



INNOVATIVE PEDIATRIC DRUG DELIVERY SYSTEMS

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Abstract: Administration of pediatric medicines needs to be accurate and to ensure the correct dose, the administration device should be easy to use and acceptable. Continuous development and maturation of pediatric organs involved in drug metabolism and clearance results in pharmacokinetic changes are focused. The review provides an overview of currently available innovative pediatric administration devices and highlights some of the challenges associated. Recent developments in oral transmucosal, parenteral, rectal, pulmonary and transdermal delivery to achieve better systemic drug levels in pediatric population are highlighted. A new nipple shield delivery system to deliver antiretroviral drug formulations to HIV infants to prevent mother-to-child HIV transmission during breastfeeding is discussed as a safe alternative. However the future of pediatric medicine is promising but challenges still remain.

Keywords: pediatric, pharmacokinetics, innovative devices, transdermal, transmucosal, pulmonary, HIV

Introduction

Pediatric age groups include individuals from birth to 18 years of age (Table 1). Patients in this population vary widely in physiologic, pharmacokinetic, pharmacodynamics, and physical capabilities. These changes makes pediatric patient care extremely challenging with respect to finding a correct drug pertaining

to patients medical condition, to identify appropriate formulations convenient for administration and largely acceptance by patients. Only 20% of medications are approved by Food and Drug Administration (FDA) for pediatric indications, thereby referring children as "Therapeutic Orphans" meaning a population excluded from medication dosing guidelines.

There is no similarity between children and adults, and it is only after puberty they become physiologically equivalent to adults. At birth they do not have fully functional organs and enzyme system, the system develops with time and at its own rate. Even the pharmacokinetic profile such as absorption, distribution,

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metabolism, biliary and renal elimination, protein fixation and action at receptor sites¹ is significantly different from adults and develops gradually. The knowledge of pharmacokinetics in children is a key to provide safe and effective therapy to the pediatric patients and to avoid therapeutic failures, adverse effects and fatality.

Table 1: Classification of pediatric age groups

Term	Age
Pediatric	0-18yr
Premature	<37 weeks (gestational week)
Neonate	1 day to 1 month
Infant	1 month to 1 year
Child	1 to 12 years
Adolescent	12 to 18 years

A. Pediatric pharmacokinetics

- **Absorption** :Early neonates (2 weeks) are in a state of achlorhydria where the gastric acid production in stomach is absent. This may significantly hamper the therapeutic efficacy of orally administered drugs which requires acidic media for drug release and absorption. Gastric pH slowly decreases and reaches adult levels by the age of 2 years. Altered gastric emptying in neonates is irregular, unpredictable and prolonged. They have protracted rate of gastric emptying which results in delayed absorption of medicament through intestines, which may increase drug degradation due to prolonged contact with gastric contents. Absorption is highly variable depending on meals and other factors. Pancreatic enzyme activity is initially low but develops gradually and affects drugs bioavailability which depends on these enzymes. Absorption via non-oral routes is different in pediatric patients since their skin surface area is thrice that of adults relative to weight, thereby increasing drug absorption applied topically. Further the skin is more hydrated and thinner than adults with increased hydration allowing

deep drug penetration but may result in increase the systemic absorption and toxicity. However, scarcity of muscle and fat tissue makes intramuscular absorption unpredictable in neonates.

- **Distribution**: Infants have high ratio of total body water to fat than adults, generating a large volume of distribution for hydrophilic drugs and low volume of distribution for lipophilic drugs. Infants have decreased level of albumin, modified protein binding characteristics, and increased competition for binding endogenous substances. A highly permeable blood brain barrier (BBB) further allows increased drug absorption. Tissue permeability, perfusion rate, tissue-drug binding, disease state, and drug interaction are major factors affecting drug distribution. Decrease in liver volume, regional blood flow of liver reduces drug biotransformation through hydrolysis, oxidation and reduction.
- **Metabolism and Elimination**: Enzyme cytochrome P-450 (CYP450) present in the liver is extensively involved in drug metabolism. Enzyme CYP450 inactivate drugs in liver via hydrolysis, oxidation and reduction (phase I reaction) and hydroxylation and conjugation (phase II reaction)¹. Other enzymes involved in infants drug metabolism such as glucuronidation enzymes are absent in the fetus and but develops gradually.

B. Challenges

Understanding the pharmacokinetic profile of pediatrics, the greatest challenge lies in design, selection and optimization of pediatric drug delivery systems². Selection of a formulation is more important than the choice of drug or brand for pediatric patients. Marketed pediatric dosage forms include solutions, syrups, suspensions, powders for reconstitution, taste masked tablets, dispersible tablets, etc.³ However limitations of these dosage forms include spillage during administration, inconvenien-

-ce during powder reconstitution, unacceptable taste and multiple dose regimens resulting in poor patient compliance^{4,5}. In order to overcome these limitations and improve pediatric patient compliance, there is an urgent need for development of innovative drug delivery systems.

C. Conventional Dosage Forms

Injections, tablets, capsules, powders, granules, suspensions, solutions etc. contributes to majority of the conventional dosage forms given through parenteral, oral or topical routes. Drug administered through these route have several limitations:

a) Parenteral Dosage Forms

- Pain at the site of injection
- Certain degree of hemolysis
- Risk of severe adverse reactions or hypersensitivity
- Requires expertise and aseptic conditions
- Patient non-compliance

b) Oral Dosage Forms

- Difficulty in swallowing
- Drug undergoes extensive first-pass metabolism in liver
- Drug metabolites formed may not be active as parent drug, and thus requires high oral dose compared to parenteral dose to achieve same clinical effects
- Rate and extent of drug absorption depends on nature of dosage form, drug interactions, presence or absence of food in the stomach and pH of GI fluids
- Irritation of GI mucosa
- Dose inaccuracy in liquid dosage affects bioavailability
- Liquid dosage form are prone to microbial contamination on storage

c) Topical Dosage Forms

- Restricted area of application
- Water-impermeable materials such as occlusive dressings, patches and high lipophilic paraffin-based formulations at application site may increase systemic exposure.

- Formulation vehicle may influence thermoregulation and transepidermal water loss in neonates.
- Permeation rate may be increased by fever and external heat radiators, hot baths

D. Innovative Pediatrics Drug Delivery Systems

Several limitations of the conventional dosage forms have resulted in the need for development of innovative dosage forms and delivery systems for pediatrics application.

Classification of Innovative Pediatric Drug Delivery Systems

- I. Oral Mucosal Drug Delivery Systems
- II. Rectal Drug Delivery Systems
- III. Transdermal Drug Delivery Systems
- IV. Pulmonary Drug Delivery Systems

I. Oral Mucosal Drug Delivery Systems

Physiological factors affecting oral drug absorption

The salivary flow rate range from 0.22–0.82 ml/min in children and 0.33–1.42 ml/min in adults. Flow rate of saliva increase up to the age of 5 to 6 years and decrease thereafter⁶. However the saliva composition and flow rate changes throughout the life period⁷. pH of the saliva plays a vital role in drug ionization and absorption. pH of oral mucosa in healthy children is slightly lower but similar to adults at a value of around 6.6^{8,9,10,11}. Saliva flow rate increase with increase in pH¹². Other factors contributing to pH of the oral mucosa include mucus membrane, diet and saliva flow rate.

Advantages of oral mucosal drug delivery systems over conventional dosage forms:

- Buccal films are strong, withstand breakage and mouth movements
- Better flexibility and comfort than conventional adhesive tablets
- Easy therapy termination by detaching the patch
- Easy administration of drugs to unconscious patients
- High patient compliance

Innovative Oral Drug Delivery Systems

- i. **Medibottle[®]:** Medibottle[®] (Figure 1) is a modified pediatric feeding bottle used as a dosing device for liquids by oral route. It consists of a traditional baby bottle and an oral dispenser that fits into the central part of the bottle. The dispenser contains the required dose of medicine which is to be inserted into the bottle filled with milk or other drinks. On drinking the dispenser plunger quickly moves down to produce a jet of medicine with every sip of the milk or drink and is swallowed by the baby¹³. Medibottle[®] is acceptable by babies and infants and to a lesser extent by older children.
- ii. **Pulp-Spoon:** Pulp-spoon (Figure 2) is developed for dosing dry medicaments. The drug in the spoon is covered by a micro-perforated foil to improve the stability of the

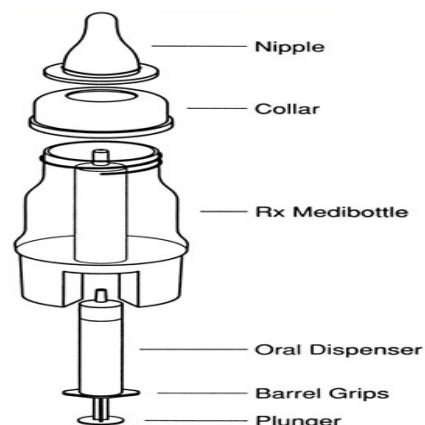


Figure 1: Medibottle[®]

product. The spoon is immersed in water for several seconds, the cover peels off and the dose is administered in form of a paste. This type of product is most suitable for young children and offers convenience of unit dose and avoids risk of spillage¹³.

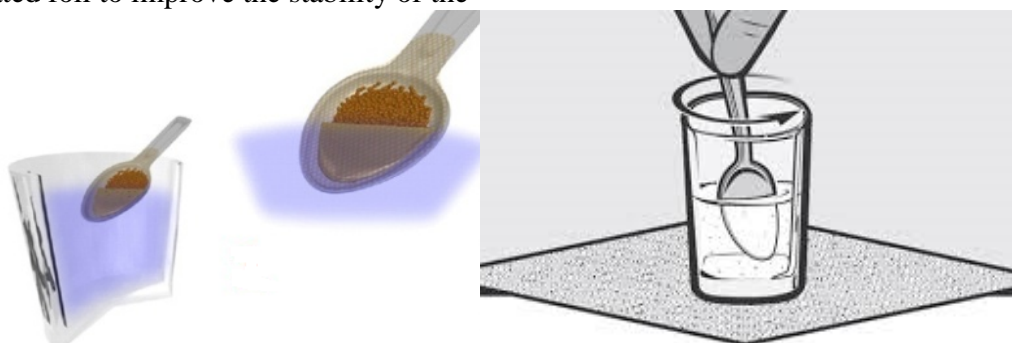


Figure 2: Pulp spoon

iii. Mini-Tablets

Mini-tablets (Figure 3) are tablets with diameter of less than 3mm¹⁴ intended for infants and children (1 month to 5 years). Infants can swallow only liquids before age of 5 month while can swallow multi-particulates depending on particle size, shape and hardness by the age of 6 month¹⁵. Thus a dosage form which disintegrates rapidly in the oral cavity with a small amount of saliva is a suitable dosage form for infants and toddlers.

iv. Orally Disintegrating Tablets (ODTs)

ODT's disintegrates in the oral cavity into small particles within 60 seconds¹⁶. ODTs offer dual

advantages of both solid and liquid dosage -



Figure 3: Mini-Tablets

forms with following advantages^{17,18,19} ODTs are unit solid dosage forms with accurate dose

- Enhanced drug bioavailability due to absorption from oral mucosa/cavity

- Rapid onset of action
- No or minimal water required for dissolution
- Easy administration to patients who have difficulty in swallowing
- Better taste masking of bitter drugs
- Good mouth feel with no residue in the mouth after oral administration
- Convenient to administer pediatric and bed ridden patients

v. **Oral Thin Films**

Oral thin films (OTFs) (Figure 4) also known as oral strips or patches are single or multi-layer system of 2-10cm² with thickness of 20-500µm. Drug can be dissolved in the matrix, emulsified or dispersed in OTFs. They are small in size, stable, durable films which dissolves rapidly without water in mouth or when applied to the oral mucosal surface. They have good flexibility, elasticity, mucoadhesive properties and resistance to breakage due to stress in oral activity²⁰. Drug from the OTFs films directly enters the bloodstream via oral mucosa, without undergoing hepatic first pass metabolism. They can enable fast or sustained release of drug from films. Films improve dosing accuracy compared to liquid formulations with rapid onset of action, dose reduction, enhanced drug efficacy and safety. They are easy to administer for local and systemic effect and improves compliance of pediatric, geriatric and neurodegenerative disease patient's where proper and complete dosing is difficult. However oral films and lyophilized wafers have a huge clinical potential for pediatric patients.

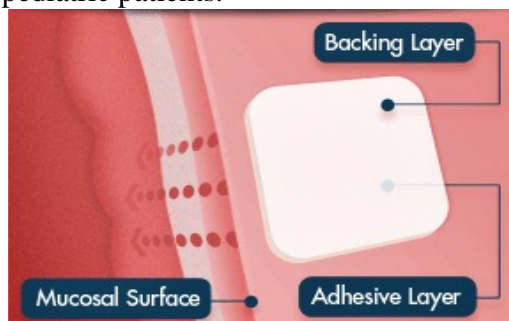


Figure 4: Oral Buccal Films

II. **Rectal Drug Delivery System**

Rectal route of administration has several

advantages over oral route. Palatability and taste, which are major focus in oral dosage forms for pediatric are successfully overcome by these systems. The rectal route of administration can be used to achieve either local (laxative, anti-inflammatory) or systemic (antipyretic, analgesic, anti-nauseant, anticonvulsive, sedative) effects. In pediatric, rectal dosage forms is indicated in patients who find oral medication difficult to swallow, have feel of nausea and vomiting, continuous nasogastric suctioning or unconsciousness and palatability issues.

Rectal Dosage Forms

Suppositories (Figure 5) are the most common rectal pediatric dosage form. Other dosage forms include creams, ointments, gels, foams, gelatin capsules and small-volume (<20ml) or large volume (>67.5ml) solution or suspension enemas.

Rectal mucosa has pH 7-8. It has abundant supply of blood vessels and lymphatic vessels and thereby bypass the first hepatic metabolism and enhance drug absorption²¹. Suppositories are available in a variety of strengths and their size should be related to the patient's age. Suppositories for infants weigh approximately 1 g, half the weight of the adult dosage form.

The volume of enemas should be related to their function (local or systemic effect) and to the age of the child. Volumes of enemas for systemic therapy in pediatric patients should be as small as possible to achieve accurate dose delivery, better absorption and no irritation. The dose delivery device should allow simple delivery; the rectal tube should not cause injury and should be of a length appropriate for the child age.

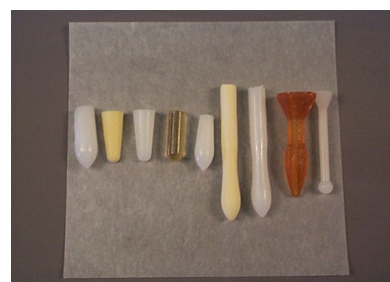


Figure 5: Suppositories

Scaled devices (pre-filled syringes with 'rectal tip') (Figure 6) facilitate individual dosing, in contrast to the 'all or none' devices, and reduce the need for several strengths or dosages.

The excipients of rectal dosage forms should not irritate the rectal mucosa of infants and children. For example, polyethylene glycol bases may lead to irritation of the rectal mucosa due to their hygroscopic nature, which may be reduced by moistening the suppository with water prior to insertion.

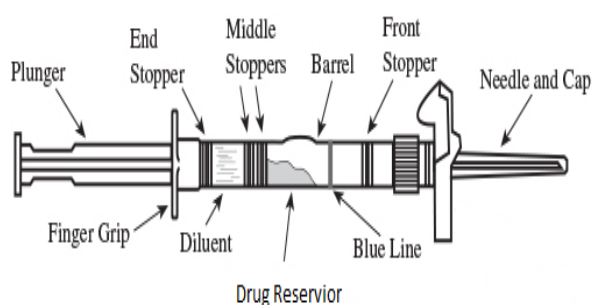


Figure 6: Prefilled syringe with rectal tip
III. Transdermal Drug Delivery System (TDDS)

TDDS is an attractive alternative to oral and parenteral routes and overcomes palatability, taste masking, gastrointestinal drug degradation, first-pass metabolism, hepatotoxicity, pain on injection, needle-stick injuries, emotional trauma of injection, prolong drug release, improve bioavailability and enhance patient compliance. Transdermal microporation technologies^{22, 23} are energy enhanced transdermal delivery of drug through use of microneedle, needle free device, jet injectors, etc.

i. Microneedles

Transdermal microneedle (Figure 7) is innovative delivery systems to deliver drug into the skin and overcome limitations of conventional passive patches. A microneedle consists of hundreds of microfabricated microneedles over a base substrate, which can pierce the stratum corneum and create transient pathways to enable penetration and delivery of drugs²⁴. Due to small needles the drug delivery

by microneedle is painless relative to hypodermic needle^{25, 26} as it reduces the nerve stimulation and pain sensation^{27,28}. It can deliver high molecular weight and water-soluble drugs. Minimal or no skin irritation²⁹, infections and bleeding³⁰ have been associated with microneedle.

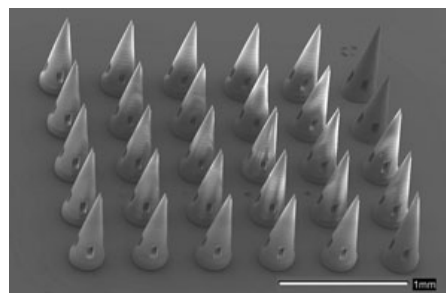


Figure 7: Transdermal Microneedle

Types of microneedle

The design and type of microneedle influences the drug delivery mechanism.

- Solid Microneedles:** They can be pressed against the skin to increase drug permeability via transdermal patch or topical formulation
- Biodegradable or water-soluble polymer based microneedles:** They have been fabricated for depot controlled release of drugs³¹

There are four types of microneedle design³² and include:

- **Solid microneedles:** For piercing the skin prior to drug application
- **Solid microneedles coated with drug:** For rapid dissolution in skin
- **Drug-free or drug-encapsulated dissolving polymeric microneedles:** For rapid or controlled drug release
- **Hollow microneedles:** For injection of drug solution

ii. Needle-free device

Needle-free devices (Figure 8) deliver drugs and large molecules such as insulin, vaccines, growth hormone and local anesthetics via both subcutaneous and intramuscular routes. These devices can deliver both liquid or powder formulations under high pressure through a very

small orifice, which penetrates the skin. Examples of these systems includes eg: PharmaJet[®] and JTip, Bioject[®]. Needle-free devices are patient friendly as they eliminate the fear of needles, providing easy handling and disposal of needles.



Figure 8: Needle free device

iii. Jet injectors

a) Liquid jet injectors

Liquid jet injectors employ a high speed jet to puncture the skin and deliver drugs without the use of needles. They operate using compressed gas or a spring mechanism which is used to eject a jet of liquid under pressure from the device onto the skin. Liquid jet and hole formation continues until the velocity of the jet can no longer penetrate deeper into the skin layers and liquid dispersion occurs³³.

A pulsed micro jet that limits the penetration depth of the jets into skin and thus potentially minimize these effects have shown effective delivery of insulin to rats³⁴ and development of such devices may improve acceptability for children. O'Hagan, Rappuoli (2006) and Baxter, Mitragotri (2006)^{35,36} reviewed that liquid jet injectors have been used to deliver a range of vaccines, proteins such as insulin, growth hormone, erythropoietin and interferon, ampicillin, lidocaine, midazolam, steroids and bleomycin.

The limitations with the development of jet injectors are the cost of the technology and the noise on activation of the devices, which may replace the fear of needles in young children.

Furthermore, strict specifications for the gas pressure and nozzle geometry of the device and

for the particle size, shape, morphology and density may pose technical challenges.

b) Powder Jet Injectors

Powder jet injectors deliver biological macromolecules as dry powder formulations. They deliver drugs into the superficial layers of skin. When actuated, a flow of compressed gas carries the drug particles out of the device nozzle, which upon impacting the skin; penetrate the stratum corneum with a significant proportion reaching the viable epidermis. They are easy to store with improved stability compared to liquid formulations³⁷

IV. Pulmonary Drug Delivery Systems

The conventional pressurized metered dose inhalers (pMDIs) are being substituted by breath actuated pressurized metered dose inhalers. These inhalers automatically release the aerosol when the patient inhales faster than a certain air flow rate. To assure that children reach the required minimal airflow rate the In-Check Dial device (Figure 9) is a valuable tool to control their peak inspiratory flow³⁸. Different air flow resistances of convenient inhalation devices can be adjusted and the suitability of each device for every individual patient can be accessed via an imprinted scale.



Figure 9: In-Check Dial device

Dry powder inhalers (DPIs) (Figure 10) are used as an alternative to pMDIs in the treatment of airway diseases as the required energy for particle dispersion is provided by the patient's peak inspiratory flow and not by propellants. Certain amount of inhalation flow rate is required to reach the lungs to generate sufficient amount of fine particles. Children below the age

of 4 years cannot normally generate an adequate inspiratory pressure to obtain the necessary flow rate. DPIs with a low air flow resistance are preferred in the group of children aged 4–6 years. Breath-actuated devices additionally assure that the aerosol is only delivered when the patient reaches a sufficient inhalation flow rate. The quality of aerosolization and the therapeutic success relies on the magnitude of the inhalation flow rate. DPIs should not be used during severe asthma attacks where breathing is impaired.



Figure 10: Dry Powder Inhalers (DPIs)

Recent Developments in Pulmonary Delivery

Various spacer/valve holding chambers have been developed during the last few years in order to improve children’s compliance and adherence towards pulmonary devices.

The Babyhaler (Figure 11) consists of a holding chamber with a valve designed for providing a comfortable mode of application for infants. A non-electrostatic holding chamber with a universal adapter for all conventional pMDIs is the Vortex equipped with funny facemasks.

The Watchhaler has an appealing design limiting the inhalation flow rate to 15 L/min with a visual feedback of successful use (Figure 12).

Another, creative development is the Funhaler which consists of a valve holding chamber with an internal spinning disc and a whistle. The disc spins and the device whistles when the child breathes normally encouraging them to take the medication (Figure 13)



Figure 11: Babyhaler

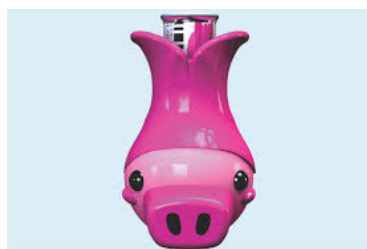


Figure 12: Watchhaler



Figure 13: Funhaler

Patents

Table 2: List of patents on pediatric drug delivery systems

Year and Patent No.	Title and Author
2014 CN103505791 (A)	Transdermal-Absorption Local-Anesthesia Painless Injection Puncture Alcohol Pad Yang Depu
2013 Mx2011011237 (A)	Compositions In Soft Chewable Gelatine Capsules With Flavour Masker. Osornio Alejandro Ortiz; Garcia Juan Carlos Villeda; Quijano Elena Maria Brito
2013 CN202844339 (U)	Disposable Pediatric Rectal Administration Device Zhang Lina , Ma Mao Lei
2011 US2011117193 (A1)	Antiretroviral Drug Formulations For Treatment Of Children Exposed To Hiv/Aids Adeyeye Moji C; Esseku Fredrick ; Joshi Anajali
2011	Drug Delivery Systems (Wafer) For Pediatric Use

WO2011020610 A1	Sascha General, Ildiko Terebesi, Adrian Funke
2010 CN201572240 (U)	Apparatus For Dripping Children's Soup Sufang Liu
2009 US2009010992 (A1)	Drug Formulations For Oral Transmucosal Delivery To Pediatric Patients Pamela Palmer, Thomas Schreck, Stelios Tzannis, Larry Hamel, Andrew I. Poutiatine
2008 US2008319079 (A1)	Method For Administering Formoterol Using A Nebulizer Stephen J. Feanny
1993 US5223264 A	Pediatric Effervescent Dosage Form Fred Wehling, Steve Schuehle, Navayanarao Madamala

Marketed products**Table 3: List of marketed preparations for pediatrics**

Dosage Form	Active Ingredient	Trade Name	Company
Dispersible Tablets	Artemether-Lumefantrine	Coartem [®]	Novartis
	Cowslip (Primula veris/elatior) Yellow gentian (Gentiana lutea). Black elder (Sambucus nigra) Common sorrel (Rumex species) Vervain (Verbena officinalis)	Sinupret [®]	Bionorica
Multiparticulates	Artesunate / mefloquine	Artequin [™] Paediatric	Mepha
	Methylphenidate hydrochloride	Medikinet [®]	Medice
Mini-tablets	Terbinafine hydrochloride	Lamisil [®] Oral Granules	Novartis
	Valproic Acid (Valproate Sodium)	Orfiril long [®] 150mg	Desitin
Orally disintegrating tablets and lyophilisates	Ondansetron	Ondansetron ratiopharm [®] ODT	ratiopharm
	Ondansetron	Zofran [®] 4mg Zydis lingual ODT	GlaxoSmithKline
Chewable tablets and chewing gums	Montelukast sodium	Singulair 4mg [®] Chewable tablets	Merck Sharp & Dohme
	Cetirizine HCl	Zyrtec [®]	Pfizer
	Dimenhydrinate	Superpep [®] Travel gum	Hermes
Oral wafers	Diphenhydramine HCl	Triaminic [®] Thin Strips [™]	Novartis Consumer Health
	Ondansetron	Setofilm [®]	Applied Pharma Research & Labtec & MonoSol Rx
Special Oral formulations	Gummy bears (eg. Pedia Lax [®] , Fleet) and lollipops (eg. Get Better Bear [®] , Helms candy)		

HIV Drug Delivery

Human immunodeficiency virus (HIV) is a retrovirus and can be transmitted sexually, vertically, through contaminated blood products or intravenous drug abuse. Vertical HIV infection can occur before birth, during delivery or after birth.

Antiretroviral therapy:

Antiretroviral (ARV) therapy is reported to benefit the pediatric populations but problems still exist with this drug therapy. The pathogenesis of HIV infection and the

antiretroviral therapy treatment for all the HIV infected patients is similar with a few different considerations in infants, children and adolescents. These considerations include changes in pharmacokinetic parameters due to maturation and development of different body organs involved in drug metabolism and clearance³⁹. The two major reasons for use of antiretroviral drugs in children is to prevent mother-to-child transmission of HIV during perinatal period and to treat children already infected with the virus³⁹.

Table 4: Antiretroviral drugs approved for HIV in adults and children

HIV Drugs	Adults	Children
Nucleoside Reverse Transcriptase Inhibitors		
Abacavir	+	>3 month
Didanosine	+	>3 month
Emtricitabine	+	>4 month
Lamivudine	+	>3 month
Non-Nucleoside Reverse Transcriptase Inhibitors		
Efavirenz	+	>3 years
Nevirapine	+	>2 month
Protease Inhibitors		
Darunavir	+	>6 years
Fosamprenavir	+	>6 years

+ indicates drugs approved in adults

The major challenges in successful delivery of ARV therapy for HIV patients include:

- Lack of pediatric ARV formulations that can be dosed in small children
- Lack of sufficient data on safety and efficacy of these therapy
- Difficult interpretation of data as the pediatric population is smaller compared to adults⁴⁰

Thus there is an urgent need for development of safe, efficacious and tolerable ARV drugs for treatment of HIV in pediatric patients⁴¹.

One such innovative system has been recently reported is a Nipple Shield Delivery System (NSDS) for oral delivery of ARV drugs in infants through breastfeeding. NSDS delivers microbicide which inactivate HIV.

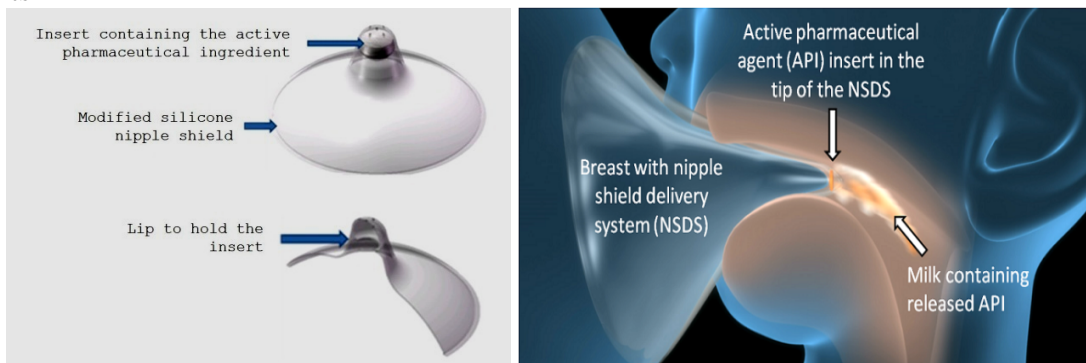


Figure 14: Nipple Shield Delivery System (NSDS)

Numerous challenges are being faced with respect to the stability, sterility and dosing of the pediatric drug delivery systems^{42, 43}. Liquid formulations being the most convenient pediatric dosage form has limited applications due to lack of access to refrigeration and potable water for reconstitution⁴⁴.

Further many current medicines used for treatment of HIV are available only in adult strengths, resulting in complications regarding safe use and dose accuracy in infants. Thus there is an urgent need for development of safe, effective, efficacious and tolerable ARV drugs for treatment of HIV in pediatric patients⁴¹. With the alarming statistics towards HIV prevention of mother to child transmission (MTCT) through breastfeeding in developing countries^{45,46}, an urgent need for appropriate medication system has been set. One such innovative system that has been recently reported is a Nipple Shield Delivery System (NSDS) for oral delivery of ARV drugs in infants through breastfeeding. NSDS delivers sodium dodecyl/lauryl sulfate (SDS) an anionic surfactant and a microbicide which inactivate HIV activity in human milk. SDS in concentration range of 0.1-1.0 weight percent has greater potential to kill sexually transmitted pathogens including HIV^{47, 48}.

NSDS is a drug-impregnated (drug in dried form) single molding of silicone insert, placed into a nipple shield to be worn by mothers during breastfeeding (Figure 14). As milk passes through the insert during suckling; the drug is released directly into the milk and enters the infant⁴⁹. Nipple shields are used to aid mothers and/or infants during breastfeeding.

Advantages of NSDS over other infant drug delivery routes and devices include:

- Simple single-use disposable low cost device with correct dosing
- Easy application
- Dry drug formulation offers improved stability over liquid formulations
- Milk may mask taste of oral administered drugs improving acceptability

- No expertise required with minimal risks associated with needle pain
- No sterilization required
- Compatible with breastfeeding and is the safest method of infant feeding
- Reduce chance of MTCT of HIV even if the mother is infected⁵⁰.

Conclusion

Design and development of innovative and appropriate delivery device is important to ensure accurate and consistent administration of drugs to pediatric patients. Innovations in drug delivery technology are leading to new alternative systems however continuous growth is required in this area of pediatric drug delivery system to serve better. Although there is a significant success of current antiretroviral therapy, however challenges still remain.

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