Multi-faceted Approach Beyond Child-Resistant Packaging: for Managing Unintentional Pharmaceutical Poisoning



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Introduction

Packaging ensures the safety and it is a cost-effective way to show, safeguard, identify, contain, make a product convenient to use, and ensure compliance with regulations during the duration of storage, transportation, display, and consumption. For the duration of the product's shelf life, the package must guarantee acceptable product stability (1, 2). COVID-19 highlighted the importance of packaging in the pharmaceutical industry. Pharmaceutical packaging companies had increased their productivity to support the rising demand for containers, vials, blister packs, containers, bottles, cartridges, pouches, and others. The global pharmaceutical packaging market generated US$ 100.9 B in 2020 and it is projected to reach US$ 267.4 B by the end of 2027. The Indian packaging market was worth $50.5 B in 2019, and it is anticipated to grow by 26.4% between 2020 and 2025 to reach $204.81 B (3).

General Classification of Packaging Requirements

Pharmaceutical packaging is classified into a primary, secondary, and tertiary levels. Primary packaging closely protects the product which is in direct contact with formulation while secondary packaging serves as branding and displays the product. The tertiary package is the outer package of secondary packaging and is used for transportation purposes. Besides, depending on the packaging requirements there are the following types of packaging as shown in fig. 1 (4). Special packaging is described as being “designed or constructed to be significantly difficult for children under the age of five to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time and not difficult for normal adults to use properly” by the Poison Prevention Packaging Act (PPPA) (5-7).

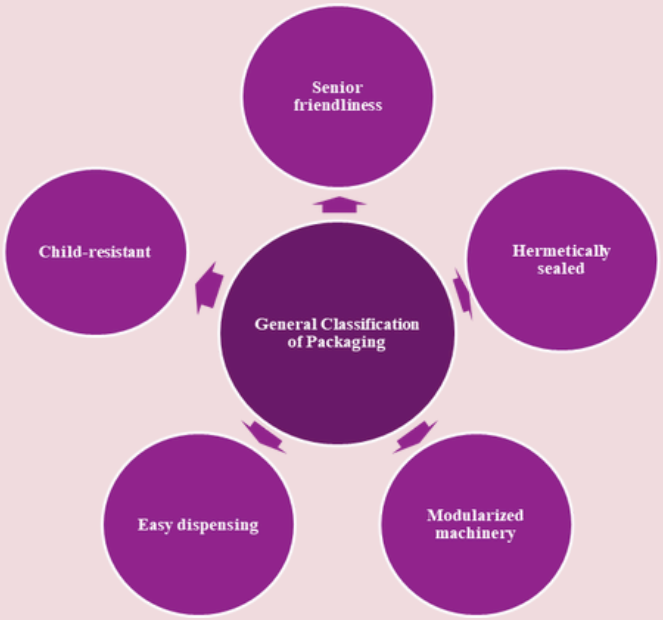

Figure. 1. Classification based on the packaging requirements

Need for Child-Resistant Packaging

Certain adult products, such as medicines, cleaning supplies, etc., can be quite dangerous when accessed by a child, mainly because of the possibility of ingestion. The most vulnerable children are those between the age of one and four since they tend to put anything they are curious about in their mouths and occasionally even swallow it. There are numerous ways that common household products can injure children, including choking hazards, unintentional poisonings, allergic responses, and chemical burns. Child-resistant packaging (CRP) 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. To ensure this, a specific safety cap with a locking mechanism is frequently employed. Despite the potential danger, the use of CRP is only mandatory for a limited number of products like OTC medications, mouthwash, dietary supplements, medications containing iron, furniture polish, turpentine, lighter fuel, various household substances, etc. Fig. 2 reveals quick facts about hazards and accidental poisonings to children (8-10). Besides, worldwide accidental data supports the importance and urgent need to address poisoning that occurred due to medicines. Across the world, various events have highlighted the importance of CRP for the prevention of medicinal hazards to children. To ensure that a product and its packaging are safe for consumers, it should always include a Design Hazard and Safety Risk Analysis (DHSRA) to review all possible risks and hazards of misusing the product, including accidental ingestion of the product by children. After a hazard review is complete, companies should review available CRP solutions. To stop children from getting access to dangerous products, the federal government and other regulatory authorities have set regulatory guidelines. The concept of CRP was introduced in the late 1960s. At the time, as per pediatricians, the most common cause of injuries in children under the age of five was accidental poisoning from ingesting specific medications and common household items. In 1970, the United States Congress passed legislation requiring specific safety measures for potentially harmful products. Despite increased legislation and regulation all around the world, which has led to the rise of the CRP industry, severe child toxicity from pharmaceuticals remains a serious global problem. Therefore, this is an opportune time

for India's developing pharmaceutical business to address child safety and implement the necessary changes in it. Engineering improvements in medicine design, enforcement measures by regulatory bodies to comply with packaging standards, and educational programs to create awareness about child safety in society are the need of the hour to ensure the rational use of medicines (11).

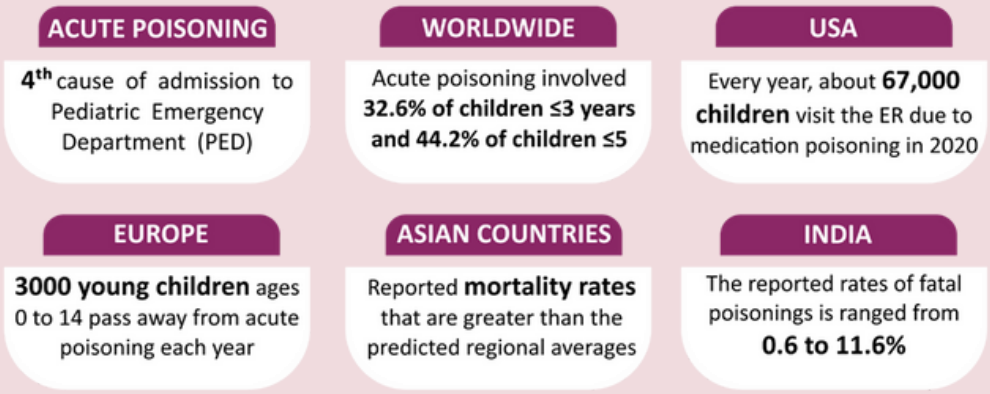

Figure. 2. Quick facts about hazards and accidental poisonings to children

Engineering Improvements to Develop CRP

The factors like changes in blister and foil materials, adhesive, blister pocket orientation, wadding materials used in closures, and the addition of liquid medication to a container-closure system can affect a child-resistant container-closure system (12). Containers and closures must be evaluated jointly to ensure that the packaging system is child-resistant (CR). In general, during the past few decades, CRP has been developed using five main activities. These include requiring the user to perform two deliberate and different simultaneous motions, to perform a hidden alignment, to have adult strength, to have an adult-sized finger or hand, and to have a tool (Chen, 2015) (13).

Principle mechanisms to develop CRP

1. Press and Turn (Two deliberate and different simultaneous motions)
2. Squeeze and Turn (Two deliberate and different simultaneous motions)
3. Combination-lock: Line-up, snap-off closures (Perform a hidden alignment)
4. Pill Closure: Considering the differences in finger size between adults and children
5. Closure with tooled access (Having a tool)
6. Press and Pull (Two deliberate and different simultaneous motions)
7. Side-Squeeze (Two deliberate and different simultaneous motions)
8. Combination-lock: require correct positioning of a series of tabs (Perform a hidden alignment)
9. Packaging with safety backing: Remove the paper then push the pill through the foil (Requiring the user to have adult strength)
10. Adding two actuating buttons: blister container with two spaced apart actuating buttons (have an adult-sized finger or hand)
11. Blister packaging with tooled access (Having a tool)
12. Tamper–evident containers: These provide a visual indication of package integrity when handled reasonably during manufacture, distribution, and retail supply.
13. Strip packages: These packages have a sealed pocket for a single dose of medicine. Two layers of films or laminates make up these packages.
14. Blister packages: These containers are made up of a base layer, cavities that resemble blisters and hold the drug, and a lid. Besides, lid is sealed with a base by heat or pressure.

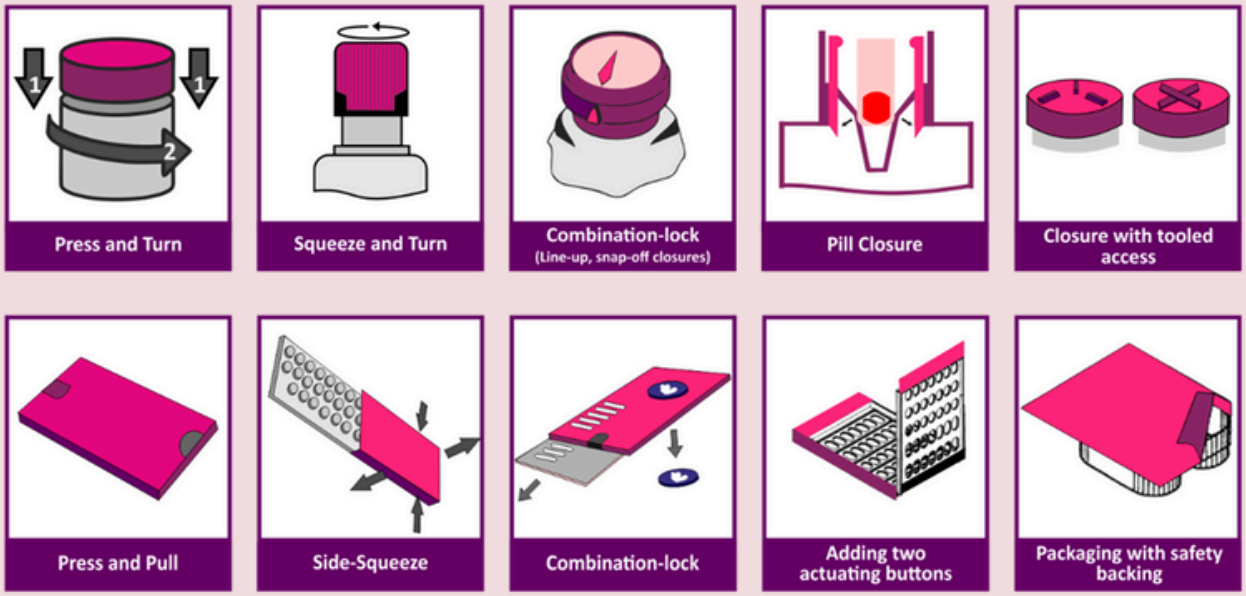

Fig. 3 Principle mechanisms to develop Child-resistant Packaging

Regulatory Framework for Child-Resistant Packaging

The European Union (EU) has enacted stringent rules to help limit and prevent unintentional child poisoning. The European Chemicals Agency (ECHA) constantly updates the Classification, Labelling, and Packaging (CLP) Regulation ((EC) No (1272/2008) to ensure that dangerous chemicals are safely contained, including CRP where necessary. Toxicity, skin corrosion qualities, and respiratory sensitization are among the conditions for substances that must be packaged in CRP, according to the law. Reclosable and non-reclosable packaging are subject to international standards, and marketing permission holders must provide proof of compliance with these standards. Drugs including aspirin, paracetamol, elemental iron, contraceptives, and many other medications must now be packed in CRP in developed nations. (14), (15).

United States: A five-person commission that administers and establishes rules for CRP on toxic substances as per the PPPA of 1970 may be appointed under the provisions of the Consumer Product Safety Act of 1970. The financial penalties for violators of industry standards are a major factor in the success and widespread adoption of CRP techniques in the US.

United Kingdom: It's worth noting that the majority of the UK's consumer legislation was passed during the 1970s. The 1975 Medicines (Child Safety) laws were one of the numerous rules that were in place at the time. Standards for CRP in the UK have included BS 5321 (1975), BS 6652 (1985), BS EN 28317 (1989), and subsequently ISO 8317, which underwent a revision in 2000.

Australia: Packaging that fulfills the specifications of the Australian Standard AS1928-2007, named CRPs. CRP is approved as child-resistant by any order made under section 10(3) of the Commonwealth Therapeutic Goods Act 1989; or complies with Section 3 of Australian Standard AS 1928-2001 CRP.

New Zealand: Caps for children must adhere to the current New Zealand Standard (NZS 5825:1991). The "palm-n-turn" style cap predominates in NZ. The "3rd generation caps" that have just been available offer a higher level of protection.

Japan: In Japan, there is no regulation as to child-resistant/ senior-friendly (CR/SF). The pharmaceutical company decides whether and how to use CRP in its products.

India: Similar to BS 7236, Indian standard IS 14233 (1995) defines blisters and strip packs and is titled "Packaging Pharmaceutical Products-CR, Tamper Proof, Packaging for Solid Dosage Forms- Code of Practice." The package is tested mechanically rather than on children.

Recent Advances in CRP

I***n-built Sensors:*** Smart packaging with in-built sensors that can identify if a product is being handled by an adult or a child with good accuracy. It uses sensors of microchips to record accurate dosing and dose monitoring. A built-in sensor will capture data each time when a patient takes a pill out of its container and sends it to the cloud (16).

Aesthetic Designs: Visual distraction technologies that distort perception and make it difficult for kids to open the package. These product designs frequently have opening features that require two independent movements, including "push and twist" caps or even blister packaging that needs to be held while being pierced by blister pieces (17).

1. Child-Resistant Blister Packaging: One of the most popular packaging options in the pharmaceutical sector is blister packing. They are inexpensive and offer excellent weather protection. For CR blister packaging, manufacturers use aluminium, PVC, PVdC, PE, PP, and Aclar films in addition to a multi-layer backing. This makes it more difficult for kids to open the packaging while adults may easily open such packages.

2. Child-Resistant Sprays: The use of CR closures makes it simple to create sprays that are both senior-friendly and CR. An additional cover that hides the spray head is usually included with nasal sprays. Manufacturers use CR caps to cover the spray head. A typical squeeze and turn mechanism, as seen in fig. 4, can be used for the cover. A new system employs bottom-lifted CR over-caps. The consumers in this case open the cap, flip it over, and push it through the bottom where it snaps into place. (18). Aptar Pharma had developed CR/SF nasal spray pump.

3. Caps and Closures: Manufacturers have used child-resistant caps and closures for a long time. The three most common mechanisms are Push and Turn, Squeeze and Turn, and Turn and Lift.

Fig. 4 Mechanism of Child-Resistant Sprays

4. Child-Resistant Sliders: Presto company has introduced a child-resistant slider and child-resistant pouches. It is a resealable pouch with a slider. The slider comes with a Press-To-Engage mechanism (PTE) shown in Fig. 5 [19]

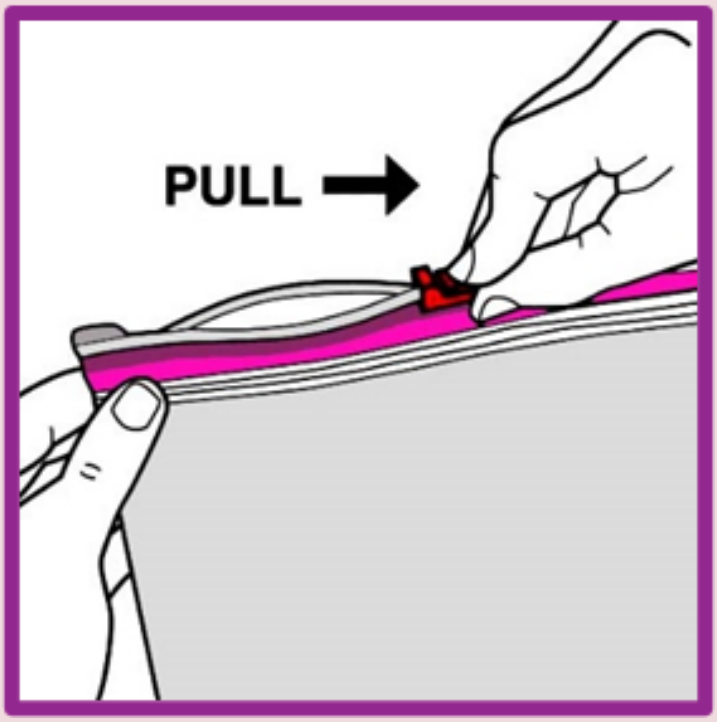

Fig. 5 Child-Resistant Sliders with Press-To-Engage mechanism

5. Re-closable CR Carton: Re-closable cartons are a low-cost and eco-friendly packing of pharmaceutical products. These are used for packing blister packs with a unit dose of medicine.
6. Locked4Kids: A plastic tray and a reclosable carton make up the Locked4Kids proprietary carton design. The plastic tray contains medicine. It can be blister packs, syringes, gelatine-coated capsules, medicine, etc. It hooks on the plastic tray and fasten it to the cardboard box from the inside. For tear resistance, the box itself has a plastic film lining. Two diagonally positioned push points on the carton must be pushed inward to release the plastic tray hook. [20].

Fig. 6 Locked4Kids with reclosable carton and a plastic tray

7. Medlock EZ: Medlock EZ is a different CR carton design that includes blister packs inside paperboard cartons. At one end of the carton, there are two push points for these cartons. By pressing down on the two push-points while sliding out the blister tray, the user can release the lock that secures the blister strip inside the carton. Cartons are highly versatile and offer a lot of space for design [21]. Colbert Packaging produces Medlock EZ packaging products.

8. Child-Resistant Pouch: Cannabis Brand Wyld Pioneers Compostable, CR Pouch for Edibles. The pouches are fully compostable, CR, and market-compliant [22].

9. Anti-counterfeit packaging: Consumers are protected from counterfeit pharmaceutical products through holograms, 2-D barcodes, forensics, radio frequency identification (RIF), overt or obvious features, concealed identifiers, serialization, and track-and-trace technologies [23].

Future Perspective of Child-Resistant Packaging

The CRP market offers tremendous growth prospects and typically exhibits superior shareholder returns. Over the next 10 years, the market for CRP will expand at a healthy rate. Throughout the projection period, new competitors are expected to flood the market, further transforming the competitive landscape of CRP [24]. The demand for CRP in the US, where India supplies around 40% of packaged OTC and prescription pharmaceuticals, as well as new sustainability rules in India, contributed to the growth of CRP solutions. Despite improved CRP designs, child poisoning remains a serious hazard. Aspirin and ibuprofen from the Kroger brand have just been recalled by Time-Cap Labs because they did not meet CRP criteria and posed a poisoning risk. Numerous studies of the EU revealed that over a quarter of the products explored were non-compliant with the classification, labelling, and packaging regulation, and nearly 44% were non-compliant with the CRF (child-resistant fastening) Regulation. The regulatory agency should take appropriate steps against those who are not able to comply with the regulatory standards. New low-cost CRP engineering mechanisms can reduce the burden on the industrial players [25].

To avoid child substance misuse, parents, guardians, and other caregivers must be involved and supportive. One of the best methods for connecting with children that adults have is through conversation. To ensure children's safety, caregivers must be cautious about the proper use and storage of medications. Fig. 7 exhibits the medication safety tips for parents [26]. Specific effective public health campaigns can be organized to raise awareness about child poisoning that may happen due to medication abuse.

Fig. 7 Medication Safety tips for preventing Pediatric pharmaceutical poisoning

Conclusion

Awareness of unintentional child poisoning has increased globally and satisfactory progress was made in poisoning prevention in the second half of the last century, particularly in reducing pediatric mortality. There are several ways to accomplish the goal of lowering the number of children under the age of five who attend the emergency room due to pharmaceutical overdoses. It will take creativity, collaboration, and commitment from the pharmaceutical industry to develop new and innovative CRP to supply the safest packaging solutions and meet the regulatory requirements to prevent unintentional deaths across the world. However, pediatric pharmaceutical poisonings can be completely routed out by working together with physicians, pharmacists, packaging professionals, pharmaceutical companies, regulatory agencies, poison preventionists, and parents. Engineering improvements, Enforcement measures, and the Educational programs (EEE) Model can all work together as a holistic strategy to reduce child poisonings from the Indian perspective.

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