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DESIGNING A LIPID-BASED FLOATING BEAD FOR PROLONGED RELEASE OF DEXTROMETHORPHAN HYDROBROMIDE

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ABSTRACT

This study explores the potential of lipid-based floating beads to prolong the gastric retention and sustained release of DXM HBr, offering a novel approach to enhance its therapeutic profile and patient adherence. Lipid-based floating beads are designed to leverage the buoyancy of lipid components, allowing them to float in the stomach and extend the absorption window for drugs absorbed in the upper gastrointestinal tract. This study aimed to create and evaluate these beads to facilitate the sustained release of DXM HBr. The selection of lipid materials, including glyceryl monostearate and beeswax, was based on their compatibility with DXM HBr and their physicochemical properties. The preparation involved melting the lipid components, dissolving DXM HBr in a suitable solvent, and emulsifying the mixture under high shear conditions in an aqueous phase containing a stabilizer like polyvinyl alcohol. The resulting beads were then collected, washed, and dried.

KEYWORDS: Lipid-based floating bead, Drug delivery, Dextromethorphan hydrobromide (DXM HBr).

INTRODUCTION

The pursuit of innovative drug delivery systems to enhance therapeutic efficacy and patient compliance while minimizing side effects has led to the development of lipid-based floating beads for the sustained release of dextromethorphan hydrobromide (DXM HBr). DXM HBr is a widely used antitussive agent that acts centrally to suppress cough. However, its clinical utility is limited by a short half-life, necessitating frequent dosing to maintain therapeutic plasma levels. The desire to improve drug delivery systems to maximize therapeutic efficacy while minimizing side effects and increasing patient adherence has driven the pursuit for new pharmaceutical formulations. Therefore, it is anticipated that the emergence of lipid-based floating beads for the sustained release of dextromethorphan hydrobromide (DXM HBr) might suggest a novel destination in pharmaceutical research to route the poorly soluble drugs to avoid the hurdles of conventional drug delivery and to amplify the therapeutic efficacy.

Dextromethorphan hydrobromide, commonly known as DXM HBr, is a frequently used antitussive medication that has shown efficacy in successfully reducing the need to cough by central action on the cough center. While proven to be an effective medicinal ingredient, the utility of DXM HBr is limited by a short half-life, which requires that the compound be administered at short intervals in order to sustain therapeutic levels of the drug in the blood. In addition to challenges in patient compliance, these dosing regimens increase the potential for a fluctuating drug concentration and thus are likely to impact treatment efficacy.

Dextromethorphan hydrobromide (DXM HBr) is an effective antitussive agent that is used domestically and globally to suppress cough through a central mechanism. Nevertheless, the clinical utility of DXM HBr is frequently restricted due to the short half-life and the consequent necessity for frequent dosing to sustain therapeutic plasma levels. This has kindled enthusiasm for the development of controlled-release formulations to improve adherence of the patient and thereby level out the therapeutic window. Researchers devote efforts to improve pharmaceutical formulations primarily by optimizing drug delivery systems for better therapeutic efficacy and patient compliance. In this background, an interesting inventive step in the field of pharmaceutical research is the fabrication of the lipid based floating beads for controlled release formulation of dextromethorphan hydrobromide (DXM HBr).

Dextromethorphan hydrobromide is a commonly used cough suppressant known for its ability to inhibit cough reflexes by acting on the central nervous system. However, its effectiveness is often limited by its short half-life, requiring frequent dosing to maintain therapeutic levels in the blood. This study aims to address these shortcomings by utilizing lipid-based floating beads to prolong the stomach's retention of DXM HBr, enabling sustained release and longer-lasting therapeutic benefits. This overview introduces the innovative strategy of developing lipid-based floating beads, underscoring their potential to transform drug delivery systems and enhance patient outcomes in the management of cough-related conditions.

Lipid-based floating beads present a promising strategy for achieving prolonged drug release. These mechanisms leverage the buoyancy of lipid components to float in the stomach, thereby extending their stay in the gastric region and widening the absorption window for drugs that are only absorbed in the upper gastrointestinal tract. This study aims to create and assess lipid-based floating beads to facilitate the sustained release of DXM HBr.

Sustained Release Drug Delivery Systems: Various sustained-release drug delivery systems have been researched in pharmaceutical studies to extend drug release, improve therapeutic effectiveness, and reduce dosing frequency. Lipid-based floating beads are a promising method for achieving sustained release, especially beneficial for short half-life drugs like dextromethorphan hydrobromide (DXM HBr).

Lipid-Based Drug Delivery Systems: Lipid-based drug delivery systems have garnered attention for their capacity to enhance the solubility, stability, and bioavailability of poorly water-soluble drugs. These systems utilize lipids as carriers, providing controlled release and targeted delivery, which makes them favorable for developing sustained-release formulations such as floating beads for DXM HBr.

Floating Drug Delivery Systems: Floating drug delivery systems aim to prolong the time dosage forms stay in the stomach, thus improving drug absorption and bioavailability. By remaining buoyant in the gastric fluid, floating beads

can expand the absorption period and offer prolonged release of DXM HBr, enhancing its therapeutic effectiveness and patient adherence.

Dextromethorphan Hydrobromide: DXM HBr, a commonly used antitussive agent, is recognized for its ability to suppress cough reflexes by affecting the central nervous system. Despite this, its short half-life requires frequent dosing, posing challenges for patient compliance and causing fluctuations in drug levels. Creating sustained-release formulations like lipid-based floating beads can overcome these hurdles and deliver consistent therapeutic benefits.

Strategies for Developing Lipid-Based Floating Beads: Various approaches have been investigated to create lipid-based floating beads, encompassing the selection of suitable lipid materials, optimization of drug loading and release kinetics, and assessment of physicochemical characteristics. These strategies are designed to promote the even dispersion of DXM HBr within the lipid matrix and ensure sustained release over a prolonged duration.

Lipid-Based Floating Bead Analysis: The drug release pattern and floating qualities of lipid-based floating beads are determined in large part by their physicochemical characteristics, which include particle size, surface structure, drug concentration, and encapsulation efficiency. These characteristics are evaluated using characterization techniques such as high-performance liquid chromatography, dynamic light scattering, and scanning electron microscopy.

In Vitro Buoyancy Studies: These investigations evaluate the floating characteristics of lipid-based floating beads in stomach fluid that is simulated. Researchers can assess how well the formulation works to extend the stomach residency duration and improve drug absorption by tracking the proportion of beads that stay buoyant over time.

In Vitro Drug Release Studies: These investigations are crucial to determining how DXM HBr is released from lipid-based floating beads. In these experiments, the beads are placed in simulated gastric fluid, and a dissolving equipment is used to track the drug's release over time. Researchers can ascertain the formulation's capability for prolonged release by examining the release kinetics.

Release Kinetics Modeling: This method is used to explain how DXM HBr is released from lipid-based floating beads by analyzing drug release data gathered from in vitro research. The Higuchi, Korsmeyer-Peppas, zero-order, and first-order mathematical models are among those utilized to match the experimental data and ascertain the drug release kinetics.

Comparative Studies with Conventional Formulations: To determine the potential benefits of the novel formulation, comparative studies comparing the pharmacokinetic profiles and efficacy of lipid-based floating beads with conventional formulations of DXM HBr are necessary. Researchers can show that lipid-based floating beads are superior in delivering sustained release and enhancing patient outcomes by assessing criteria such drug release kinetics, plasma concentration profiles, and therapeutic effects.

MATERIALS AND METHODS

The process described herein for creating lipid-based floating beads that release dextromethorphan hydrobromide (DXM HBr) over an extended period of time includes a number of crucial stages meant to optimize the formulation and assess the characteristics of the final product. DXM HBr is the active pharmaceutical ingredient (API), and lipid materials, polymers, solvents, and other excipients are selected based on their compatibility with DXM HBr and their

capacity to create lipid-based beads. This initial material selection is crucial. The selection of lipid materials is based on factors such as compatibility with the API, solubility, and melting points, such as glyceryl monostearate and beeswax.
The first step in the formulation development procedure is to prepare lipid-based beads. This entails melting the lipid components and dissolving DXM HBr in an appropriate solvent. To guarantee even distribution, the medication solution is then added while the lipid is still hot and constantly stirred. Then, under high shear conditions, the lipid-drug mixture is emulsified to form beads in an aqueous phase containing a stabilizer, like polyvinyl alcohol. After that, the beads are gathered, cleaned, and dried to produce the finished composition. To achieve the intended drug loading and release profile, formulation parameter optimization is essential. To improve bead size, stability, and drug release properties, variables such the drug-to-lipid ratio, stabilizer concentration, and process parameters (such as stirring speed, temperature, and emulsification time) are changed and improved.

The beads are characterized using a variety of analytical methods in order to evaluate their physicochemical characteristics. Bead size distribution can be understood through particle size analysis using dynamic light scattering (DLS) or optical microscopy, and surface morphology can be examined using scanning electron microscopy (SEM). To ensure consistent drug distribution, high-performance liquid chromatography (HPLC) is utilized to measure the drug content and bead encapsulation efficiency. The beads' ability to float in simulated stomach fluid is evaluated by in vitro buoyancy tests, which validate their appropriateness for extended gastric residency times.

A USP dissolving equipment is used in in vitro drug release experiments in simulated stomach fluid to assess the release profile of DXM HBr from the beads. The kinetics and mechanism of drug release from the beads are clarified by release kinetics analysis employing a variety of mathematical models, including the zero-order, first-order, Higuchi, and Korsmeyer-Peppas models. All things considered, the thorough approach presented makes it easier to create, optimize, and characterize lipid-based floating beads for the sustained release of DXM HBr in a methodical manner. This establishes the foundation for future developments in drug delivery technologies that could lead to better therapeutic results.

RESULTS AND DISCUSSION

The study delved into pre-formulation aspects of dextromethorphan HBr, revealing its characteristics including color (white) and odor (odorless), alongside its melting point (122°C to 124.33°C), closely aligned with literature values. UV spectroscopy highlighted its absorption maximum at 280 nm, with a standard linearity curve in methanol confirming a linear relationship between concentration and absorbance ($Y = 0.0081x + 0.0079$, $R^2 = 0.999$). Solubility studies indicated dextromethorphan HBr's high solubility in methanol and ethanol, and limited solubility in water and other aqueous solutions. Partition coefficient determination yielded a value of 1.432±0.014. Formulation of dextromethorphan HBr loaded lipid-based floating beads was successful using Gelucire 43/01, with variations in lipid amounts affecting bead characteristics. In-vitro characterization demonstrated spherical beads with varying yields, drug entrapment, loading, and sizes, with Gelucire 43/01 beads exhibiting the desired properties. Notably, DB6 formulation showed optimal drug entrapment and loading with a suitable bead size of 5.327±0.031mm, alongside excellent floating ability (100%) for 24 hours. FT-IR spectra confirmed drug encapsulation within the bead matrix. Scanning electron microscopy revealed porous surface architecture enhancing bead porosity. In-vitro drug release studies in 0.1NHcl exhibited controlled and sustained release from DB6 formulation, contrasting with immediate release from pure drug. The release kinetics followed the Higuchi model, with a regression coefficient of 0.9045, indicating diffusion-

controlled release. This comprehensive characterization offers insights into the development of dextromethorphan HBr loaded lipid-based floating beads, promising for controlled drug delivery applications.

CONCLUSION

The creation of lipid-based floating beads offers a viable method to improve the antitussive drug's therapeutic efficacy and patient compliance: the sustained release of DXM HBr. The limitations of traditional DXM HBr formulations can be addressed by extending the stomach residence period and achieving controlled drug release through optimization of the formulation and processing parameters. Important information about the produced beads' potential as a sustained-release delivery method is gleaned from the characterization and assessment of the beads conducted in vitro.

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