutical packaging closing systems for solid forms:

We should pay attention to the securing against tampering of pharmaceutical packages, as it is considered the first obstacle for the child before opening the package for the first time, so it must be taken into consideration.

- Tamper–Evident Containers:

Are closed containers fitted with a device that irreversibly indicates if the container has been opened. As shown in figure 2 & figure 3. (Shete et al, 2020)

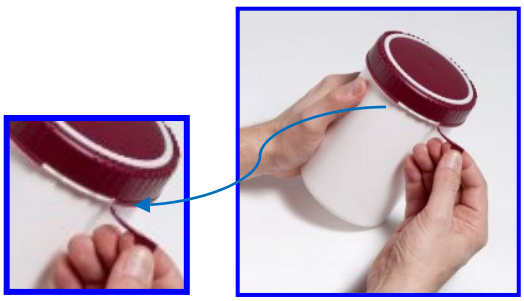


Figure 2: Tamper–Evident Containers

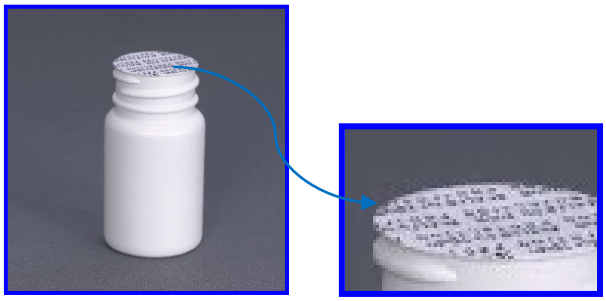


Figure 3: Tamper–Evident Containers

We should also pay attention to the effect of the cap design in the repeated opening operations, as a large proportion of medicines require taking them for a certain period, not once, and throwing the package after that. Therefore, attention must be paid to the repeated use of different caps
There are many shapes and designs for caps, and some but not all of them will be covered in the evaluation process later.

- Strip packages:

Figure 4, have at least one sealed pocket of material with each pocket containing a single dose of the product. The package is made of two layers of film or laminate material. The nature and level of protection which is required by the contained product will affect the composition of these layers. (Shete et al, 2020)

Figure 4: Strip packages

- Blister packages:

Figure 5, Are composed of a base layer, with cavities called blisters which contain the pharmaceutical product, and a lid. This lid is sealed to the base layer by heat, pressure or both. They are more rigid than strip packages and are not used for powders or semi-solids. In tropical areas blister packages with an additional aluminum membrane is used which provide greater protection against high humidity. (Shete et al, 2020)

Figure 5: Blister packages

- Child Resistant Containers:

Figure 6 & Figure 7, commonly referred to as CRC's, are designed to prevent the child accessing the potentially hazardous product. (Shete et al, 2020)

Figure 6: child-resistant Containers

Figure 7: child-resistant Containers

It should be noted that there are many designs of caps to secure against opening by children and the most common is what has been mentioned.

3. REQUIRMENTS TO DEVELOP CHILD RESISTANT PACKAGING

In essence, there are five principle activities that have been used to develop child resistant packaging over the past several decades. These include, requiring the user to (Chen, 2015):

1. Perform two deliberate and different simultaneous motions.
2. Perform a hidden alignment.
3. Have adult strength.
4. Have an adult-sized finger or hand.
5. Have a tool.

Through this table1, the main points will be reviewed in detail for developing the child-resistant packaging feature, with illustrations showing the required movement.

Table 1 (part1): Main Principles to develop Child-resistant Packaging

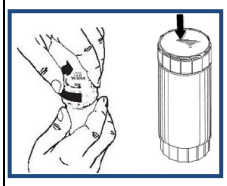
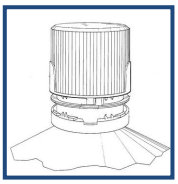
Primary Package								
Child-resistant features	Main Principles to develop Child-resistant Packaging.							
			Two deliberate and different simultaneous motions	Perform a hidden alignment	Requiring the user to have adult strength	have an adult-sized finger or hand	Having a tool	Illustration
	1. Closures	**Press and Turn**	●					
		Squeeze and Turn	●					
		Combination-lock (Line-up, snap-off closures).		●				

Table 1 (part2): Main Principles to develop Child-resistant Packaging

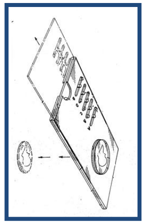
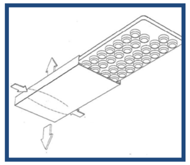
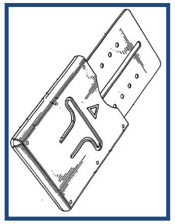
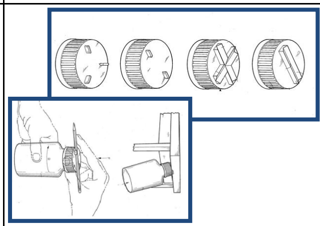
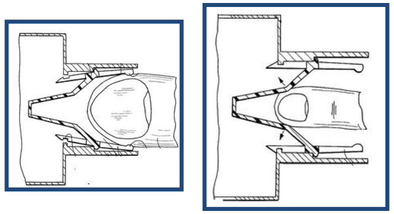
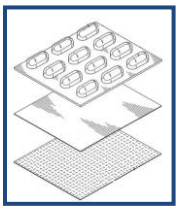
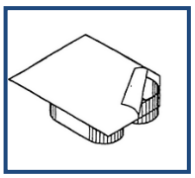
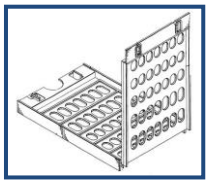
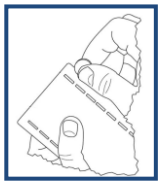
2. Blister & strip pack				
Combination-lock (require correct positioning of a series of tabs)	Side-Squeeze	Press and Pull	closure with tooled access	**Pill Closure** (considering the differences in finger size between adults and children)
	●	●		
●				
				●
			●	
				

Table 1 (part3): Main Principles to develop Child-resistant Packaging

		Packaging with safety backing. (Remove the paper then push the pill through the foil).			●			 
		Adding two actuating buttons (blister container with two spaced apart actuating buttons)				●		
		Blister packaging with tooled access					●	 

4. RESULTS & DISCUSSION

After reviewing the Egyptian pharmaceutical market, it was found that one of the characteristics of protecting children from the danger of poisoning has been applied, which is the child resistant features by applying it at the cap of medicine bottles, but when looking at the strip and blister packaging, there was no application for the child-resistant features except for the feature "Packaging with safety backing" on some medicines only. While the child-resistant features have not yet been implemented at the rest of the medicine, as shown in Table 2.

Table 2: Availability of child-resistant features at pharmaceutical packaging in Egypt.

Child-Resistant Features	Closures	Strip &blister Packs
1. Press and Turn	●	–
2. Squeeze and Turn	●	–
3. Combination-lock (Line-up, snap-off closures)	●	–
4. Pill Closure	–	–
5. Closure with tooled access	–	–
6. Press and Pull	–	–
7. Side-Squeeze	–	–
10. Packaging with safety backing	–	–
11. Adding two actuating buttons	–	●
12. Blister packaging with tooled access	–	–
13. Closure with tooled access	–	–

From Table 2, it can be summarize that in Egypt we can find the child-resistant features has been applied in the caps of pharmaceutical bottles, but in the blister & strip pack was found that it applied only with the features “packaging with safety backing” and wasn`t applied with the other types of medicines.

5. CONCLUSION

As a final result, the researchers can conclude the importance of the presence of the property of Child-resistant features in all types of medicines, especially in primary packaging, and we can notice that the developed countries of the world besides some of the developing are continuously creating and developing guidelines for each type of pharmaceutical packaging, it`s noticed that in Egypt, for example, there are some bottled medicines with Child-resistant features, but the cartoon types (blister and strip packaging) with child-resistant features have not yet been fully produced. But they have been started to produce one type until now from the child resistant blister & strip packaging. So this research highlights the importance of reaching the implementation of Child-resistant features in the blister and strip pharmaceutical packaging, as a complement to the protection of children under the age of five years.

6. REFERENCES

[1] Chen, R.: "Visual distraction as a means of enhancing child resistance", MSc thesis, Michigan State University, 2015.
[2] Fuente, C.J.: "The use of a universal design methodology for developing child-resistant drug packaging", MSc thesis, Michigan State University, 2006.
[3] Kulkarni, S., Agrawal, A.: "Creative Innovations in Pharmaceutical Packaging", Indian Journal of Pharmacy and Pharmacology 2 (4), 230-235, 2015. doi: 10.5958/2393-9087.2015.00009.6.
[4] Lorenzini, G.C.: "Toward inclusive pharmaceutical packaging an innovation and design process perspective", MSc thesis, University of Lund, 2018.
[5] Lyashenko, V., Sotnik, L., Babker, A.M.: "Features of Packaging from Polymers in Pharmaceutics", Saudi Journal of Medical and Pharmaceutical Sciences 4 (2), 166-174, 2018, doi: 10.21276/sjmps.2018.4.2.2.
[6] Maklad, A.I., Emara, A., Elmadah, E.: "Pediatric poisoning in egypt", Journal of Applied Pharmaceutical Science 2 (2), 01-06, 2012.
[7] Malhotra, S., Arora, R.K., Singh, B., Gakhar, U., Tonk, R.: "Child Resistant Packaging: A Prime Concern for Packaging of Medicinal Products", International Journal of Pharmaceutical Sciences Review and Research 22 (2), 2013.
[8] Nasa, P.: "A review on pharmaceutical packaging material", World Journal of Pharmaceutical Research 3 (5), 344-368, 2014.
[9] Sangeeta, S., Gupta, M.: "Critical survey on the guidelines under recommendation of child resistant packaging for pharmaceutical products", International Journal of Drug Regulatory Affairs 3 (3), 36-41, 2018. doi: 10.22270/ijdra.v3i3.170.
[10] Shete, N.A., Mohan R.S., Kotame R.N., Gore S.J. and Tagad R.R.: "Changing scenario of packaging in pharmaceutical industry", World Journal of Pharmaceutical Research 9 (1), 1728-1808, 2020. doi: 10.20959/wjpr20201-16569.
[11] Zadbuke, N., Shahi, S.: "Recent trends and future of pharmaceutical packaging technology", Journal of Pharmacy and Bioallied Sciences 5 (2), 2013. doi: 10.4103/0975-7406.111820.