



Overcoming Challenges in Paediatric Formulation in Patient-Centric Design Approach: A Proof of concept Study on design of Oral Solutions of Bitter Taste

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Abstract

Paediatric medication formulation faces unique challenges due to children's distinct physiological needs and preferences, particularly with bitter-tasting drugs that hinder adherence. This review emphasizes the importance of a patient-centric design approach, involving children, caregivers, and healthcare providers, to enhance palatability, dosing flexibility, and treatment success. Key barriers, including bitterness, dosing accuracy, and excipient safety, are examined alongside innovative advancements in oral solution technologies. Strategies such as encapsulation, ion-exchange resins, flavour modifiers, and novel formulations like liquid suspensions and microencapsulation are discussed. A proof-of-concept case study highlights the impact of integrating advanced taste-masking techniques and patient feedback in improving medication acceptability and adherence, demonstrating the effectiveness of user-centered formulation methodologies.

Keywords: Sensory Evaluation, Paediatric Formulation, Patient-Centric Design, Oral Solution.

I.Introduction

Paediatric medication formulation presents unique challenges due to children's distinct physiological and behavioural characteristics, including differences in drug absorption, metabolism, and taste preferences. Bitter-tasting drugs often hinder adherence, making palatability a critical focus in paediatric pharmaceutical development. Traditional taste-masking methods, such as sweeteners, are often inadequate, necessitating advanced approaches like microencapsulation, ion-exchange resins, and lipid-based systems. A patient-centric design, involving children, caregivers, and healthcare professionals, has emerged as a vital strategy to ensure formulations are therapeutically effective, safe, and acceptable. This review examines these challenges and explores innovative taste-masking techniques and user-centered methodologies, highlighting their potential through a case study on a bitter oral solution. By integrating patient feedback and advancing formulation strategies, this approach aims to improve paediatric treatment outcomes and adherence.



Age Classification of Paediatric Formulation.

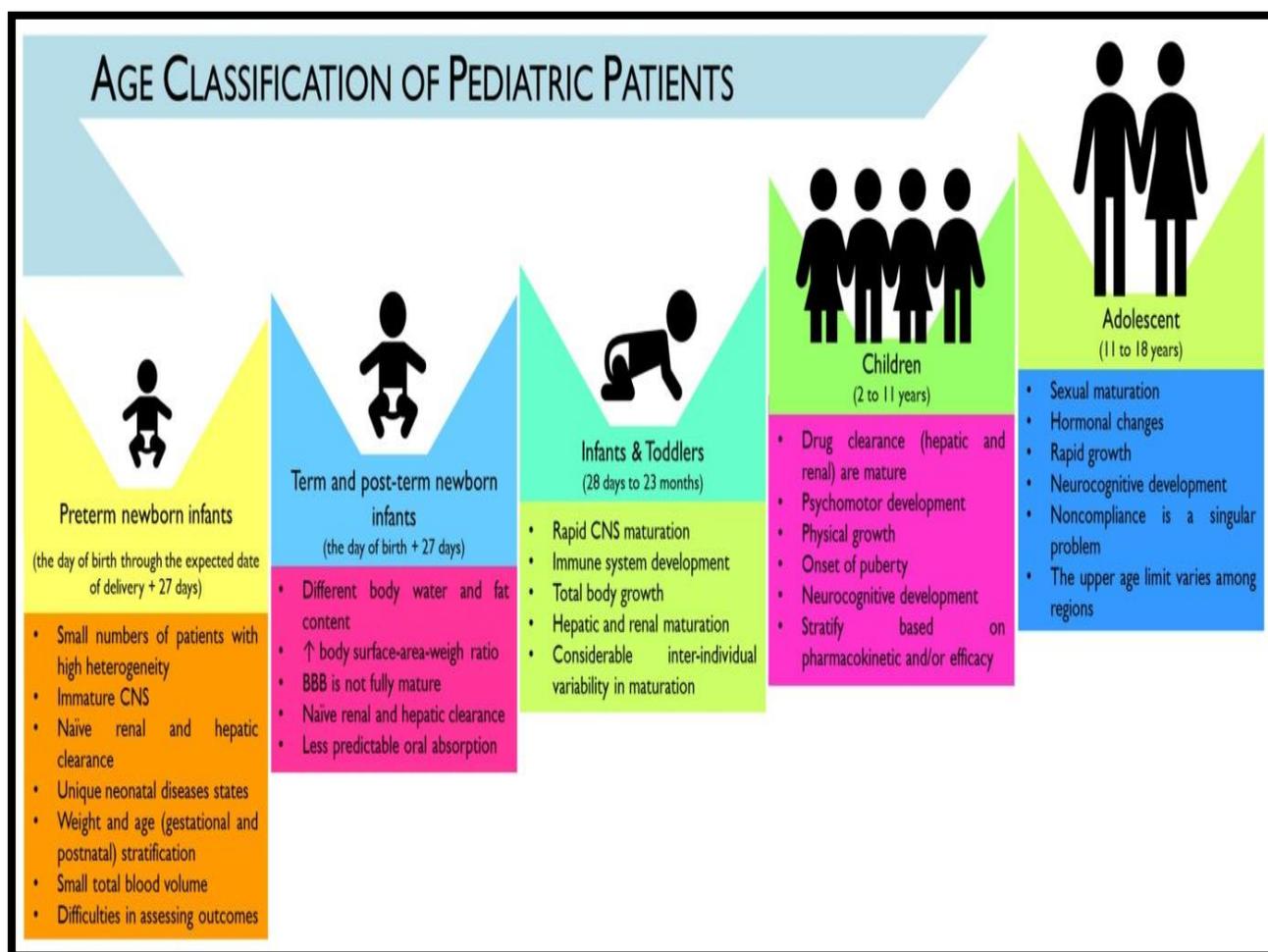


Figure 1 : Infographic of the age categorization of paediatric patients according to the International Council for Harmonization (ICH) guidelines E11(R1).As summarized ,there is a considerable heterogeneity in developmental categorization (e.g.physical,cognitive,and psychological)across paediatric ages .Central nervous system (CNS),blood –brain barrier (BBB),increase.

II.Challenges in paediatric formulation

2.1 taste and palatability

Taste and palatability are essential for paediatric medication adherence, as children are sensitive to bitter drugs. While sweeteners and flavour enhancers are commonly used, they may be unsuitable for certain dietary needs. Advanced techniques like encapsulation, microencapsulation, polymer coatings, and ion-exchange resins effectively mask bitterness by preventing interaction between the drug and taste receptors or controlling drug release, ensuring both palatability and therapeutic effectiveness.

2.2 Dosing Accuracy

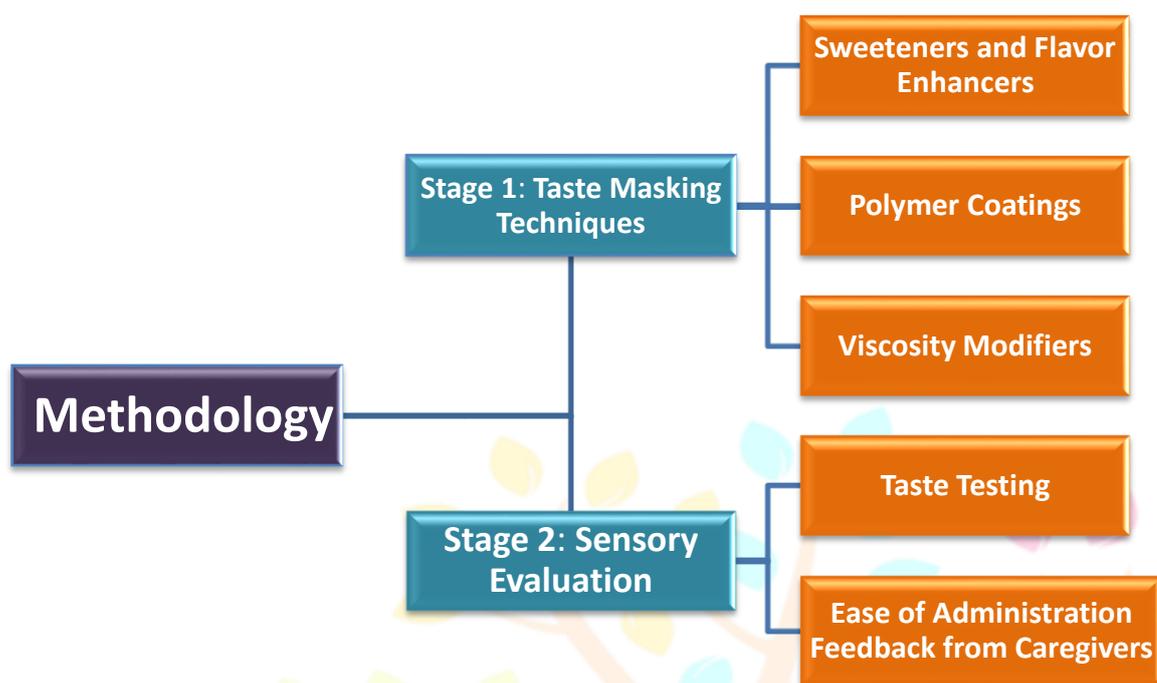
Accurate dosing in paediatric formulations is crucial due to variations in children's weight and development. Liquid formulations, such as oral solutions and suspensions, are preferred for easy dose adjustments, particularly for young children who cannot swallow tablets. However, challenges like stability, taste, and accurate measurement persist. While dose-measuring devices like oral syringes and dosing cups help improve accuracy, dosing errors are still common, especially with household tools. Clear labelling and standardized dosing instruments are essential to reduce the risk of under- or over-dosing.

2.3 Safety and toxicity

The safety of paediatric formulations is critical, as children are more susceptible to adverse effects from excipients that are safe for adults. Substances like benzyl alcohol and propylene glycol can be toxic to neonates and infants due to their immature metabolic

systems. Regulatory bodies, such as the FDA and EMA, stress the importance of excipient safety assessments in paediatric drug development. Safety considerations.

III. Methodology :



The methodology for the study was designed as a two-stage process to optimize the oral solution of a bitter drug for paediatric use. This approach aimed to ensure both effective taste-masking and high acceptability based on feedback from the target age group and their caregivers.

1. Stage 1: Taste Masking Techniques

1.1. Sweeteners and Flavour Enhancers : To counteract bitterness and enhance taste, natural and artificial sweeteners were used alongside fruit-flavoured enhancers. This combination was designed to create a sweet and appealing flavour, particularly for children.

1.2. Polymer Coatings: Polymer coatings were used to encapsulate the API, preventing direct contact with taste buds and masking bitterness. Advanced techniques like microencapsulation ensured the coating dissolved only in the stomach's acidic environment, minimizing unpleasant taste during administration

1.3. Viscosity Modifiers: Gelling agents or viscosity enhancers were added to alter the mouth feel and ensure that the oral solution had a smoother consistency, which could improve the acceptance among children.

2. Stage 2: Sensory Evaluation :

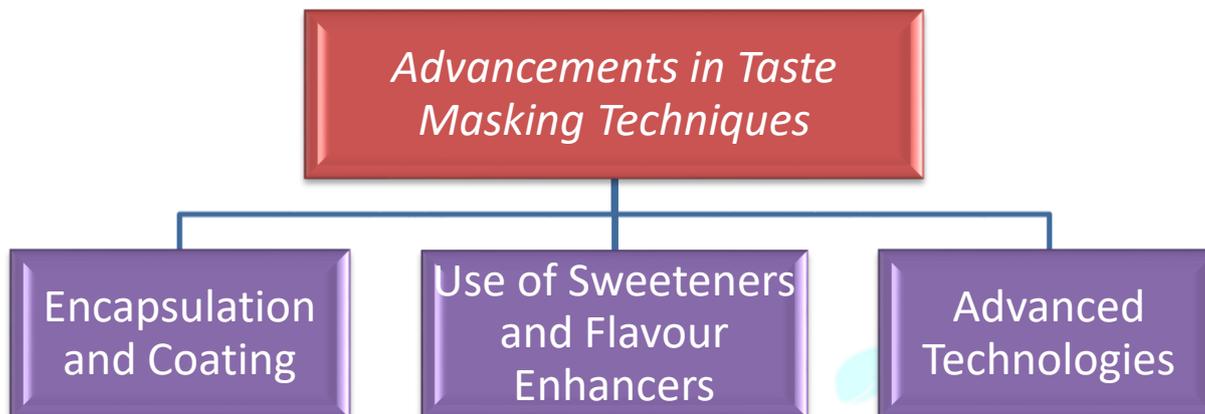
2.1. Taste Testing:

The children were asked to rate the taste of the oral solution using a standardized hedonic scale (e.g., faces representing different levels of liking). This helped assess whether the taste-masking strategies were effective in improving palatability.

2.2. Ease of Administration Feedback from Caregivers:

Caregiver feedback on administration ease, including dose measurement, spill resistance, and packaging convenience, informed iterative refinements to the formulation and design. This patient-centric approach in paediatric drug development leveraged real-time insights and statistical analysis to evaluate the impact of changes across formulation iterations.

IV. Advancement in taste masking techniques



A) Encapsulation and Coating :

Microencapsulation is an effective technique for masking the bitterness of oral drugs, particularly in paediatric formulations. This method involves encasing the API in a polymeric coating designed to dissolve at specific pH levels, typically in the gastrointestinal tract, delaying taste release and enhancing palatability. Common polymers, such as ethyl cellulose and polyvinyl acetate, enable controlled release and improve drug stability by protecting against environmental degradation. Studies show that microencapsulated formulations significantly improve taste acceptance and adherence in children, supporting better treatment outcomes.

B) Use of Sweeteners and Flavour Enhancers:

The use of non-nutritive sweeteners, such as sucralose and aspartame, along with natural flavour enhancers like fruit extracts and essential oils, is a proven strategy for improving the taste of oral solutions. These sweeteners effectively mask bitterness without adding significant calories, while natural flavours enhance palatability and create a balanced taste profile. Additionally, flavouring agents can stimulate salivation and improve mouth feel, increasing patient acceptance and adherence, particularly in paediatric populations.

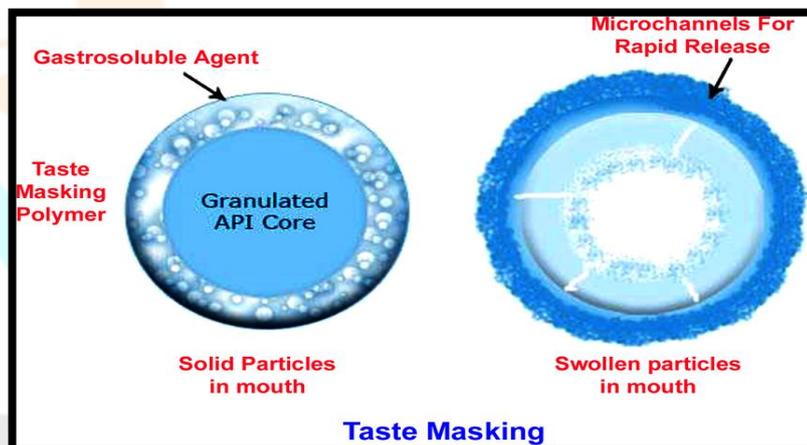


Figure 9 : Taste masking in Fast melt technology

C) Advanced Technologies

In addition to traditional taste-masking techniques, more advanced methodologies are being explored to address the challenges of bitter drug formulations.

Ion-Exchange Resins:



Figure 10: Advanced Technologies in Ion-Exchange Resins

V. Discussion:

Paediatric drug formulation development faces challenges related to children's physiological traits, taste preferences, and dosing needs, with bitterness being a key barrier to adherence. Effective taste-masking techniques, such as sweeteners, encapsulation, and ion-exchange resins, are essential for improving palatability. A patient-centric approach that involves children and caregivers enhances medication

VI. Result :

The proof-of-concept study yielded promising results, indicating that the patient-centric approach to the formulation had a significant impact on improving the acceptability and ease of administration of the oral solution.

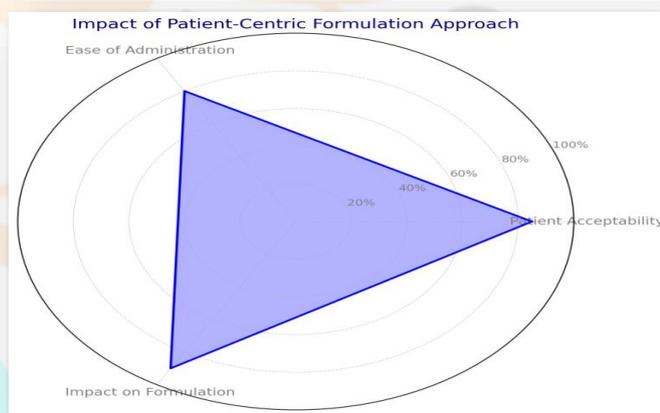


Figure 12 : Impact of patient –centric formulation Approach

VII. Conclusion :

Paediatric formulation faces unique challenges, including taste masking, accurate dosing, and excipient safety, which affect medication adherence. A patient-centric approach, involving children and caregivers, helps create palatable and user-friendly medications. Techniques such as taste masking with sweeteners, encapsulation, and advanced technologies like ion-exchange resins have proven effective in improving oral medication acceptability. Regulatory guidelines ensure safety and efficacy, while market demand for child-friendly medications continues to grow. Future advancements will rely on integrating innovative taste-masking methods and patient-focused design to improve adherence and therapeutic outcomes for children.

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