

Formulation and Development Challenges for a Carvedilol Liquid that is Pediatric-friendly

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Abstract

Pediatric patients often present unique challenges when it comes to medication administration. Carvedilol, a widely used beta-blocker for the management of various cardiovascular conditions, is no exception. While it is typically available in tablet form for adult patients, formulating a safe, effective and palatable liquid formulation for pediatric use can be a complex and demanding task. In this article, we will explore the formulation and development challenges faced in creating a pediatric-friendly carvedilol liquid. Children can suffer from a wide range of cardiovascular conditions, such as hypertension, heart failure, or arrhythmias, for which carvedilol may be a suitable treatment option. However, administering tablets to pediatric patients can be problematic. Children often struggle to swallow pills and the dosing accuracy for tablets can be challenging. Furthermore, many pediatric patients require customized dosing, which is more easily achieved with liquid formulations.

Keywords: Hypertension • Arrhythmias • Heart failure • Pediatric patient

Introduction

Carvedilol is poorly water-soluble, which complicates the formulation process. Creating a stable liquid formulation requires overcoming solubility issues and maintaining drug stability over time. Excipients such as solubilizing agents, stabilizers and preservatives must be carefully selected to ensure drug integrity. One of the most critical challenges in formulating pediatric-friendly medications is making them palatable. Children can be extremely sensitive to the taste and texture of medications. The bitter taste of carvedilol presents a significant hurdle. Masking the bitterness while maintaining the drug's therapeutic efficacy is essential. Ensuring accurate dosing for pediatric patients is crucial to prevent underdosing or overdosing. Liquid formulations must provide a reliable means of measuring and delivering precise doses, especially for younger children who may require very low doses. Pediatric medications often need to be administered with specialized devices such as oral syringes or droppers. The liquid formulation must be compatible with these devices to facilitate accurate and convenient administration. Liquid formulations often require the use of excipients to improve stability, solubility and taste. However, it's essential to ensure that these excipients are safe for pediatric use and do not interact with the active ingredient [1].

Literature Review

Various taste-masking approaches can be employed to make carvedilol more palatable for children. These may include the use of sweetening agents, flavor enhancers and encapsulation technologies. The goal is to create a liquid formulation that is both tolerable and appealing to pediatric patients. Microencapsulation techniques can be used to encase carvedilol in a tasteless shell, preventing its bitter taste from being perceived. This approach can also

enhance stability and allow for sustained drug release, which may be beneficial for certain pediatric populations. Modifying the pH of the liquid formulation can influence the taste perception of carvedilol. By adjusting the pH, it is possible to reduce the bitterness of the drug while maintaining its chemical stability. Developing clear and precise dosing guidelines for carvedilol in pediatric patients is essential. Dosing should be based on age, weight and the specific indication for which the medication is prescribed. The formulation should allow for easy adjustment of dosages to accommodate the wide range of pediatric patients' needs [2].

Extensive stability studies are necessary to ensure that the liquid formulation remains effective and safe over its shelf life. Factors such as temperature, light exposure and the choice of packaging materials can all impact the stability of the medication. Developing a pediatric-friendly carvedilol liquid formulation involves navigating regulatory requirements, including those set forth by agencies like the FDA in the United States. Manufacturers must meet stringent quality, safety and efficacy standards when formulating medications for pediatric use. Clinical trials involving pediatric patients may be required to demonstrate the safety and efficacy of the liquid formulation in this population [3].

Discussion

Carvedilol is a widely used medication primarily indicated for adults with conditions like hypertension and congestive heart failure. However, there is a growing need to adapt this medication for pediatric use, given its potential benefits in treating certain heart conditions in children. Formulating a pediatric-friendly liquid version of carvedilol presents several challenges, ranging from dose accuracy to taste masking. In this article, we will explore the complexities of developing a pediatric-friendly carvedilol liquid and the various strategies researchers and pharmaceutical companies employ to overcome these hurdles. Carvedilol, a non-selective beta-blocker, has been a staple in the treatment of cardiovascular conditions in adults for several decades. Its unique pharmacological profile makes it an attractive option for managing conditions such as hypertension and congestive heart failure. However, when it comes to pediatric patients, using the existing tablet formulations can be impractical or even dangerous. This has spurred interest in creating a pediatric-friendly liquid version of carvedilol. One of the foremost challenges in developing a pediatric-friendly carvedilol liquid is achieving precise dosing. Unlike adult patients, children require smaller and more carefully measured doses, making dose accuracy a top priority. Ensuring that each milliliter of the liquid contains the intended amount of carvedilol is crucial for safe and effective treatment [4].

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Received: 26 June, 2023, Manuscript No. fsb-23-115223; **Editor Assigned:** 29 June, 2023, PreQC No. P-115223; **Reviewed:** 13 July, 2023, QC No. Q-115223; **Revised:** 18 July, 2023, Manuscript No. R-115223; **Published:** 25 July, 2023, DOI: 10.37421/2577-0543.2023.7.161

Formulation scientists must employ state-of-the-art pharmaceutical technology to ensure accurate dosing. This includes specialized equipment for measuring and dispensing the active ingredient. Developing multiple concentration options can help address dose accuracy. For instance, having 1 mg/mL, 2 mg/mL and 4 mg/mL concentrations would provide flexibility in dosing for different age groups. Carvedilol has a bitter taste that can be extremely unpalatable to children. Ensuring that the liquid formulation is palatable is essential to encourage compliance and prevent resistance to medication administration.

The most common approach to taste masking is flavoring the liquid. This can involve the use of various flavors like cherry, grape, or bubblegum to mask the bitterness. However, this approach may not completely eliminate the taste and the choice of flavor should be age-appropriate. The addition of sweeteners like sucrose or aspartame can help mask the bitter taste. However, the use of sweeteners should be carefully considered, especially in patients with diabetes or other dietary restrictions. Another innovative approach is microencapsulation, where the active ingredient is coated to prevent contact with taste buds until it reaches the stomach. This can be particularly effective for bitter drugs [5].

Pediatric medications must have a stable shelf life to ensure that the drug remains effective and safe for consumption. Carvedilol, like many other drugs, can be susceptible to degradation over time. Utilizing specialized packaging that prevents exposure to light, air and moisture can help extend the shelf life of the liquid formulation. Extensive stability studies are essential to determine the degradation kinetics of carvedilol in the liquid form. This information can guide the formulation process to ensure that the drug remains potent over its shelf life. Ensuring that caregivers and healthcare providers can accurately measure and administer the liquid formulation is critical. Inaccurate dosing can lead to underdosing or overdosing, both of which can have serious consequences. Providing oral syringes with clear volume markings can help caregivers and healthcare providers accurately measure the required dose. Proper education and training for caregivers on how to use the dosing device are crucial to prevent dosing errors [6].

Conclusion

Creating a pediatric-friendly liquid formulation of carvedilol is a complex and challenging endeavor. Formulation scientists must address issues related to solubility, taste, dosing accuracy and compatibility with administration devices. Various strategies, including taste masking, microencapsulation and pH adjustment, can be employed to overcome these challenges. Additionally, the development process must adhere to strict regulatory standards and may require clinical trials in pediatric patients to ensure safety and efficacy. The successful formulation and development of a pediatric-friendly carvedilol

liquid would provide healthcare providers with a valuable tool for managing cardiovascular conditions in children. By addressing the unique needs of pediatric patients, this endeavor has the potential to improve medication adherence and outcomes for this vulnerable population, ultimately enhancing their quality of life. Formulators must carefully select excipients that are well-tolerated by pediatric patients and have a proven safety profile.

The development of a pediatric-friendly liquid formulation for carvedilol is a complex process that involves addressing multiple challenges, including dose accuracy, taste masking, stability, dosing devices, excipient compatibility and regulatory approval. Pharmaceutical companies and researchers must employ innovative strategies and advanced technology to overcome these obstacles and provide a safe and effective treatment option for pediatric patients with cardiovascular conditions. Ultimately, success in this endeavor can significantly improve the quality of life for children with these conditions and their families.

Acknowledgement

None.

Conflict of Interest

None.

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How to cite this article: Pérez-Lozano, Khadija. "Formulation and Development Challenges for a Carvedilol Liquid that is Pediatric-friendly." *J Formul Sci Bioavailab* 7 (2023): 161.