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Review article

Novel Approaches in Pediatric Drug Delivery System

Paramita Dey*, Saheli Bairagi, Sandip Kumar Mondal

Bengal School of Technology, Hooghly, West Bengal, India.

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ABSTRACT

The development of medication delivery technology has led to an increase in the popularity of pediatric formulations. However, there is absence of secure and efficient drug delivery mechanism for pediatric patients. It is crucial to design and create a novel and suitable delivery system to guarantee precise and reliable medication administration to pediatric patients, as their pharmacokinetics and pathophysiologic profiles differ from those of adults. Under this heading, discussion will be carried out in order to increase stability; new medication delivery techniques and technology are being developed to enhance the stability, toxicity, flexibility, moreover security aspects of pediatric oral formulations. Specifically, issues with patient acceptability and manufacturability are discussed in this section, and innovative medication delivery methods are examined to address current issues.

Introduction

Creating secure and efficient preparation for juvenile patients is a significant task because their pharmacokinetic and pathophysiologic profiles differ from those of adults. Considering other populations youngsters may take in, disperse, remove, and retain substances in various methods.[1] Therefore, young people cannot take contemporary adult prescription drugs. A child's ability to absorb drugs is significantly impacted by changes in the stomach's emptying time and pH.[2] In particular, the pH of the stomach drops two to three days after birth from its neutral state at birth. The acidic pH of an adult stomach is not attained until after weeks or years of this procedure.[3] It has been noted that infants six to eight months old have slower gastric emptying times due to the immaturity of the neuroregulation of stomach motility.[4]

Furthermore, compared to an adult, a child's body has a higher water content and a lower concentration of plasma protein. This leads to varying medication distribution rates throughout a child's organs. An additional crucial aspect to take into account is the potential existence of metabolic abnormalities in newborns, which could lead to decreased medication excretion and an extended drug half-life. Renal clearance declines due to immature tubular reabsorption, tubular secretion, and glomerular filtration, particularly in babies.[2,5] Therefore, it is crucial to ascertain the appropriate and safe dosages of medications meant for prescription to children, neonates, and babies. Therefore, while using medications in children, it is imperative to comprehend their pharmacokinetics and pharmacodynamics in order to attain an appropriate concentration.[1] To determine the optimal and appropriate dosage, clinicians should consider the aforementioned factors as well as the distinct clinical manifestations of each pediatric patient. There are several ways to administer drugs to kids, including oral, rectal, intramuscular, dermal-transdermal,[6] and inhalation methods.[7] As it is easier to

***Corresponding Author:** Dr. Paramita Dey

Address: Bengal School of Technology, Hooghly, West Bengal, India.

Email ✉: paramita@bstpharmacy.in

Tel.: +91-9051477424

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carry out than other conventional formulations, the oral pathway is the most preferred method of administration for treating chronic diseases, while the intravenous route is crucial for treating acute disorders.

The biggest issue with oral dosage forms, however, is getting kids to swallow the medication or accept it without complaining. Furthermore, children can acquire the ability to swallow at approximately 6 years of age. Because various sweeteners and flavors can mask the obnoxious taste or odor of the formulation, it is therefore advised to use liquid formulations at younger ages.[8] However, a lot of oral medications are still sold in larger or tablet form, and these medications not only make it difficult for children to swallow them but also make them behave badly. Because of this, physicians and parents may want to consider alternative delivery methods, like breaking, crushing, or incorporating the medication into meals, which could reduce the medication's therapeutic effectiveness.[9,10] Granules or orodispersible tablets can be used to get around this issue, but the taste of bulking agents in these formulations ought to fall inside tolerable bounds for pediatric individuals. Transdermal application is an additional route of administration that offers several benefits. Because the skin is the human body's biggest organ—it offers an alternative method of administering medications to pediatric patients.

The medications can enter the systemic circulation by penetrating the skin layers in transdermal application. Still, the skin serves as an obstacle that prevents drug intrusion and dehydration, particularly in older children and infants. However, having such a barrier function could be helpful in achieving therapeutic concentrations that are appropriate without running the risk of toxicity. Nowadays, pediatric patients receive different transdermal patches with active pharmaceutical substances like fentanyl, clonidine, and scopolamine, though not all drugs are covered by them.[6] Inhalation products are the primary treatment for the majority of pediatric patients suffering from asthma and chronic obstructive pulmonary disease (COPD). Another crucial route for administering medication to children is intramuscularly. When it comes to pharmacokinetic parameters like the amount of time needed to reach the target drug concentration, this route has certain drawbacks. In infants, it is particularly unreliable.

However, medication molecules such as ampicillin and aminoglycosides exhibit comparable pharmacokinetic characteristics in newborns, kids, and adults, such as the quantity of time needed to attain the maximal plasma concentration. For patients who are unable to take oral dosage forms, rectal administration is recommended because the rectum is well vascularized, resulting in the appropriate adsorption.[11] People in the pediatric age range are those who are under 18 years old. The physiologic, pharmacokinetic, pharmacodynamic, and physical capabilities of the patients in this group differ greatly. These modifications make it very difficult to provide pediatric patient care in terms of selecting the right medication for the patient's condition, identifying convenient formulations for administration, and gaining the patient's acceptance. Children who are not included in the medication dosing guidelines are referred to as "Therapeutic Orphans." Children and adults are not similar, and they do not become physiologically equivalent to one another until they reach puberty. Their organs and enzymatic systems are not fully developed at birth; these things happen gradually. Even the pharmacokinetic profile, which gradually develops and differs greatly from adults in terms of absorption, distribution, metabolism, biliary and renal excretion. Understanding pediatric pharmacokinetics is essential to giving pediatric patients safe, effective treatment and preventing side effects, therapeutic failures, and death.

Pediatric Age Grouping

- <38 weeks is called premature
- Baby with 1 day to 1 month is called neonate
- Baby with 1 month to 1 year is called infant
- 1 to 12 years of age is called child
- 12 to 18 years of age is called adolescent
- 0 to 18 years of age is called pediatric

Pediatric Pharmacokinetics

Absorption

Early neonates (less than 2 weeks old) experience achlorhydria, a condition in which the stomach does not produce any gastric acid. The therapeutic effectiveness of medications taken orally, which depend on acidic media for drug release and absorption, may be severely hampered by this. At 2 years old, the pH of the stomach gradually drops to adult levels. Neonatal with altered stomach emptying have prolonged, erratic, and irregular stomach emptying. The medication absorption via the intestine is delayed by prolonged how quickly the stomach empties, potentially increasing drug degradation as a result of prolonged contact with the contents of the stomach. The rate of absorption varies greatly regarding food and other variables. Although enzyme activity in the pancreas is minimal, it potentially increases moreover influences the bioavailability of drugs that are dependent on these enzymes. Since children's skin is three times larger than an adult's in relation to weight, absorption through non-oral routes is different in this age group. This increases the absorption of topically applied drugs. In addition, compared to adults, the skin is thinner and more hydrated, which permits deep drug penetration but may also raise toxicity and systemic absorption. However, intramuscular absorption in neonates is unpredictable due to the lack of muscle and fat tissue.

Distribution

Because infants possess a greater total body water to fat comparatively speaking to adults, drugs that are hydrophilic will have a larger volume of distribution,

while those that are lipophilic will have a smaller volume. Babies have lower albumin levels, different protein-binding properties, and more competition when it comes to binding endogenous substances. Additional enhancement of drug absorption is possible due to a highly permeable blood-brain barrier (BBB). The main factors influencing drug distribution are permeation through tissues, perfusion speed, binding of tissue with drug, type of disease and interaction with drugs. Reduced liver volume and regional hepatic blood flow inhibit the hydrolysis, oxidation, and reduction of drugs during their biotransformation.

Metabolism and elimination

The liver's cytochrome P-450 (CYP450) enzyme is heavily involved in the metabolism of APIs. APIs are inactivated in the hepatic organ by the enzyme CYP450 through hydroxylation and conjugation moreover hydrolysis, oxidation, and reduction. The fetus lacks certain enzymes that are crucial for the drug metabolism of infants, like glucuronidation enzymes, which develop gradually.

Most Frequently used Pediatric Formulations and Preferable Administration Routes

Oral dosages

- Solid (tablets, pills)
- Liquid (syrup, suspensions)
- Chewable tablets

Transdermal patches

- Microneedles
- Iontophoretic
- Drug in adhesive

Rectal formulations

- Creams- ointments
- Suppositories
- Foams
- Sprays
- Enemas

Conventional Formulations for Pediatric Usage

Drug distribution to pediatric patients is restricted when using traditional liquid drug formulations like solutions, emulsions, and suspensions and solid dosage forms like tablets and capsules (Table 1).

Specifically, issues with patient acceptability and manufacturability are discussed in this section, and innovative medication delivery methods are examined to address current issues.

Liquid dosage forms

Due to their difficulty in swallowing when administered orally, liquid formulations are typically recommended over capsules and tablets, especially for young children. Furthermore, because of the huge size of traditional solid dosage forms and their high active ingredient content, youngsters should not use them. Splitting tablets to administer them usually makes it more difficult to get the desired, safe treatment. However, suspensions are frequently recommended in pediatric patients because certain active ingredients are not soluble in water.

However, there are also some significant restrictions when it comes to using liquid dose forms on young children. The necessity of consistent dose in order to maintain the blood level of active componentis the first of these issues. The challenge of hiding an unpleasant taste is another issue. Milk has been utilized as a transporter for this purpose in recent years, but not enough progress has been made. Furthermore, it's challenging to ensure the amount of homogeneity in liquid dosage forms, even with the use of syringes and other administration tools.

For all of these reasons, it is thought that innovative drug delivery methods, like ODTs or tiny tablets, which combine the benefits off or pediatric patients both solid and liquid medication delivery methods, may be the answer to the aforementioned issues rather than traditional liquid dose forms.

Solid dosage forms

Often, solid dosage forms are preferred over liquid ones, because of their long-term stability and inexpensive production costs, even though they are not appropriate for patients who have trouble swallowing as adults or children. The ability to more readily mask the formulation's bitter taste is another benefit of traditional solid dose forms like tablets and capsules. For this reason, simple-to-use formulations that boost patient compliance are developed, particularly with the advent of coated tablets and encapsulating technologies.

However, dose flexibility in treatment is not possible with traditional solid dosage forms. Recently, an application tool known as a "solid dosage pen" to give dose flexibility, particularly with tablets. With the help of this device, the tablet can be sliced to the appropriate length, allowing for quantity adjustments.

Still, questions remain about how safe and useful the device is.

Owing to the benefits associated with solid dosage forms, the use of ODMTs, which can be administered to pediatrics as soon as possible, has expanded in recent years, with a particular focus on pediatric use.

Advancement of novel dosage form

Scientists have created various liquid formulations of pediatric products to be used, but liquid formulations easily undergo hydrolysis instability and are prone to microbial growth. Oral administration is the best option for administering and manufacturing in the form of tablets. But, tablets have better taste, swallowing, and size for pediatric patients.[12]

Infants and newborns experience fast, parallel organ growth phases, as well as wide variations in their

Table 1: Benefits and drawbacks of the administration route in pediatrics

Administration path	*Benefits*	*Drawbacks*
Suspensions	Offers sustained medical care. Flexibility in dosage administration.	Initial pass effect Stability issues
Solutions, syrups	Ensures uniform dosing.	Stability issues. Issues with dose measurement.
Granules powders	Delivering a customized release of the medication.	Difficulties with dose measurement.
Tablets	Acceptance by the children	Ingesting issues.
Capsules	Adaptability of dose Elevated stability.	Criteria for taste masking.
Parenterals	Primary path in the event of an emergency. Rapid and high blood drug concentration.	More costly. A little discomfort during injection.
Suppositories	No difficulty in swallowing.	Restricted bioavailability and size concern.

medication sensitivity and metabolizing capacities. It is necessary to conduct an empirical search for drug response patterns related to age in order to identify the most suitable treatments and those that should be given to pediatric populations.[13]

In order to identify specific treatment approaches as a body matures and develops aqueous defensive mechanisms that protect against germs and infective agents. One of the main objectives of pharmacogenetic research is to identify the variability of genes that affect drug response. This includes analyzing the pattern of gene expression interaction between these products and their role in the pathogen of pediatric diseases.

Oro-dispersible tablets

Tablets which are dispersed orally are made to dissolve in buccal cavities in just a few seconds (Fig. 1), no need for swallowing. However, the formulation design of these tablets does not offer any dose flexibility over conventional tablets; instead, different dose strengths would be required to satisfy the need of entire population. The usage of dispersible tablets needs to be made clear in order to prevent medication errors because the drug's bioavailability is affected by the formulation's retention period in the mouth. Super disintegrants such as carboxymethyl cellulose, cross-linked cellulose, polyvinyl pyrrolidone, and sodium stars glycolate are added to these formulations, which allows them to dissolve in the mouth in a fraction of a seconds.[13]

Drug bioavailability can rise due to pregastric and oral absorption, resulting in fast disintegration upon coming into contact with water or saliva, hence lowering the

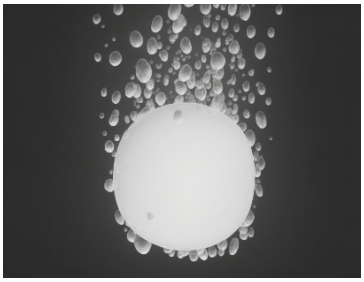

Fig. 1: Oro-dispersible tablets

first-pass metabolism in the GIT. Compared to semi-solid or liquid dose forms, they are more stable.[14] For ODTs, drug loading is extremely high. Because it is simple to administer, no measuring equipment is needed. When hydrophobic and insoluble medications are given to pediatric patients as oral disintegration tablets (ODTs), the tablet gradually dissolves and disintegrates, increasing the bioavailability of the medication. Preservatives are not necessary because the dispersible dosage form with numerous excipients has a suitable safety profile. For the production of ODTs, direct compression and lyophilization are two popular processes. Compared to compressed tablets, lyophilized ODTs are more mechanically delicate. Compressed ODTs are also needed to improve packaging in order to guarantee stability.[13]

Compression tablets dissolve more slowly than lyophilized ODTs. Lyophilized ODTs can typically be delivered at recommended doses of 60 mg for the water-miscible drug and less than 400 mg for the weakly water-soluble drug. Furthermore, it can take a while to grow because it can be difficult to find the ideal ratio between rapid breakdown and sufficient mechanical power. A recently promoted ODT has been approved for use in one-year-old toddlers. The medication can be administered straight into the patient's mouth, by an oral syringe, or through a nasogastric tube combined with water.[14]

Mini-tablets

For infants and children, mini tablets are the solid dosage form with a diameter of 2 to 4 mm (Fig. 2). Infants can only ingest liquids; however, by the age of six months, they can swallow a variety of particles based on their size, shape and hardness. A dosage form with a rapid oral dissolution rate and with a minimal quantity of saliva is a suitable dosage form for infants and toddlers.[15]

2 mm

When these are placed on the tongue, the medication is released instantly whether they are coated or not. Mini tablets need to be used with a tablet dispenser and can be used by anyone six months of age or older. The benefits of tiny tablets include ease of swallowing, adjustable dosage, non-refrigerated storage, excellent portability, and the option to take multiple tablets as a single dose when combined with jelly.

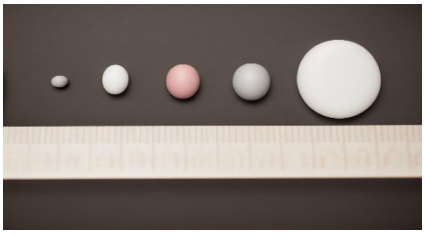

Fig. 2: Mini tablets

4 mm

Parents can administer these at home, giving children the opportunity to get instant medication release starting at age one year old. Benefits include being more often accepted than powder, syrup or suspension. Tablet dispenser not required.[16]

Pill Swallowing Cup

It's not always easy to swallow pills, but with the right tools and technique, you can down the tablet quickly along with your beverage. The oralflo cup, which resembles a sipping cup (Fig. 3), is one of these cups. It is accessible to anyone and appropriate for both adults and kids four years of age and up. Millions of people who would have previously had to choke, gag, and suffer while attempting to take the drug have benefited from it. Oral flow is a cutting-edge new medical tool that assists physicians, nurses, pediatricians, parents, elders, and other caregivers in giving pills to patients. It makes it possible to naturally and safely swallow pills of any size, doing away with the need to hold a dry tablet in your tongue and easing the worry associated with taking medications. The distinctive design makes sure the tablet and water combine in your mouth. in order for you to swallow the tablet without difficulty when your swallow reflex kicks in. Depending on the size of the pill, you might not even detect the field.[17]

Medicated Dosing Straw

When a child is sick, they prefer to drink liquid medication instead of swallowing big tablets, which makes them reluctant to take the medication.[18] Granulated medication can be administered with ease because it has previously been accurately pre-dosed in a straw (Fig. 4). Taking out the straw, the patient pours his favorite drink inside, removes the end cap, and sucks after tearing open the sealed single pack. As you take the medication, a device inside the straw known as a controller rises. At the top, the controller remains until the entire dosage is consumed. Additionally, drugs are simply dosed on an individual basis.[19,20] The device serves two purposes: it facilitates easy consumption by drinking straws and allows for individual dosage. Using a dosing ring with defined phases, the user can modify the dosage that the doctor has prescribed. This personalized adjustment enables each patient to receive the individualized care that is necessary in today's modern medicine.[21] Extra features include detachable caps for

Fig. 3: Pill swallowing cap

Fig. 4: Medicated dosing straw

Fig. 5: Solid dosage pen devices

straws with pre-measured medication doses to prevent medication straw walls that are flexible to enable breaking up medication pills inside the straw, preventing loss while handling or storing, disposable funnels for feeling the straw that has the appropriate amount of meditation, and funnels that can attach to pill crushers.

Solid Dosage Pen Device

A wonderful dosing tool for individual therapy, the solid dosage pen allows for flexible oral individual therapy dosage for a wide range of targeted populations. Solid dose pens are produced using the wet extrusion method. These extrudates can be placed using the solid dose pen (Fig. 5), and an adjustable screw is used to select the dosage. Finally, the extrudates can be snipped off to directly supply individual dosed tablets, such as slices.[17,22]

Medi-bottle

Utilized as a liquid dosage tool for oral administration, the Medi bottle is a modified pediatric feeding bottle. The components of this system include an oral dispenser that inserts into the middle of a conventional infant bottle.[23]

Fig. 6: Medi-bottle

Fig. 7: Nipple shield delivery system

To put the prescribed dosage of medication into a container filled with milk or other liquid, insert the dispenser's contents (Fig. 6). The infant swallows the medicine as soon as the dispenser plunger descends, producing aexplosion of medication with each gulp down milk or other beverage. Babies and young children accept the Medi bottle, and older children take it to a lesser extent.[24]

Nipple Shield Delivery System

When nursing, a newborn may receive nutrition and medication safely through a breast shield that wouldn't transfer illness. In order to utilize these delivery systems, a mother places the device with the pre-loaded tablet insert over her breast before nursing her child (Fig. 7). As the child suckles, the milk flows through the apparatus, releasing the drug particles straight into the breast milk and onto the child. The gadget will be pre-loaded, disposable, and designed to minimize material thickness while optimizing skin-to-skin contact with the baby. Antibiotics, antimalarials, antivirals, vitamins, minerals, and probiotics are among the medications that are delivered by this method. Requiring portable water to dissolve a dry tablet is not necessary because the sterile device uses human milk as the dissolving agent.[25]

Oral Thin Films

Oral thin films, sometimes referred to as buccal patches or strips, are monolayer or multilayer systems that range in length from 2 to 10 cm and thickness from 20 to 500 µm. Medication might be spread in oral thin films, emulsified, or dissolved in the matrix. These are thin, sturdy, long-lasting films that quickly dissolve when placed to the oral mucosa surface or without water in the mouth (Fig. 8). They are resilient to breaking from the stress of oral action and have good mucoadhesive, elastic, and flexible characteristics. Without going through hepatic first-pass metabolism, the medication from the films enters the systemic circulation straight through the oral mucosa. They can facilitate the drug's quick or continuous release from films.[23] With a quicker start of action, lower dosage requirements, improved drug efficacy, and safety, films offer more precise dosing than liquid formulations. These are simple to manage for both regional and systemic effects, and they increase geriatric, pediatric, and neurodegenerative disease patients' compliance when accurate and comprehensive dosing is challenging. However for pediatric patients, lyophilized wafers and oral films offer enormous therapeutic potential.[26]

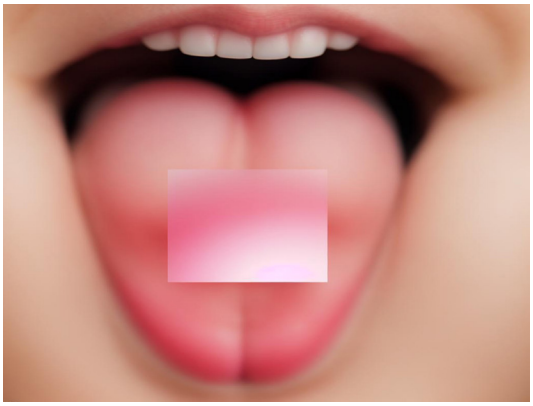

Fig. 8: Oral thin films

Pulmonary Drug Delivery System

Breath-actuated pressurized meter dose inhalers are replacing traditional pressurized metered dose inhalers. At the patient breathes more quickly than above a specific air flow rate, these inhalers instantly release the aerosol. Children's peak inspiratory flow can be effectively controlled with the use of the in-check dial device (Fig. 9), which ensures that they achieve the necessary minimal air flow rate. Convenient inhalation devices have adjustable airflow resistances, and an imprinted scale makes it possible to determine which device is best for each patient. In the treatment of airway diseases, powder inhalers are used instead of pressurized meter dose inhalers because the patient's peak inspiratory flow provides the necessary energy for particle dispersion rather than propellants.[23] A specific flow power during breathing is needed to arrive in the lungs in order to produce a minimum number of tiny particles. Typically, kids under 4 years old are unable to produce sufficient inspiratory pressure to achieve the required flow rate. For children ages 4 to 6, low airflow resistance dry powder inhalers are the ideal choice. Additionally, a breath-actuated device guarantees that

the aerosol is only administered once the patient achieves a suitable flow rate during inhalation. When breathing is difficult due to a severe asthma attack, dry powder inhalers should not be used.[27]

Recent Developments in Pulmonary Delivery

In recent years, a number of spacer/valve-holding chambers have been created with the goal of enhancing children's adherence to and compliance with pulmonary devices. The Babyhaler is made out of a holding chamber with a valve that allows babies to apply medication in a pleasant way (Fig. 10). The vortex, which comes with amusing facemasks, is a holding chamber that is non-electrostatic having a universal adaptor for all ordinary PMDIs.

With a visually pleasing design that limits the inhalation flow rate to 15 L/min, the Watchhaler is an attractive tool to use.

The Funhaler is another inventive invention that comprises a whistle and an internal spinning disk housed in a valve-holding chamber. When the youngster breathes regularly, the disc rotates and the gadget whistles, encouraging them to take the prescription.[23]

Transdermal Drug Delivery System

Palatability, taste masking, gastrointestinal drug degradation, first-pass metabolism, hepatotoxicity, pain during injection, needle-stick injuries, injection-related emotional trauma, prolonged drug release, improved bioavailability, and improved patient adherence are all overcome by TDDS, making it a desirable substitute for oral and parenteral routes. Energy-enhanced transdermal drug delivery by the use of jet injectors, needle-free devices, microneedles, etc., is known as transdermal microporation.[23,28]

Fig. 9: Inhaler devices

Fig. 10: Funhaler

Microneedle

The transdermal microneedle is a novel drug delivery technology that circumvents the drawbacks of traditional passive patches by delivering medication directly into the skin (Fig. 11). A microneedle is made up of hundreds of microfabricated microneedles layered on a basic substrate.[28,29] It can penetrate the stratum corneum and open temporary passageways for medication delivery and penetration.[30,31] In comparison to hypodermic needles, drug administration with microneedles is painless because of their tiny needles, which lessen pain perception and nerve stimulation (Fig. 12).[32,33] It can transport water-soluble and large molecular-weight medications. Microneedles have been linked to bleeding, infections, and little to no skin discomfort.[34]

- *Types of microneedles*

The drug delivery method is influenced by the type and design of microneedle.

- Solid microneedle can be applied topically or applied as a transdermal patch to improve the permeability of a medication.
- Water-soluble or biodegradable polymer-based microneedles: These have been developed for depot-controlled medication release.[35]

Four varieties of microneedle designs exist,[36] which comprise:

- Solid microneedles: To puncture the skin before applying medication
- Solid microneedles with medication coating: For quick skin disintegration
- Polymeric microneedles that dissolve quickly and can be regulated in their drug release: either drug-free or drug-encapsulated.
- Hollow microneedles: For injecting medication.
- Needle-free device: Both subcutaneous and intramuscular delivery methods are used by needle-free devices to administer medications and big molecules, including insulin, vaccinations, growth

Fig. 11: Microneedle

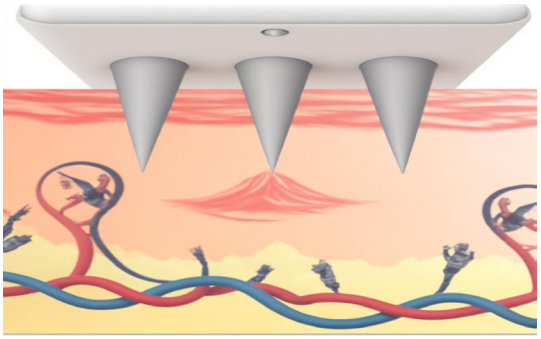

Fig. 12: Stimuli responsive microneedle

hormone, and local anesthetics. Through a tiny skin-piercing hole, these devices can administer formulas in either liquid or powder form under high pressure. These systems include, for instance, PharmaJet, JTip, and Bioject. Needles are essentially easy to handle and dispose of. Needle-free devices help patients overcome their dread of needles.

Rectal Dosage Form

The rectal method of administration is superior to the oral route in a number of ways. These methods successfully address palatability and taste, two key concerns in oral dose forms for pediatric patients. Both regional (laxative, anti-inflammatory) and systemic (antipyretic, analgesic, anti-nauseant, anticonvulsive, sedative) effects can be obtained by the rectal route of administration. Rectal dose forms are recommended for young patients who have difficulty swallowing oral medications, experience nausea or vomiting, require continuous nasogastric suctioning, are unconscious, or have palatability problems.

The most used rectal dose form for pediatric patients is suppositories. Additional dose forms consist of gelatin capsules, lotions, ointments, gels, foams, and small- or large-volume (<20 mL) solution or suspension enemas.

pH of the rectal mucosa is 7 to 8. Its extensive blood and lymphatic artery supply allows it to avoid the initial stage of hepatic metabolism and improves medication absorption.[37] Suppositories come in a range of strengths, and the size of the tablet should correspond to the patient's age. Infant suppositories have a weight of about 1 g, which is half that of the dose form for adults.

The function (local or systemic effect) and age of the kid should be taken into consideration when determining the volume of enemas. The smallest enemas' volume is ideal for precise dosage distribution, optimal absorption, and minimal irritability. The rectal tube should be safe to use and the right length for the child's age; the dose delivery mechanism should make straightforward distribution possible.[37]

Challenges of Novel Dosage Form

When creating pediatric formulations, the delicate nature of the formulation is prioritized. Masking the flavor of the API during preparation is a challenging undertaking because the patient would never experience the API's flavors during administration. The absence of *in-vitro* testing is the biggest drawback of delicacy valuation. The intelligence of medicinal delicacy differs in adults and children, and in children who are ill and those who are well. As a result, only children were used in clinical experiments, albeit this raised some ethical concerns. For this reason, the "swill and spit" method can be helpful in assessing delicacy. Pediatric patients have difficulty understanding the acceptability and palatability of medications.[38]

On the other hand, it might be appreciated by regularly prescription medication to patients as opposed to giving them a single dose. In actuality, a deficiency of assessment methods leads to formulation issues. Incorporating flavors that children like—like chocolate, cherry, strawberry, and apple—into a liquid preparation will help increase adoptions and help overcome delicacy value challenges.

The creation of a traditional dosage form is the primary goal of developing suitable formulation qualities for teenage dosage forms while developing a new formulation intended for oral administration. While newborns prefer liquid formulations, younger and older children prefer oral solid formulations.[39] When creating a formulation, physicochemical, biopharmaceutical and physical parameters are taken into consideration as the most important elements. Therefore, taste is not a consideration. It can be difficult to determine a drug's soluble qualities for pediatric formulations. When a medicine has a high solubility, it can be difficult to disguise its flavor and create a suspension or liquid formulation because the drug dissolves readily in a medium. The drug's high solubility, which causes it to dissolve easily in the mouth, makes flavor concealing difficult in solid dosage forms, including chewable formulations and ODTs. Therefore, other methods such as drug coating, film-coated pellet formulation, and micro tablets have gained attention.

Conclusion

Considerable progress has been made in the area of baby medication delivery from the standpoint of formulation and dosage form. It can be difficult for parents and healthcare professionals to give a baby a liquid dosage form, and the entire amount is rarely given without difficulty. For older infants, the dosage form can be mixed with food without risk of choking, thanks to mini-tablet and sprinkle formulations. Rather of attempting to modify adult formulations, age-appropriate devices have been devised to satisfy the need of oral doses in newborns. Our capacity to modify dosage forms for infants will significantly improve with the quick development of 3D printed technologies and their application in hospital and pharmacy settings. Covers, chewable, or thin-films to genuinely transform dosage forms that are patient-centric. It is crucial to design and create a novel and

suitable delivery system to guarantee precise and reliable medication administration to pediatric patients. While new alternative medication delivery systems are being created as a result of advancements in drug delivery technology, the pediatric drug delivery system needs to continue growing in order to provide better care. Notwithstanding the substantial progress made by contemporary antiretroviral therapy, many obstacles persist.

To increase patient acceptability and compliance, several eye-catching technologies might be employed. These cutting-edge methods can be used to improve the stability, toxicity, flexibility, and safety aspects of pediatric oral formulations. The choice of a suitable formulation for a certain target demographic for a given product needs to be thoroughly thought out.

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