DEVELOPMENT AND EVALUATION OF GASTRORETENTIVE SOLID ORAL DRUG DELIVERY SYSTEM OF DROTAVERINE HYDROCHLORIDE

[1] Dr.Paras Babarao Pophalkar, [2] Prof.Sachin Ushaji Hole, [3]Prof.Nayankumar Nilkanth Bondhare

[1]Associate Professor, [2]Assistant Professor, [3]Assistant Professor
[1]Department of Pharmaceutics,
[1]Sudhakarrao Naik Institute of Pharmacy, Pusad, Maharashtra, India

Abstract : Drotaverine hydrochloride is an antispasmodic agent widely used in the treatment of gastrointestinal disorders. However, its short biological half-life and absorption predominantly in the upper gastrointestinal tract necessitate frequent dosing, leading to poor patient compliance. The present study aimed to develop and evaluate a gastroretentive solid oral drug delivery system of Drotaverine hydrochloride to enhance gastric residence time and sustain drug release. Floating tablets were prepared by direct compression using hydrophilic polymers such as hydroxypropyl methylcellulose (HPMC K4M and K15M) along with gas-generating agents. The prepared formulations were evaluated for precompression parameters, postcompression characteristics, in vitro buoyancy, swelling behavior, drug content uniformity, and in vitro drug release. All formulations showed acceptable physicochemical properties. The optimized formulation exhibited a floating lag time of less than one minute and remained buoyant for more than 12 h. In vitro dissolution studies revealed sustained drug release up to 12 h following Higuchi diffusion kinetics. The results indicate that gastroretentive floating tablets of Drotaverine hydrochloride can be successfully formulated to improve gastric retention and therapeutic efficacy.

Keywords: Drotaverine hydrochloride, gastroretentive drug delivery system, floating tablets, sustained release, HPMC

INTRODUCTION

Oral drug delivery remains the most preferred route of administration due to patient convenience, cost-effectiveness, and ease of formulation. However, conventional oral dosage forms often exhibit limitations such as variable gastric emptying time, short gastrointestinal transit time, and reduced bioavailability of drugs that are absorbed primarily in the upper gastrointestinal tract.

Gastroretentive drug delivery systems (GRDDS) are designed to retain the dosage form in the stomach for a prolonged period, thereby improving drug bioavailability, reducing dosing frequency, and enhancing therapeutic effectiveness. Several approaches have been explored to achieve gastroretention, including floating systems, bioadhesive systems, expandable systems, and high-density systems. Among these, floating drug delivery systems have gained considerable attention due to their simplicity and effectiveness.

Drotaverine hydrochloride is a phosphodiesterase-IV inhibitor with potent antispasmodic activity. It is widely used for the treatment of gastrointestinal and genitourinary spasms. The drug exhibits better solubility in acidic pH and is absorbed mainly from the stomach and upper part of the small intestine. Its relatively short half-life necessitates frequent administration, which may result in reduced patient compliance.

Considering these factors, Drotaverine hydrochloride is an ideal candidate for formulation as a gastroretentive drug delivery system. The objective of the present study was to develop and evaluate gastroretentive floating tablets of Drotaverine hydrochloride to achieve prolonged gastric retention and sustained drug release.

Materials and Methods

Materials

Drotaverine hydrochloride was obtained as a gift sample from a reputed pharmaceutical manufacturer. Hydroxypropyl methylcellulose (HPMC K4M and HPMC K15M), sodium bicarbonate, citric acid, lactose monohydrate, magnesium stearate, and talc were of pharmaceutical grade and used without further purification.

Preformulation Studies

Identification of Drug

The identity of Drotaverine hydrochloride was confirmed by determination of melting point and Fourier transform infrared (FT-IR) spectroscopy.

Solubility Studies

Solubility of Drotaverine hydrochloride was determined in distilled water, 0.1 N hydrochloric acid, phosphate buffer pH 6.8, and methanol.

Drug–Excipient Compatibility Studies

FT-IR spectra of pure drug and physical mixtures of drug with excipients were recorded to study possible drug–excipient interactions.

Formulation of Gastroretentive Floating Tablets

Floating tablets were prepared by the direct compression method. The drug and excipients were passed through a 60-mesh sieve, blended uniformly, and lubricated with magnesium stearate and talc. The blends were compressed into tablets using a rotary tablet compression machine.

Table 1: Composition of Drotaverine Hydrochloride Floating Tablets

Ingredients (mg)	F1	F2	F3	F4	F5
Drotaverine HCl	40	40	40	40	40
HPMC K4M	60	80	100	–	–
HPMC K15M	–	–	–	80	100
Sodium bicarbonate	20	20	20	20	20
Citric acid	10	10	10	10	10
Lactose	q.s	q.s	q.s	q.s	q.s
Magnesium stearate	5	5	5	5	5
Talc	5	5	5	5	5
Total weight	250	250	250	250	250

Evaluation of Powder Blend

The prepared powder blends were evaluated for bulk density, tapped density, angle of repose, Carr's index, and Hausner's ratio to assess flow properties.

Evaluation of Tablets

Physical Characteristics

Compressed tablets were evaluated for weight variation, thickness, hardness, and friability according to pharmacopoeial standards.

Drug Content Uniformity

Tablet powder equivalent to 40 mg of Drotaverine hydrochloride was dissolved, suitably diluted, and analyzed spectrophotometrically at 230 nm.

In Vitro Buoyancy Studies

The floating lag time and total floating duration were determined by placing tablets in 0.1 N hydrochloric acid at 37 ± 0.5°C.

Swelling Index

Swelling behavior of tablets was studied by measuring weight gain after immersion in 0.1 N hydrochloric acid at predetermined time intervals.

In Vitro Drug Release Studies

Dissolution studies were carried out using USP type II dissolution apparatus at 50 rpm in 900 ml of 0.1 N hydrochloric acid maintained at 37 ± 0.5°C. Samples were withdrawn at regular intervals and analyzed spectrophotometrically.

Drug Release Kinetics

The dissolution data were fitted to zero-order, first-order, Higuchi, and Korsmeyer–Peppas models to determine the drug release mechanism.

Results and Discussion

Preformulation studies confirmed the purity of Drotaverine hydrochloride and the absence of any significant drug–excipient interactions. The powder blends exhibited good flow properties with acceptable values of angle of repose, Carr's index, and Hausner's ratio.All tablet formulations complied with pharmacopoeial limits for weight variation, hardness, friability, and drug content uniformity. Floating lag time was found to be less than 60 s for optimized formulations, and the tablets remained buoyant for more than 12 h.

Swelling studies indicated gradual hydration of polymer matrices, contributing to sustained drug release. In vitro dissolution studies showed that an increase in polymer concentration resulted in a slower release rate. The optimized formulation demonstrated sustained release of Drotaverine hydrochloride over a period of 12 h.

Drug release kinetics revealed that the release followed the Higuchi model, indicating diffusion-controlled drug release with non-Fickian transport behavior.

Conclusion

Gastroretentive floating tablets of Drotaverine hydrochloride were successfully developed using hydrophilic polymers. The optimized formulation exhibited satisfactory buoyancy, sustained drug release, and acceptable physicochemical characteristics. The developed gastroretentive system may improve bioavailability, reduce dosing frequency, and enhance patient compliance.

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