

Goodbye Bitter, Hello Better: Taste Masking in Pediatric Oral Medicines

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ABSTRACT

Poor taste, particularly bitterness, is a major factor contributing to poor medication adherence in children, potentially compromising treatment efficacy and clinical outcomes. Therefore, the development of palatable and child-friendly formulations is an essential consideration in paediatric drug delivery. This review provides an overview of the physiological basis of taste perception in children and highlights the importance of palatability in improving medication acceptance and compliance. This review covers both conventional and advanced taste masking strategies, including sweeteners and flavouring agents, polymer coating, microencapsulation, complexation, ion exchange resins, hot melt extrusion, spray drying and solid dispersion. Their use in various paediatric dosage forms such as oral liquid and suspension, powders and granules, chewable tablets, orally disintegrating tablets, and oral thin films, with suitable examples. By integrating scientific insights with practical formulation strategies, this review highlights key strategies for designing safe, effective and child-friendly medicines which may improve medication adherence and lead to better therapeutic outcomes in children.

Keywords: paediatric medicines, taste masking, palatability, oral formulations, oral thin films, sweeteners.

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1. INTRODUCTION

Poor adherence to prescribed medications among children is a common problem that can lead to serious clinical consequences(1). The preference for sweet flavours is an inherent evolutionary trait present from birth, which likely evolved to encourage the intake of safe, energy-rich nourishment such as breastmilk(2). A natural dislike for bitter-tasting medicines is one of the main reasons why children often refuse to take their medication properly. Unlike adults, children may not fully understand the long-term benefits of the treatment that are more important than the unpleasant taste of the medicine. For many children, the taste of the medicine plays a major role in deciding whether it is swallowed, spat out, or completely refused(3). Children have different taste physiology that makes them more sensitive to bitter compounds than adults, mainly due to developmental and evolutionary factors(4).

Scientific evidence suggests that newborns have a stronger natural aversion to unpleasant taste, which serves as an evolutionary defence mechanism to protect against the ingestion of potentially harmful compounds. While both toddlers and adults possess the same family of 25 functional bitter taste receptors (TAS2Rs), the expression and sensitivity of these receptors vary significantly across different age groups(5). To overcome the innate sensory challenges experienced by children, regulatory authorities have established strict guidelines for paediatric formulations. Both the US-FDA and EMA require comprehensive plans that consider acceptability and palatability as essential components of paediatric drug approval(6).

To maintain pharmacokinetic effectiveness while ensuring sensory acceptability, taste masking strategies for paediatric formulation require careful optimisation. This is necessary because coatings that effectively mask bitterness often alter the dissolution kinetics of the formulation. Similarly, viscous

suspensions that improve oral coating may create challenges in achieving accurate dose measurement across different paediatric age groups(7). The development of paediatric formulation is limited by the toxic effects of certain excipients such as ethanol, propylene glycol, and benzyl alcohol, which may be safe for adults but are unsuitable for neonates and infants. In neonates, ethanol may cause hypoglycaemia and CNS depression, propylene glycol can lead to renal and CNS toxicity, and benzyl alcohol has been associated with gasping syndrome in preterm infants(8).

The selection of paediatric dosage forms must consider developmental physiology and the child's ability to administer the medication. For instance, infants require preservative-free liquid formulations with minimal flavouring to ensure accurate dosing with syringes, whereas toddlers require palatable suspension with optimised viscosity to facilitate administration by caregivers. Preschool children can use orodispersible tablets with enhanced sensory modulation, such as cooling agents to improve acceptability, and school-aged children can tolerate mini tablets (≤ 2 mm) when their appearance and organoleptic properties are properly optimised(9). This review provides a practical approach to the development of palatable paediatric oral medications. It summarises the major taste masking strategies and their applications in paediatric dosage forms, including orally disintegrating tablets, mini tablets and liquid suspension. By integrating scientific knowledge with practical formulation strategies, this review aims to support the development of safe, effective and child-friendly medicines that enhance medication adherence among children(10).

2. PHYSIOLOGY OF TASTE PERCEPTION IN CHILDREN

Approximately 2,000-8,000 taste buds are present on the human tongue, with each taste bud composed of 50-100 sensory receptor cells. Children exhibit a wider distribution of taste buds throughout the oral cavity and have a higher density of fungiform papillae, making children more sensitive to taste than adults(11,12). Infants have approximately 10,000 taste buds, with this number gradually declining with age, and children with more fungiform papillae are more sensitive to bitter taste(11).

At the cellular level, humans perceive bitter taste through TAS2R (Taste Receptor Type 2) family of G-protein-coupled receptors. These receptors show considerable variation among individuals, indicating that genetic variations play an important role in bitter taste sensitivity. Unlike bitter taste, sweet taste is mediated by the TAS1R2/TAS1R3 receptor, which is highly expressed from birth and contributes to natural preferences for sweet flavours in infants(13). Sour and salty tastes are mediated by different ion channels, while sour taste is mediated

by the PKD2L1 channel, and the ENaC channel is responsible for salty taste(14,15).

Newborns and infants typically reject bitter compounds through facial grimacing, tongue protrusion, and head turning, with this response being stronger and less influenced by learning than in adults. However, studies suggest that rejection of bitter taste emerges at approximately 4 months of age(16). Sweet taste is typically more appealing to children than to adults, and children require a higher sucrose concentration to identify and enjoy sweet flavours. Studies have shown that children prefer sucrose concentrations that are approximately 50% higher than those preferred by adults. This natural preference can be used in paediatric formulations by adding more sweeteners to improve taste and increase medication acceptance among children's(4,16). Bitter sensitivity generally decreases as children grow older, but genetic differences in TAS2R receptors can cause variations in how individuals perceive bitter taste. Infants and young children strongly dislike bitter taste and require effective taste masking, while adolescents typically have taste preferences similar to adults. Understanding TAS2R receptor function may aid the development of improved taste masking strategies for paediatric medicines(17–19).

A large proportion of taste perception (approximately 75-85%) is influenced by retro-nasal olfaction, a process in which aroma compounds released in the mouth travel through the nasopharynx to the olfactory epithelium during chewing and swallowing. Therefore, aroma plays an equally important role as taste in determining overall palatability, particularly in paediatric formulations(20).

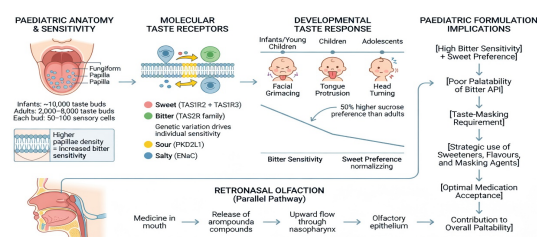


Figure 1: Age-related dynamics of taste perception and paediatric formulation

3. CHALLENGES IN PEDIATRIC TASTE MASKING

Taste masking in paediatric formulation is challenging because many medicines have a naturally bitter taste, and children are particularly sensitive to unpleasant flavours. Even a slight bitter taste or an unpleasant aftertaste can cause children to refuse medication, making it difficult to ensure proper treatment adherence. Differences in taste preferences across age groups, together with the need to preserve drug effectiveness, stability, and safety, make the development of paediatric formulations more challenging(21).

Taste preferences change with age, with infants preferring simple sweet tastes, toddlers favouring familiar fruit flavours, and school-aged children being more accepting of complex flavour profiles. A formulation that is acceptable to a 3-year-old child may not be well accepted by a 10-year-old because taste and flavour preferences change with age. Infants and children generally prefer sweeter and saltier tastes than adults, and these preferences often persist until late adolescence(22).

A major challenge in taste masking is ensuring that the strategy does not affect the drug performance, as reducing bitterness while maintaining rapid drug release, stability and therapeutic efficacy require careful formulation design. Coatings used to mask bitterness can sometimes slow drug dissolution and affect bioavailability, requiring a careful balance between effective taste masking and timely drug release(21).

Another challenge in paediatric formulation development is the absence of a universally accepted method for assessing the palatability of medicines. Although several methods are available to assess the palatability of medicines, each has its own limitations, and many are not well-suited for use in young children. This makes it difficult to accurately evaluate the taste and overall acceptability of paediatric medicines(23).

4. FACTORS INFLUENCING TASTE MASKING EFFECTIVENESS

4.1 Drug properties

The success of taste masking largely depends on the properties of the drug. Highly water-soluble drugs dissolve rapidly in saliva, making their bitter taste more noticeable as they come in contact with taste buds more quickly. Drugs with a strong bitter taste usually require more effective taste masking techniques to improve their palatability, while high doses are more difficult to taste mask because a larger amount of drug can come into contact with taste receptors. In addition, a drug's chemical structure and its ability to bind to bitter taste receptors can influence the intensity of bitterness and the difficulty of developing a palatable formulation(7,24–26).

4.2 Formulation type

Taste masking needs vary between syrups, suspensions, tablets, orally disintegrating tablets, and oral films. This is because each dosage form affects the extent and duration of the drug's contact with the taste buds. Oral liquids such as syrups and suspensions are generally more difficult to taste mask because the drug is already present in the liquid, and its taste can be detected immediately after administration. In contrast, solid dosage forms can more effectively mask bitterness through techniques such as coating, encapsulation, or complex formation, which limits the drug exposure to taste receptors(27).

4.3 Drug release characteristics

The bitterness of a medicine depends largely on the amount of drug released into saliva because taste receptors in the mouth can detect dissolved drug molecules. Rapid drug release can increase the perception of bitterness, especially in ODTs and rapidly dissolving dosage forms, where the amount of drug release in the saliva becomes high enough for its bitter taste to be detected before swallowing(28).

4.4 Patient age and sensory perception

People's taste preferences and sensitivity can change as they grow older. Children generally prefer sweeter tastes and respond to flavours differently from adults. In addition, cultural background, previous experiences and individual preferences can influence how a medicine or flavour is perceived(29).



Figure 2: Overview of factors influencing taste masking effectiveness

Table 1: Conventional taste masking strategies(25,30–33)

Strategy	Description	Examples
Sweeteners	To make medicines more palatable to children, a sweetener is added in paediatric formulations to mask bitterness and improve overall taste	Sucrose, glucose, fructose, sorbitol, saccharin, sodium, aspartame, sucralose
Flavouring agents	Flavouring agents are often used alongside sweeteners to improve the taste of medicines and make them more	Strawberry, grape, cherry, orange, banana, mango, mint, vanilla, bubblegum.

	acceptable for children	
Bitter blockers	Bitter blockers are a promising taste masking strategy that reduces bitterness by preventing the perception of bitter taste	Sodium acetate, sodium gluconate, adenosine 5'-monophosphate
Salt and acid modulators	A small amount of salt and organic acids can alter taste perception and help improve the overall flavour of oral medicines	Citric acid, malic acid, sodium chloride
Cooling agents	Cooling agents can create a cooling sensation and help reduce unpleasant taste, hence improving the overall flavour and acceptability of oral medicines	Menthol

5. FORMULATION-BASED TASTE MASKING APPROACHES

5.1 Coating techniques

Coating is a widely used approach for taste masking because it creates a protective layer around the drug particles by delaying the release of the drug in the mouth and reducing direct contact with taste receptors. By controlling how long and how much drug is exposed in the mouth, coating techniques help reduce the unpleasant taste and improve the palatability of oral formulations. Limiting drug

release in mouth coating techniques helps reduce bitterness and improve palatability(34).

Polymer coating is a commonly used approach for taste masking, where polymers such as ethyl cellulose and cellulose acetate create a protective layer around the drug, which limits the drug release in the saliva and reduces the contact with the taste receptors(35). Another technique involves film coating, where a thin polymer layer is applied to tablets, pellets, or granules to improve the palatability without affecting the drug performance. **Error! Not a valid filename.** Also, techniques such as microencapsulation encapsulate drug particles within a polymeric or lipid layer, which reduces the exposure of the drug in the saliva and taste buds and thereby improves the palatability. It is also used for controlled drug release and reducing the bitter taste of a drug(36).

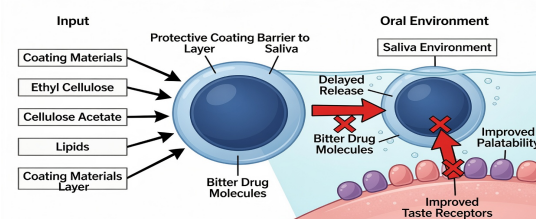


Figure 3: Taste masking coating techniques

5.2 Complexation techniques

Complexation is a useful approach for improving the taste of medicine for children by limiting the drug's contact with the taste receptors, thereby decreasing bitterness and increasing palatability(37).

Cyclodextrin reversibly binds to drug molecules, thereby reducing the amount of drug released in the saliva, thereby helping to reduce the bitter taste. They are commonly used in paediatric oral liquid formulations to enhance palatability(24). Ion exchange resins interact with charged drug molecules to form a drug resin complex, which helps reduce the drug release in the mouth and minimise unpleasant taste. After swallowing this complex breakdown in the GIT, which allows the drug is released(38).

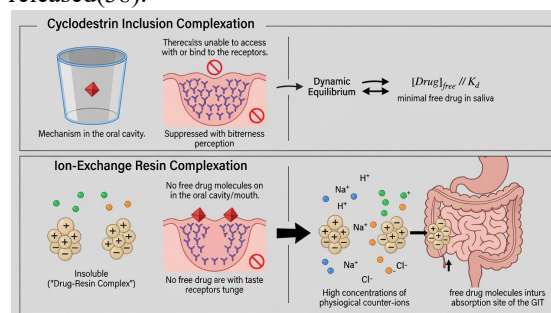


Figure 4: Cyclodextrin complex for taste masking

5.3 Granulation and matrix system

Granulation and matrix-based systems can enhance the taste and acceptability of paediatric medicines by reducing the amount of drug that comes into contact with saliva and taste receptor(39). Wet granulation can help mask bitterness by incorporating the drugs

into granules. Dry granulation limits the direct interaction of drug particles with taste buds, helping to reduce bitterness, making it particularly suitable for moisture-sensitive drugs. The lipid matrix system incorporates the drug into a lipid carrier, thereby controlling the drug release and minimising its exposure in the oral cavity(40).

5.4 Multiple emulsions and lipid-based systems

Multiple emulsion and matrix systems can help improve the taste and acceptability of paediatric medicines by enclosing drug molecules and limiting their release in the oral cavity. Water-in-oil-in-water emulsion (W/O/W) can help mask the bitterness of the drug by trapping bitter-tasting drugs within the internal phase. Liposomes can entrap drugs within phospholipid vesicles, thereby limiting their interaction with the taste receptors, while solid lipid nanoparticles incorporate the drug into a lipid matrix, thereby delaying drug release until after swallowing(41)

Table 2: Advanced taste masking strategies(42–44)

Techniques	Description
Hot melt extrusion	Hot melt extrusion can incorporate drugs into polymer matrices, thereby allowing controlled release in oral formulations.
Spray drying	Spray drying can generate amorphous solid dispersion or microparticles with modified surface characteristics and controlled drug release, thereby supporting taste masking strategies
Solid dispersion	Solid dispersion can help improve drug dissolution and regulate drug release by dispersing the drug in a carrier matrix, thereby limiting drug release in the oral cavity
Polymeric nanoparticles	A polymeric nanoparticulate system can be used to improve taste masking by entrapping the drug molecules and limiting their contact with taste receptors

Nano capsules	The nano capsule system is often used for taste masking and oral delivery
Nano emulsion	Nanoemulsions and related lipid nano-carriers are also used to mask the taste of bitter drugs

6. TASTE MASKING IN DIFFERENT PAEDIATRIC DOSAGE FORMS

Taste masking strategies vary according to the dosage forms to enhance the palatability and acceptance of paediatric medicines(37).

6.1 Oral liquids and suspension

Oral liquid and suspension often contain flavouring agents, sweeteners, and ion exchange resins to improve palatability and make them more acceptable to children. Sweeteners and flavouring agents are commonly used in liquid formulations, whereas ion exchange resins help mask taste by forming drug resin complexes, which minimise drug release in the mouth and allow it to be released after swallowing. For example, amoxicillin suspension flavoured with strawberry and banana(45).

6.2 Powders and granules

Granulation, polymer coating, and microencapsulation are widely used to enhance the palatability of powders and granules. These approaches help limit the contact of the drug with saliva and reduce its interaction with taste receptors, and provide controlled drug release. Crfixime dry suspension granules are a common example of this approach(46).

6.3 Chewable tablets

Chewable tablets commonly incorporate sweeteners, flavours, and taste masking coatings to improve their acceptability in children. Cherry-flavoured Montelukast chewable tablets are a typical example of this approach(47).**Error! Not a valid filename.**

6.4 Oro dispersible tablets (ODTs)

Since ODTs dissolve in the mouth, proper taste masking is important. Common taste masking strategies include coating, complexation, and ion exchange resins, which help minimise the interaction of bitter drugs with taste buds before swallowing. Ondansetron ODTs formulated with ion exchange resin complexes are a well-known example of this strategy(48).

6.5 Oral thin films

Since oral thin films dissolve quickly in the mouth, proper taste masking is essential. Common taste masking approaches include cyclodextrin complexes, polymer film coating, and other formulation techniques that help minimise bitterness. Cetirizine is a typical example of fast-dissolving oral films. ODT and lyophilisate formulations have also been prepared using β

cyclodextrin or hydroxypropyl β cyclodextrin to improve palatability and acceptability(49).

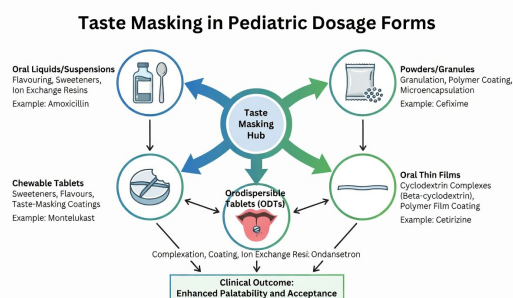


Figure 5: Taste-masking strategies in paediatric oral formulations

7. CONCLUSION

Taste masking is a key consideration in the development of paediatric oral formulations as unpleasant taste continues to be a major barrier to medication acceptance and adherence in children. A wide range of conventional and advanced taste masking strategies have been developed over the years, including sweeteners and flavouring agents, coating, microencapsulation, complexation, ion exchange resins, spray drying, hot melt extrusion, etc., to enhance taste while preserving therapeutic effectiveness. The selection of an appropriate taste masking strategy depends upon the physical and chemical properties of the drug as well as the dosage forms in which the drug is intended to be delivered, such as liquids, granules, oral films or chewable tablets. Ensuring the use of safe excipients, suitable manufacturing approaches, and proper evaluation techniques is also important for successful paediatric formulations and acceptability by patients. As formulation technologies continue to evolve and a deeper understanding of how children perceive taste is gained, further paediatric formulation is expected to become more acceptable and patient-friendly. Overall, effective taste masking strategies can help improve medication adherence and help achieve better therapeutic outcomes in children.

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