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Pediatric and Geriatric Formulation Tailoring Dosage Form for Age-Specific Needs

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Abstract

This comprehensive review addresses the critical challenges and advancements in the formulation of oral medications for pediatric and geriatric populations, who often face unique pharmacokinetic and pharmacodynamic differences. The World Health Organization highlights that nearly 50% of long-term medications are not adhered to, with significant implications for health outcomes. Pediatric patients, due to their developmental stages, and geriatric patients, due to age-related physiological changes, require tailored drug formulations to enhance safety, efficacy, and acceptability. The review discusses the anatomy and physiology of the pediatric gastrointestinal tract, emphasizing how these factors influence drug absorption, distribution, metabolism, and elimination. It also explores various oral dosage forms, including solutions, suspensions, orally disintegrating tablets (ODTs), and chewable formulations, assessing their advantages and limitations in terms of patient compliance. Furthermore, the review highlights the importance of taste, texture, and volume in medication acceptability, particularly for children and older adults with dysphagia. Recent innovations in drug delivery systems, such as 3D printing and personalized medicine, are examined as potential solutions to improve adherence and therapeutic outcomes. The conclusion underscores the need for ongoing research and regulatory support to develop age-appropriate formulations that meet the specific needs of these vulnerable populations.

Keywords: Age-appropriate formulations, pediatric pharmacokinetics, geriatric drug delivery, oral dosage forms, patient compliance, tailored drug therapy

INTRODUCTION

The World Health Organization (WHO) reports that around 50% of long-term medications are not taken as prescribed, and approximately 10% of medicines for children are used off-label or without a license [1]. Effective pharmacotherapy is essential for improving disease outcomes, enhancing quality of life, and reducing complications. Pediatric patients differ significantly due to anatomical, physiological, and developmental changes, which impact drug safety, toxicity, and acceptability. Understanding these variations is crucial to predicting drug behavior and minimizing adverse effects.

Pharmacokinetic (PK) changes in children can alter drug absorption, metabolism, and elimination, requiring careful dose adjustments to prevent toxicity [2]. Excipients, often considered inert, may also accumulate due to immature organ function, increasing toxicity risks [3]. From a formulation perspective, pediatric medicines must

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be safe, effective, and easy to administer to ensure adherence. Various dosage forms, including oral liquids, mini-tablets, chewable tablets, and Oro dispersible formulations, have been developed, with small, flexible solid forms showing superior acceptability. Unlike adults, children's acceptance of medications depends on age, ability, and development [4].

Pediatric and geriatric patients require modified dosage forms to ensure adherence to prescribed regimens due to age-related differences. Table 1 presents the classifications for pediatric, adult, and geriatric patients. Non-compliance in these age groups is a concern, often due to poor taste and difficulty swallowing (dysphagia). Most drug formulations worldwide are developed primarily for adults, given their larger market size. Consequently, off-label use, such as crushing tablets or mixing capsule contents with liquids, poses safety and efficacy concerns for pediatric patients. Hospital pharmacies frequently prepare extemporaneous formulations, but their safety and effectiveness remain a challenge for both pediatric and geriatric populations.

The lack of pediatric-specific formulations is primarily due to limited clinical data, studies predominantly conducted on adults, small pediatric patient populations, and business priorities favoring larger adult markets. Geriatric patients also struggle with swallowing large tablets and capsules, while polypharmacy increases the complexity of medication management. Memory loss, multiple comorbidities, and difficulty handling small pills contribute to poor adherence in the elderly [5].

To address these challenges, there is a growing need for patient-centric formulations suitable for both pediatric and geriatric patients. Developing age-appropriate pediatric formulations is particularly complex, requiring consideration of drug properties, excipient safety, volume, dosage form, size, taste, and acceptability. The oral route remains the most common for both age groups, with marketed dosage forms including solutions, syrups, suspensions, granules, tablets, orally disintegrating tablets (ODT), chewable tablets, dispersible tablets, capsules, oral thin strips, chewing gums, and troches [6, 7].

Chewable tablets, ODTs, orally disintegrating mini-tablets, andoral dispersible films (ODF) are particularly beneficial for school-aged children and elderly patients due to their ease of administration and reduced swallowing difficulties. Flexible formulations, such as chewable tablets, ODTs, and dispersible tablets, can be taken whole, chewed, or mixed with water, while flexible granules, pellets, or powders can be swallowed directly or dispersed in liquid. Notable innovations include solid oral flexible tablets (OFT) using ion exchange resins for taste masking (e.g., cetirizine) and extended-release OFTs using ethyl cellulose for controlled drug release (e.g., carbamazepine) [8]. Additionally, the USFDA recently approved 3D-printed rapidly disintegrating levetiracetam tablets (Spritam) for oral suspension, highlighting advancements in patient-friendly drug delivery.

Pediatric patients require specialized oral drug delivery systems due to their ongoing development, making conventional formulations unsuitable [9]. As a result, manipulation and compounding are common practices. Age-appropriate formulations are essential to ensure proper dosing, safety, and efficacy. Similarly, geriatric patients would benefit from patient-centric designs due to impaired physiological functions.

Developing such formulations is complex, considering pharmacokinetic variability, excipient safety, palatability, swallowing ease, and caregiver dependence. Additionally, manufacturing, processing, and packaging must ensure quality, affordability, and accessibility. Flexible technology platforms are needed to accommodate different drugs and dosing requirements. Regulatory changes have driven innovations in pediatric formulations, leading to novel dosage forms (e.g., dispersible tablets, oral films, and minitablets) and administration devices (e.g., medicated straws) [10–18]. Table 1 describes the preferred dosage forms according to age of patients.

Table 1. Preferred dosage forms according to age of patients.

Classification	Age	Currently Marketed Dosage Form
Preterm newborn infants	23 w to 25 w gestation	Liquids.
Term newborn infants	0–27 d	Liquids.
Infants and toddlers	1 to 23 months	Liquids.
Pre-school children	2–5 y	Liquids, multiparticulate, dispersible tablets, chewable tablets and ODT.
School going children	6–11 y	Liquids, multiparticulate, chewable tablets, ODT, dispersible tablets.
Adolescents	12 to 16–18 y	Liquids, multiparticulate, chewable tablets, ODT, dispersible tablets, swallowable tablets, and capsules.
Adults	18–60 y	Swallowable tablets, dispersible tablets, capsules.
Geriatrics	60–65 y, 65–70 y, 75–80 y, >85 y.	Swallowable tablets, dispersible tablets, capsules.

ANATOMY AND PHYSIOLOGY OF PEDIATRIC GI TRACT

Several routes of administration are possible within the pediatric population; however, the oral route is the most preferred, as it is simple, convenient and non-invasive [19–22]. After oral administration, the drug/pharmacological substance is subjected to several processes before being eliminated from the body; the gastrointestinal (GI) tract is an organ system, composed of the oral cavity, oesophagus, stomach and intestines that serves to transport, digest, absorb and expel food and pharmacological substances [23]. In medicine, identifying the anatomical and physiological differences of components of the GI system between pediatrics and adults is paramount to achieving safe, non-toxic and effective therapeutic concentrations of pharmacological substances. Furthermore, the effect of physiological differences should better inform pediatric drug development and assist regulatory reviews [24].

Oral Cavity

Digestion begins in the mouth, where saliva aids in swallowing. In newborns, the tongue is short and broad, and the larynx is positioned higher, with the soft palate touching the epiglottis. By age four, these structures change, increasing the risk of aspiration as the larynx descends and the pharynx connects to both the airway and food pathway. These developmental changes, along with motor skill limitations, restrict the use of solid oral dosage forms in young children. Additionally, the small oral cavity limits the size and volume of medication that can be administered [25–28].

Oesophagus

The oesophagus is a fibrous tube that transports food from the mouth to the stomach, with contractions continuing the digestive process. In neonates, the oesophagus measures 18 cm, growing to 25 cm by age 10 [29]. Differences between children and adults include the length and diameter of the oesophagus, which affect transit time. Younger children, with shorter oesophagi, empty food into their stomach more quickly. Oesophageal transit time (OTT) can also vary based on body position. Additionally, immature peristalsis and the lower oesophageal sphincter in neonates can lead to Gastroesophageal Reflux Disease (GORD), affecting drug absorption as contents may be regurgitated [30–31].

Stomach

The stomach continues digestion by breaking food into a liquid form before moving it to the intestines. Differences in stomach physiology, such as gastric pH, fluid volume, and emptying time, can affect drug absorption in children. Gastric acid secretion begins after birth, but in preterm infants, it develops more slowly [32]. At birth, gastric pH is neutral, becoming acidic within 24–48 hours, and only reaches adult levels by age 2 [33]. Drugs, like phenytoin and phenobarbital, which rely on an

acidic environment for absorption, may have reduced bioavailability in children due to higher gastric pH. On the other hand, the higher pH can protect acid-labile drugs and increase absorption of weak bases like penicillin. Most drug absorption occurs in the small intestines, and gastric emptying and intestinal motility are key limiting factors. Newborns and neonates have slower and more variable gastric emptying, leading to delayed absorption. Additionally, stomach capacity increases with age, which can affect the dissolution and absorption of drugs, particularly those with low solubility (BCS Class II and IV) [34].

Small Intestine

After gastric digestion, the contents move into the small intestine, where further digestion and absorption into the bloodstream occur. Several physiological factors in the intestine, such as transit time, permeability, bile secretion, microflora, and active transport, differ between children and adults, affecting drug absorption [35]. The small intestine is made up of the duodenum, jejunum, and ileum, each responsible for processing and absorbing nutrients. At birth, the small intestine measures 300–350 cm, growing to adult length by age 20 [36]. Intestinal permeability is higher in newborns than adults, due to an immature mucosal barrier, but decreases as the child grows. The gut microbiota also differs between children and adults, influencing development and drug absorption [37–47]. Active transport systems, which are less mature at birth, reach full functionality around four months. P-glycoprotein (P-gp), which regulates drug absorption and elimination, is limited in newborns, gradually reaching adult levels by age 2. However, studies show varied timelines for the maturation of P-gp expression in the pediatric population [48–53]. The comparative difference between anatomical and physiological GIT of pediatrics and adults is shown in Table 2.

Table 2. Comparison of anatomical and physiological differences in the gastrointestinal (GI) tract between pediatrics and adults.

GI Tract Component	Aspect	Pediatrics	Adults
Oral Cavity	Anatomical	*Tongue:* short and broad in newborns – Tongue proportionally larger in young children – Soft palate in contact with epiglottis – *Epiglottis:* longer, floppy, U-shaped – *Larynx:* more anterior and superior	*Tongue:* proportionally smaller – Soft palate and epiglottis contact lost – *Epiglottis:* shorter, stiff – *Larynx:* posterior and lower.
Oesophagus	Anatomical	*Neonates:* ~18 cm – Age 3: ~20 cm – *Vertebral column location:* C4–T9	*Measures:* ~25 cm – *Vertebral column location:* C6–T11
Stomach	Anatomical	*Neonatal capacity:* 10–20 mL – Age 2 capacity: 200 mL	≥16 years capacity: 1500 mL
	Physiological	*Gastric pH:* neutral at birth – *Gastric emptying:* ↓ and linear (until 6–8 months)	*Gastric pH:* 2–3 – *Gastric emptying:* ↑ and bi-phasic
Small Intestine	Anatomical	*At birth:* ~300–350 cm – Age 10: ~500 cm – Fewer circular folds – Reduced absorptive surface area	~575 cm in adults – Increased circular folds – Higher absorptive area
	Physiological	*Intestinal permeability:* 3–4× greater – *Microbiota:* High levels of microbes supporting development (e.g., mean bifidobacteria in infants: $4.4 \pm 8.6 \times 10^{10}$ CFU/g) – *Transport system:* P-gp limited during birth – *Intestinal transit time:* ↑ in neonates/infants – *Bile salt secretion/activity:* ↓ in neonates/infants	*Intestinal permeability:* mature – *Microbiota (mean bifidobacteria):* $1.03 \pm 1.7 \times 10^9$ CFU/g – *Transport systems:* mature – *Bile salt secretion and activity:* mature

PHARMACOKINETICS OF PEDIATRIC

As children's anatomy and physiology evolve with age, so do their pharmacokinetic (PK) profiles, which are non-linear. PK studies how a drug is absorbed, distributed, metabolized, and eliminated. Differences between children and adults can significantly impact the concentration of drugs or

excipients, requiring careful dose adjustments [49]. Despite the growing amount of data on pharmacokinetics, the effects of age-related changes on PK profiles and dose requirements are still not fully understood [40]. While excipients are well-studied in adults, their safety in children is less explored, and they can cause adverse effects if used inappropriately [50]. Excipients should be selected based on research and guidance from regulatory agencies like the EMA. Due to the lack of authorized formulations for children, off-label and unlicensed medicines are often used, but their excipient content may not always be safe. A deep understanding of how anatomical and physiological differences affect PK is essential to ensure the safe use of drugs and excipients in children [51, 52].

Absorption

Bioavailability is influenced by the development of the gastrointestinal (GI) tract, with factors like surface area, intestinal permeability, gastric pH, gastric emptying, GI motility, and bile secretion affecting absorption. At birth, gastric p235H is neutral but decreases over time, reaching adult levels (pH 2–3) by age 3. These changes impact the absorption of weakly acidic or basic drugs. Gastric emptying is slower in infants up to 6–8 months and then becomes more adult-like. Intestinal transit time is initially longer in neonates due to slower GI motility but decreases as GI function matures. Shorter intestinal transit time in infants may reduce drug absorption. Bile salts, which help solubilize fats, are less effective in neonates and infants due to immature bile secretion, limiting the absorption of fat-soluble and lipophilic drugs. Bile secretion matures after 3–7 months, highlighting the need for careful dose adjustment during this period [53–60].

Distribution

After absorption, a substance is distributed based on its physicochemical properties. As a child grows, total body water content decreases from 80–90% in neonates and infants to 55–60% in adults. Hydrophilic substances, like phenobarbital, have a larger volume of distribution in neonates due to higher body water content, requiring larger doses per weight for the same therapeutic effect as adults. The blood–brain barrier (BBB) is also immature in neonates, increasing the risk of toxicity as substances more easily enter the central nervous system, especially with excipients like ethanol and propylene glycol. Additionally, neonates have lower plasma protein binding, resulting in a higher fraction of unbound drug and potentially more active substance. Therefore, drug doses should be carefully adjusted to avoid toxicity in different age groups [61–65].

Metabolism

The liver plays a key role in metabolizing drugs into less toxic, water-soluble compounds for easier excretion. In neonates, immature liver enzymes reduce metabolism efficiency, increasing the risk of toxicity due to substance accumulation. Cytochrome P450 (CYP) enzymes, responsible for oxidizing toxic substances, are only about 50% as active in children aged 6–12 months compared to adults. Hepatic blood flow is reduced in neonates but reaches adult levels by infancy. Despite this, liver size relative to body weight is larger in infants, leading to increased hepatic clearance of substances, particularly those undergoing extensive metabolism, like allopurinol and benzyl alcohol [66–69].

Elimination

Elimination is the process by which drugs and their metabolites are excreted from the body, primarily through the kidneys. Key factors affecting elimination include glomerular filtration rate (GFR), tubular secretion, and reabsorption, all of which vary with renal blood and plasma flow. In newborns, renal excretion is low but improves as the renal system matures, with adult-like blood flow achieved by age 2. GFR is also low at birth, increasing rapidly in the first two weeks and reaching adult levels by age 1. Tubular reabsorption and secretion mature over the first few years of life, with full maturation by 1–3 years for reabsorption and 7–12 months for secretion. The reabsorption of weak acids is influenced by urinary pH, which is higher in neonates and infants, enhancing the reabsorption of weak acids. While the kidneys are the primary route for elimination, some substances are secreted into the bile and excreted in feces. Differences in renal and hepatic function between children and adults lead to varying pharmacokinetic profiles, meaning drugs for adults cannot be assumed to be safe for pediatric use [70–75].

MARKETED ORAL FORMULATIONS

Different formulations, such as solutions, suspensions, Oro dispersible tablets (ODTs), and chewable tablets, are prescribed together with classical orally swallowable tablets and capsules for pediatrics and geriatric patients based on the literature currently available and review of the approved products over the world [68]. It is because all the formulations are unique in their design, meeting that criteria require careful selection of these processes or material → excipients. For each of the formulations, the quality attributes of the formulations were distinct to each. Taste masking and stability, for instance, are complex quality attributes for a solution, syrups, drops and suspension formulations. Strength and chewing ability are important properties for chewable tablet formulations. Dispersibility and stability of the dispersion are quality attributes in front boiled for dispersible tablet formulation. One of the critical properties for ODTs includes rapid in vitro and in vivo disintegration, hardness, friability, and stability. Since these formulations are formulated based on adult patients' safety and efficacy profile, their compatibility with pediatrics patients used excipients in these formulations is worrisome [76–79]. Marketed formulations of pediatrics and geriatrics are shown in Tables 3 and 4, respectively.

Table 3. Marketed oral pediatric formulations.

Formulation Type	Features	Examples (Brand Names)
Syrups / Solutions	Easy to swallow, flavored for taste	Crocin DS (Paracetamol), Ibugesic Plus (Ibuprofen), Zifi Syrup (Cefixime)
Oral Drops	High concentration, suitable for infants	D-rise drops (Vitamin D3), Calpol drops (Paracetamol), Zincovit drops
Oral Dispersible Tablets (ODTs)	Disintegrate quickly in mouth, no water needed	Emeset ODT (Ondansetron), Cefolac-OD (Cefixime), Montair LC Kid (Montelukast)
Orodispersible Films (ODFs)	Thin films, dissolve on tongue	Zuplenz (Ondansetron), Risperdal Quicklet (Risperidone)
Chewable Tablets	Flavored, chewable, for older kids	Zentel chewable (Albendazole), Montair-LC Kid, Shelcal chewable
Granules for Reconstitution	Powder to be mixed with water before dosing	Augmentin Duo (Amox+Clav), Omnicef (Cefpodoxime), Azithral (Azithromycin)
Mini tablets/ Pellets	Sprinkled on food/liquids, ideal for infants/toddlers	Prevacid Sprinkle (Lansoprazole), Omez Insta (Omeprazole), Creon Micro (Pancreatin)

Table 4. Marketed geriatric formulations.

Brand Name	Drug Name	Dosage Form	Indication	Special Feature For Geriatrics
Aricept	Donepezil	Orodispersible tablet	Alzheimer's disease	Easy to swallow; dissolves in mouth
Exelon Patch	Rivastigmine	Transdermal patch	Dementia (Alzheimer's, Parkinson's)	Avoid swallowing; steady drug delivery
Glucophage XR	Metformin	Extended-release tablet	Type 2 Diabetes	Once-daily dosing; minimizes GI upset
Xarelto	Rivaroxaban	Film-coated tablet	Anticoagulation (DVT, AF)	Lower bleeding risk; once-daily dosing
Plavix	Clopidogrel	Oral tablet	Antiplatelet therapy	Simple dosing: minimal monitoring required
Mylanta	Aluminum hydroxide + Mg OH	Oral suspension	Gastric acidity	Liquid form easier for dysphagia
Senokot	Senna	Oral tablet or syrup	Constipation	Gentle on bowel; syrup version for easy intake
Fortisip	Nutritional supplement	Ready-to-drink liquid	Malnutrition or frailty	High-calorie, nutrient-dense for elderly nutrition
Memantine	Namenda	Oral tablet or solution	Moderate to severe Alzheimer's	Available in liquid form
Evista	Raloxifene	Oral tablet	Osteoporosis in postmenopausal women	Convenient dosing, reduces fracture risk

ADVANTAGES AND DISADVANTAGES OF MARKETED FORMULATIONS

Most oral tablet formulations on the market are mainly used for adults and elderly patients. For kids under 2 years old, liquid options, like solutions and suspensions, tend to work better. Meanwhile, older children (those over 2) often prefer easier-to-take forms, like dispersible tablets, orally disintegrating tablets (ODTs), and chewable tablets, to help with swallowing. However, one big issue is that many of these popular forms are often turned down because of their bad taste. A lot of medicines, especially antibiotics and some for the brain and nerves, are known for their bitterness, and unfortunately, they do not always have good taste masking [80]. There has been a lack of personalized drug development for kids, which means that things, like colors, flavors, and preservatives, are added to the liquid forms and chewable options given to children. Sadly, some of these additives can cause side effects in young patients. When it comes to giving liquid medicine in the right dose, that's where things can get tricky [81]. If the dose is not measured properly, it can lead to issues like toxicity or not working effectively. The bitterness, gritty texture, large volume of doses, big tablet or capsule sizes, high costs, and simply not having the right forms available make it hard for both kids and elderly patients to stick to their treatment. Because patients of different ages have different needs, picking the right medication form based on a person's age is essential for many over-the-counter (OTC) drugs. Unfortunately, in many developing countries, drug products often lack important information such as safety guidelines, dosage instructions, and warnings on their labels [82–84].

NOVEL APPROACHES TO AGE-APPROPRIATE ORAL DRUG DELIVERY

This section reviews new formulation design approaches, including multiarticulate drug delivery systems, oro dispersible tablets (ODTs), oro dispersible films (ODFs), and chewable formulations.

Oro Dispersible Tablets

ODTs are formulated to rapidly disintegrate in the oral cavity and do not require swallowing of whole tablets. They do not need water in most instances, and are, therefore, particularly appropriate for children, the elderly or patients who are dysphagic. They have flexible administration methods: dissolving in the mouth or swallowing whole, or pre-dispersion in a liquid that can improve patient adherence [85–88].

ODTs are easy to administer; however, their dosing granules are often no more flexible than those of regular tablets. Multiple dosage strengths are still needed to adjust dosing, and these ODTs provide a much too delicate ondansetron for splitting. This restricts the use of individualized dosing, but the recent appearance of ODMT may offer a viable strategy to alleviate this as it combines the advantages of ODTs with multiparticulate systems [89–91].

ODTs are basically formulated to permit absorption of the drug through the GI tract after disintegration. Oral retention may offer a buccal or sublingual route for absorption which could optimize onset and bioavailability. Buccal-Oriented oromucosal tablets (ODTs) can be formulated with bioadhesive coatings to improve formular retention and mucosal permeation.

Accurate labeling is important too, given its potential effect on bioavailability(taste). As ODTs are tasted by taste buds, the great importance of taste masking mainly for bitter taste APIs cannot be overemphasized [92]. Although sweeteners and flavors are often added, they may be unnecessary and pose safety issues for young children. Particle coating is a more efficient flavor-encapsulation method, albeit a difficult technological task.

These unsolved issues have been addressed by current patented ODT technologies, based mainly on the microencapsulation of APIs or the use of polymer coatings for controlled release and better taste. These advances enhance patient compliance and broaden the therapeutic utility of ODTs [93–99].

Oro Dispersible Films

Made from polymeric matrix, Orally Disintegrating Films (ODFs) are thin, stamp-like strips that disintegrate rapidly in the mouth and release the active medication without the need for water [100]. They give benefits comparable to those of orally disintegrating tablets (ODTs), making them particularly desirable for individuals who have trouble swallowing. Flexible dosing – films can be sliced to achieve varying strengths – is an additional advantage [101–105].

ODFs, which are mostly made by solvent casting or hot-melt extrusion, contain the medication in addition to excipients, plasticizers, and film-forming polymers. Cutting-edge techniques, like ink-jet printing and electrospinning, are becoming popular. However, because of size and thickness limitations, drug loading is usually restricted to less than 60–70 mg, while future technologies might permit up to 100 mg [106–110].

Chewable Formulations

Chewing gums differ from tablets; in that the gum base is not meant to be swallowed. Therefore, it is important to specify on the label how long the product should be chewed to ensure complete drug release. Due to insufficient safety data, these gum-based formulations are generally only recommended for children aged six and above [111–115]. There is also the risk of children mistaking these medicated gums or chews for candy, leading to misuse. Chewable tablets are typically produced through a compression process, like ODTs but without disintegrants. Some patented production techniques, such as those introduced by Paulsen et al., allow for manufacturing without using water or high heat, which can enhance stability [116–120]. Other methods utilize modified soft gelatin capsules that include chewable ingredients, providing the benefits of soft gels without requiring them to be swallowed whole. Pharmaceutical chewing gum is made by blending resins, waxes, and elastomers into the gum matrix through compression or extrusion. This technology has proven effective for targeted delivery of agents like fluoride and chlorhexidine. Overall, chewable formulations are a practical and appealing option, especially for children. While they improve compliance and ease of administration, challenges related to taste masking, dose flexibility, and user-dependent effectiveness remain important considerations [121–124].

THE FUTURE DIRECTION OF PHARMACEUTICAL DEVELOPMENT OF MEDICINES FOR PEDIATRICS AND GERIATRIC USE

Swallowing difficulties are a common concern among both elderly and pediatric patients, especially those at the age extremes, highlighting the importance of adaptable dosing and age-appropriate drug formulations. In older adults, research and development in pharmaceuticals should concentrate on neurological disorders, such as Alzheimer's, Parkinson's, stroke, and epilepsy, which arise from degenerative changes or neurological damage. These conditions require formulations that are easier to administer, especially by caregivers [125]. Similarly, in children, neurodevelopmental disorders, like autism, cerebral palsy, and epilepsy, present challenges that call for thoughtfully designed medications to ensure effective administration and better compliance. Palliative care is another vital area needing improved drug delivery systems. With an increasing elderly population [126–128], there is a growing demand for medications that can be easily administered at home. Many drugs currently used for quick symptom relief in palliative settings rely on injections. However, newer non-invasive dosage forms, like orodispersible and oromucosal tablets, are being explored to replace these. Pediatric palliative care is even more complex, often requiring very small and accurate doses to prevent overdosing, making formulation precision crucial. Selecting the right dosage form and production method involves evaluating the drug's properties and the needs of the patient group [129]. Advanced manufacturing technologies, such as 3D and inkjet printing, are emerging as promising tools for creating tailored medications for individuals in both industrial and localized settings.

The World Health Organization recognizes that flexible solid oral dosage forms – such as orodispersible, chewable, and soluble tablets – are the most appropriate for children. These formats dissolve in the mouth or a liquid, helping children swallow them more easily. They combine the

benefits of liquid forms (such as dosing flexibility) and solid forms (like durability and low cost), while minimizing their respective drawbacks [130]. The pharmaceutical industry is now focusing on developing these user-friendly dosage forms, especially multiparticulate options like mini-tablets, powders, and granules. One significant initiative is the European LENA project, which developed orodispersible mini-tablets of enalapril to meet pediatric needs, potentially qualifying for Pediatric Use Marketing Authorization (PUMA), and paving the way for more suitable, child-friendly formulations [131–141].

CONCLUSIONS

Pediatric and elderly patients show considerable variation in how they process and respond to medications compared to the general adult population. These differences mean that drugs must be carefully dosed and formulated, with particular attention to excipients used. While both age groups often prefer dosage forms that are easy to take and pleasant in taste, each group has specific needs that require individualized formulation approaches. To address these challenges, newer drug delivery systems – such as multiparticulates and fixed-dose combinations – are being developed to improve compliance and therapeutic benefits. Regulatory bodies have begun offering more structured guidance and incentives to encourage the creation of age-appropriate medicines. One such initiative is the 2007 Pediatric Regulation in Europe, which introduced the Pediatric Use Marketing Authorization (PUMA) to support the development of pediatric formulations, especially for older, off-patent drugs. Still, the overall impact has been limited, with only 221 new pediatric formulations or indications launched by 2016, highlighting a gap between policy goals and actual outcomes. In pediatric care, the widespread use of unlicensed or off-label medications often leads to adherence issues due to factors such as poor taste, swallowing difficulties, or excipient-related safety concerns. This underscores the need for pediatric-specific drug delivery systems that are safe, palatable, require minimal dosing, and are suitable across age groups. Involving children directly in research is proving valuable, as their input – when gathered through age-appropriate methods – helps shape more effective and acceptable medications. For both children and older adults, the physical design of a medication is vital to ensure it is well-tolerated and accepted. In older patients, preventing problems, like choking or oesophageal retention, is especially important. Although the European Medicines Agency recommends initially focusing on a few widely suitable dosage forms, a single formulation cannot meet the needs of all patients due to wide physiological variation within these populations. Customizing drug formulations for different subgroups is, therefore, essential to balance cost-effectiveness with therapeutic success. Ultimately, progress in developing medications for pediatric and geriatric populations depends on a combination of regulatory backing, patient-focused formulation design, technological advances, and meaningful involvement of patients themselves. These efforts are essential to ensure the availability of safe, effective, and user-friendly medications for vulnerable age groups.

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