Ind. J. Pharm. Edu. Res., 2026; 60(4):1416-1424.
https://www.ijper.org

Original Article

Design and Development of Pulsatile Drug Delivery System of Bambuterol for Asthma Treatment

Sanjay Jayaram, Manjunath Kopparam*, Abdul Waris Khan

Department of Pharmaceutics, Sree Siddaganga College of Pharmacy, Tumkur, Karnataka, INDIA.

ABSTRACT

Aim/Background: The objective of this study was to create a pulsincap system designed to target the Gastrointestinal Tract (GIT) and administer the asthma drug bambuterol. **Materials and Methods:** *In vitro* release tests and Fourier-Transform Infrared Spectroscopy (FTIR) analysis were used to assess the physicochemical characteristics of Bambuterol Hydrochloride (BHC) granules. Based on these findings, the most promising formulation was selected for the pulsincap's continued development. An *in vitro* assessment was subsequently conducted on the final pulsincap formulation. **Results:** The FTIR spectra confirmed the absence of any interaction between the polymer and BHC. Preformulation analyses demonstrated the granules possessed good flow characteristics. The *in vitro* release analysis of BHC granules showed rapid drug release, which was dependent on the dose of super disintegrants utilized; specifically, formulation F6, which contained 20 mg of crospovidone, achieved a 95.65% release after 15 min. In the pulse formulation containing karaya gum and lactose (F6-P5), a 5-hr lag time was observed in the *in vitro* dissolution of BHC from the pulsincap. **Conclusion:** The study concluded that BHC granules can be effectively directed towards the GIT. The release of the medicine started after the 5-hr lag time, and 91.87% of the medicine had been released overall by the 9th hr.

Keywords: Bambuterol Hydrochloride (BHC), Lag time, Gastrointestinal Targeting (GIT), Asthma, Pulsatile drug delivery, Formaldehyde treatment.

Correspondence:
Dr. Manjunath Kopparam
Professor and Head, Department of Pharmaceutics, Sree Siddaganga College of Pharmacy, Tumkur, Karnataka, INDIA.
Email: manju_kop@yahoo.com

Received: 11-05-2026;
Revised: 05-06-2026;
Accepted: 27-07-2026.

INTRODUCTION

Pulsatile drug delivery systems, as a Novel Drug Delivery System (NDDS) or Chronotherapeutic Drug Delivery System (ChrDDS), have the potential to enhance their market value and competitiveness while extending their patent life. In the 21st century, the pharmaceutical industry faces significant challenges due to escalating costs associated with successful drug discovery and development, coupled with the need to maintain affordability. These systems offer a promising solution to meet the demands of emerging global trends in drug research and innovation.[1] Various techniques have been employed to delay drug release, including osmotic mechanisms, hydrophobic or hydrophilic coatings around a drug-loaded core, and the use of erodible or swellable plugs that encapsulate the drug within an insoluble capsule. A pulsatile drug release profile is defined by a lag phase, during which no drug is released, followed by a sudden and complete release of the drug. These formulations offer several advantages, including the ability to delay the start of drug release, which is beneficial for conditions like bronchial asthma[2] minimal dosage, avoidance of adverse side effects, and nearly consistent drug levels at the target site.

Pulsatile Drug Delivery Systems (PDDS) have garnered significant attention for their advantages over conventional dosage forms. These systems enhance therapeutic outcomes by ensuring the medication is delivered at the optimal time, targeted to the site of action, and in the precise dosage, ultimately improving patient adherence.[3] Asthma, a chronic inflammatory condition of the airways, is characterized by airway narrowing, structural remodelling of airway walls, excessive mucus production, and Bronchial Hyper-Reactivity (BHR). It involves a complex interplay of innate and adaptive immune system cells along with epithelial cells. In the United States, asthma imposes an economic burden of over $18 billion annually in direct medical expenses and indirect costs from lost productivity. While most patients manage the disease with a combination of inhaled corticosteroids (to reduce inflammation) and β2-adrenergic agonists (to relax bronchial smooth muscle), approximately 5-10% of individuals do not respond to corticosteroids and may require hospitalization, particularly during respiratory viral infections such as those caused by rhinoviruses.[4]

In 28 countries, the β2 adrenergic agonist terbutaline's biscarbamate ester prodrug, bambuterol, has been authorised for the management of asthma. Tablets containing 10 and 20 mg (25

DOI: 10.5530/ijper.20261636

and 50 µmol) of the hydrochloride salt are available. Lung tissue is capable of this metabolic route, and butyrylcholinesterase is the primary enzyme that hydrolyses bambuterol to terbutaline. Bambuterol is stable to presystemic elimination. It also undergoes oxidative metabolism to produce compounds that terbutaline can hydrolyse.[5] For at least half of the 14-day run-in period, patients showed a nighttime decline in Peak Expiratory Flow (PEF) of at least 20 percent. Subsequently, they were randomly assigned to receive two 14-day treatment periods consisting of a placebo and 20 mg of bambuterol nocte.[6] In individuals with allergic asthma, the effects of oral β-agonist bambuterol and inhaled corticosteroid budesonide on the nocturnal exacerbation of asthma were investigated.

A controlled onset, pulsatile, chronopharmaceutical drug delivery system was created to use an FT-IR instrument for monitoring interactions between the medication and the excipients in the formulation. To prepare a pulsatile capsule, it must be cross-linked through chemical treatment, filled with various chemicals, polymers, and excipients, and then evaluated for different physicochemical properties. Additionally, its release kinetics need to be predicted, and short-term stability studies should be conducted according to ICH guidelines.

MATERIALS AND METHODS

Materials

Bambuterol, HPMC-E15, crospovidone, ethyl cellulose, concentrated HCl, karaya gum, isopropyl alcohol, and sodium starch glycolate were obtained from Yarrow Chem (Mumbai). We purchased formaldehyde, talc, starch, and croscarmellose sodium from SD Fine Chem. Ltd., (Mumbai). Research-Lab Fine Chem Industries (Mumbai) provided the microcrystalline cellulose and guar gum, while Loba Chemie Pvt. Ltd., (Mumbai) provided the magnesium stearate.

Methods

BHC was identified via melting point analysis, solubility tests, and FTIR spectrophotometry. When creating pharmacological dosage forms, preformulation testing is a crucial first step. It entails evaluating the chemical and physical characteristics of the medication both by itself and in conjunction with excipients. Preformulation testing's primary objective is to give formulators information they may utilise to develop stable, mass-producible, and bioavailable dosage forms.

UV spectroscopy

Estimation of BHC

Estimation of BHC was carried out using various buffer such as 1.2 pH acid and 6.8 pH phosphate buffer.[7]

Preparation of 1.2 pH acid buffer

2.0 g of sodium chloride was dissolved in water and 7 mL Conc. HCl was added and made upto volume with water to make 1000 mL of buffer solution.

Determination of BHC in 1.2 pH acid buffer

Stock solution was prepared by dissolving 50 mg of drug in 50 mL of 1.2 pH acid buffer. The solution was than scanned under UV range of 200-400 nm. Maximum absorbance was found at 263 nm.

Preparation of 6.8 pH phosphate buffer

11.45 g of potassium dihydrogen orthophosphate and 28.20 g of sodium dihydrogen orthophosphate were dissolved in water and then adjusted to 6.8 pH with NaOH and made up to 1000 mL with water.

Determination of BHC in 6.8 pH phosphate buffer

To prepare the stock solution dissolve 50 mg of drug in 50 mL of 6.8pH phosphate buffer in volumetric flask with vigorous shaking. The solution was than scanned under UV range of 200-400 nm.

Calibration curve of BHC

Aliquots of 100, 150, 200, 250, 300 and 350 µg/mL were prepared their absorbance was measured at 263 nm using UV spectrophotometric against blank of 1.2 pH acid buffer and pH 6.8 phosphate buffer.

Fourier-Transformation Infrared (FTIR) spectroscopy

Drug polymers and polymer-polymer interactions were investigated. Regarding the KBr disc, dry KBr was combined with 2% (w/w) of the sample. An agate mortar was used to grind the combination into a fine powder, and a hydraulic press was used to compress it into a KBr disc at 1000 pressure. Apodization was used to scan each KBr disc sixteen times at a speed of 2 mm/sec and a resolution of 4 cm^{-1}.

Formulation design

Preparation of crossed-linked gelatin capsule using formaldehyde

About fifty size "1" firm gelatin capsules were taken. After being taken off the cap,[8-11] their body was put on a wire mesh. A beaker containing 25 mL of a 15% v/v formaldehyde solution was placed inside an empty glass desiccator. Potassium permanganate (0.5 mg) was added to this. A wire mesh holding the capsule's body was placed on top of the beaker, and the desiccator was promptly sealed and snugly closed. For 12 hr, the capsule's body was exposed to formaldehyde fumes. To complete the reaction between gelatin and formaldehyde vapors, the capsules were removed and placed on filter paper before being dried in an oven at 35°C for 60 min. They were then left in an open area to allow

any residual formaldehyde to evaporate. The capsule bodies were sealed with untreated caps and stored in a polyethylene bag for further use.

Evaluation of treated capsules

Different evaluation tests were performed for the formaldehyde treated capsules.

Identification attributes

The size "1" capsules that were selected had a translucent coloured body and cap and were opaque. They were of the locking variety, odourless, and pliable to the touch of a moist hand. Other than their stickiness, the capsules did not significantly change after being treated with formaldehyde. Even when handled with a damp hand, the capsule's body remained firm and non-stick.

Visual defects

Out of the fifty capsule bodies that underwent formaldehyde treatment, three to five were observed to have completely lost their moisture, causing them to shrink or take on unusual shapes.

Solubility test for treated capsules

Using a magnetic stirrer, empty capsule was aggressively agitated in 100 mL of dissolving medium in a 250-mL beaker. Water, 1.2 pH, and 6.8 pH phosphate buffer served as the dissolving medium. It was recorded when the capsule dissolved or turned into a mushy lump.

Dimensions

The size differences between the capsule's treated with formaldehyde and those that were not treated was examined, using a calliper, the capsule's diameter and length were measured both before and after the treatment.

Chemical test: Qualitative test

To prepare the sample, 25 treated residues were broken into small pieces and placed in a beaker containing 40 mL of distilled water. A standard formaldehyde solution with a concentration of 20 µg/mL was prepared by diluting an appropriate amount of formaldehyde solution with water. The sample was stirred with a magnetic stirrer for 1 hr to dissolve any free formaldehyde. After stirring, the solution was filtered into a 50 mL volumetric flask, rinsed with distilled water, and diluted to a final volume of 50 mL.

Procedure

To prepare the test solution, 4 mL of water and 5 mL of acetylacetone solution were added to 1 mL of the sample solution in a test tube, which was then placed in a water bath at 40°C for 40 min. Simultaneously, a reference solution was prepared using 1 mL of the standard formaldehyde solution following the same procedure. If the colour of the sample solution matches that of the reference solution, it indicates that each of the 25 capsule bodies contains less than 20 µg/mL of free formaldehyde.

Preparation of BHC Granules

Powders and starch were mixed as part of the wet granulation process. The granulating agent was isopropyl alcohol. The resultant granules were then dried for an hour at 50°C after the wet material was run through a #12 mesh screen. Table 1 discusses how BHC granules are made.

Characterization of BHC granules

The flow properties of the produced granules that were assessed included the following: dissolving profile, compressibility index, Hausner's ratio, bulk density, tapped density, angle of repose, and drug content. Using a UV spectrophotometric technique, absorbance measurements were made at 263 nm to determine the drug content.

Bulk density (Db)

Bulk density is defined as the mass of a powder divided by its bulk volume. It is affected by factors such as particle cohesion, shape, and size distribution. To determine bulk density, a measured quantity of powder is poured through a large funnel into a graduated cylinder, and the initial bulk volume is noted. The Bulk density (Db) is then calculated using the formula: Db=M/Vo is then used to get the Bulk density, where Db is the bulk density (g/cc), M is the powder's mass (g), and Vo is the bulk volume (cc).

Tapped Density (Dt)

A total of 10 g of powder was added to a cleaned and dried 100 mL measuring cylinder. After tapping the cylinder from a predetermined height 100 times, the tapped volume was recorded. The tapped Density (Dt) was calculated using the formula Dt = M/Vt, where M represents the mass of the powder in grams and Vt is the tapped volume in Cubic Centimeters (cc). Tapped density is expressed in grams per cubic centimeter (gm/cc).

Compressibility index

The Carr's compressibility index was used to calculate the powder's compressibility. It is calculated as:

$$[(TBD-LBD)\times 100] / TBD$$

Where LBD stands for loose bulk density and TPD for taped bulk density.

Angle of repose (θ)

Once the funnel was filled, the test sample was allowed to flow freely through the opening under the influence of gravity. The area of the resulting pile, which provided insights into the granules' flowability, was measured based on the cone-shaped pattern formed on a graph sheet. Additionally, the height of the

Table 1: Formulation of BHC granules.

Ingredient (mg)	F1	F2	F3	F4	F5	F6
Bambuterol	40	40	40	40	40	40
CCS	15	30	-	-	-	-
SSG	-	-	15	30	-	-
CP	-	-	-	-	15	30
Talc	5	5	5	5	5	5
Starch	5	5	5	5	5	5
Magnesium stearate	5	5	5	5	5	5
MCC	80	65	80	65	80	65
Total weight	150	150	150	150	150	150

Table 2: *In vitro* drug release conditions for BHC pulsin cap

Apparatus	USP type II Dissolution apparatus
Dissolution medium	HCl 1.2 pH and 6.8 pH buffer
Temp	37±0.5°C
RPM	75
Volume taken and replaced (mL)	5
λ_{max} (nm)	263
Blank solution	HCl 1.2 pH and Phosphate buffer of 6.8 pH
Time of study (hr)	12
Volume of medium (mL)	900

pile was recorded. The angle of repose (θ) was calculated using the formula $\theta = \tan^{-1}(h/r)$, where r represents the radius of the pile's base and h is the height of the pile.

The Hausner ratio

It assesses the friction between particles. The flow characteristics are evaluated using the compressibility index.

Hausner ratio= bulk density/tapped density

In vitro drug release study

Procedure

In vitro drug release studies were conducted using a USP type II dissolving equipment (Electro Lab, Mumbai, India). For the first 2 hr, the dissolution medium was an acid buffer with a pH of 1.2, and for the next ten, it was a phosphate buffer with a pH of 6.8. The tests were run at 37±0.5°C and 75 rpm. At regular intervals, 5 mL samples were collected and replaced with freshly prepared buffer. These samples were filtered using Whatman filter paper and diluted as needed, and the drug release was measured using a UV spectrophotometer set to 263 nm. Three duplicates of the study were conducted. Table 2 discusses the BHC pulsin cap's *in vitro* drug release conditions.

Formulations of hydrogel plug

Using a rotary tablet press and 6 mm punches and dies, equal volumes of different polymers were compressed to create the hydrogel plug. Table 3 discusses the pulsating cap formulation.

Evaluation of hydrogel plug

Hardness

The hardness of the hydrogel plug was measured using a Monsanto Hardness Tester and expressed in kilograms per centimetre. The mean and standard deviation were calculated based on three randomly selected tablets from each formulation.

Thickness and diameter

For consumer approval and to guarantee tablet consistency, it is essential to regulate the physical parameters of tablets, such as their thickness and diameter. Vernier callipers were used to measure the tablet's diameter and thickness, and the results were reported in millimetres.

Formulation of pulsin cap

The bodies and caps of size "1" firm gelatin capsules that had been treated with formaldehyde were physically separated prior to their use in the formulation. Carefully measured 40 mg BHC granules were manually placed into the treated capsule bodies. Subsequently, various polymers were added to the capsules containing BHC granules in differing amounts, including hydroxyl propyl methyl cellulose E-15, ethyl cellulose, xanthan gum, Karaya gum, and guar gum. The connection between the capsule body and cap was sealed using a small amount of a 5% ethyl cellulose ethanolic solution.

Evaluation of pulsin cap

Weight variation

The weights of the individual capsules were compared to the average weight after randomly selecting and weighing 20 capsules from each batch. None of the individual weights deviated from the average by more than the percentage indicated in the table,

and no weight differed from the average by more than double that percentage.

The percentage variation is calculated by dividing the individual weight by the average weight multiplied by 100.

Drug content

The granules were added separately to a 50 mL volumetric flask after being precisely weighed to equal 40 mg of BHC. 50 cc of methanol solution was added. A 100 mL volumetric flask containing pH 6.8 phosphate buffer is then filled with 10 mL of the previously mentioned solution after it has been diluted. The same buffer solution is then used to increase the volume to 100 mL, and a membrane filter is used to filter the combination. UV spectrophotometry was used to measure the filtrate at 263 nm after 5 mL of it had been diluted to 50 mL using the same buffer solution.

In vitro drug release profile

The *in vitro* dissolution profile of each formulation was determined using a paddle-style USP type II device over a 2-hr period in various media, including simulated gastric fluid with a pH of 1.2 and simulated gastrointestinal fluid with a pH of 6.8 during the subsequent hours (as the stomach typically empties in 2 hr). The paddle was rotated at 75 rpm to maintain the dissolution media at a temperature of 37±5ºC. BHC pulsin pills were placed in each dissolution vessel. At appropriate intervals, 5 mL of samples were withdrawn from the dissolution media, and an equal volume of fresh buffer was added. The absorbance of the samples was measured at 263 nm.

Kinetic release of *in vitro* Release Rates of BHC Pulsin cap

The *in vitro* release profile results for formulation F6-P5 were plotted using various data treatment methods as follows:

Table 3: Formulation of the pulsing cap.

Composition of hydrogel plug (mg)	Different polymers and in combination with lactose				
	F6-P1	F6-P2	F6-P3	F6-P4	F6-P5
HPMC E-15	100	100	-	-	-
Ethyl Cellulose	-	-	-	-	-
Xanthan Gum	-	-	50	-	-
Guar Gum	-	-	-	50	-
Karaya Gum	-	-	-	-	50
Lactose	-	-	50	50	50
Total	100	100	100	100	100

* 150 mg of BHC granules (containing 40 mg of the drug) were placed inside the capsule body, with a 100 mg polymer plug placed on top.

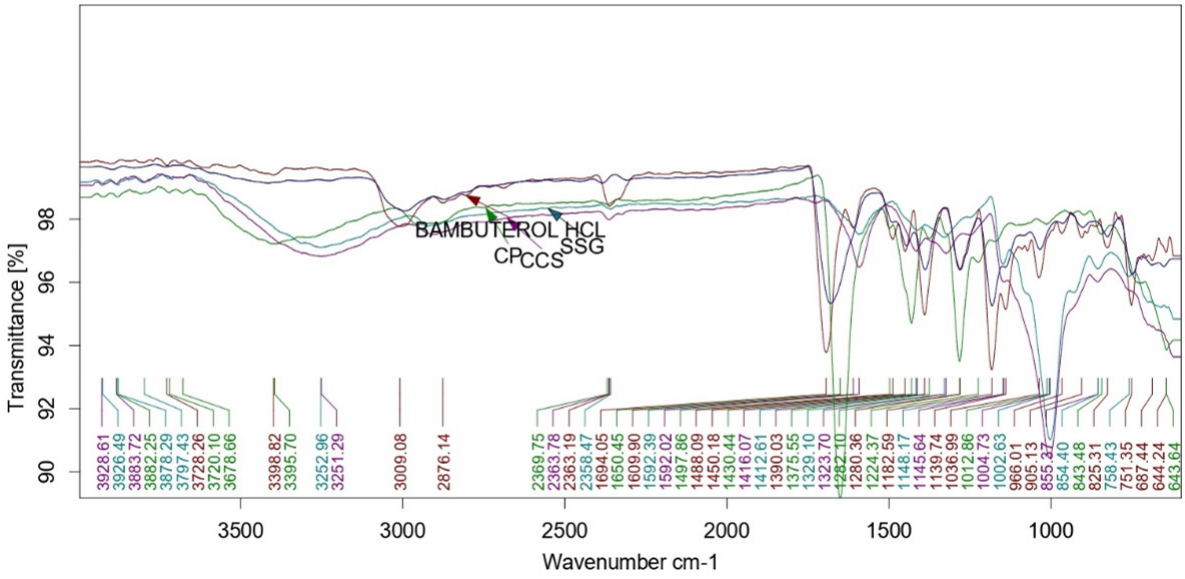

Figure 1: FTIR spectra of drug and excipients.

1. A plot of the cumulative percentage of drug released against time (T) is known as the zero order kinetic model.
2. The first order kinetic model is a plot of time (T) against the logarithm of the cumulative percentage of medication left.
3. A plot of the cumulative percentage of drugs released against the square root of time (T) is known as Higuchi's Model.
4. The fourth model is the Korsmeyer/Peppas Model, which plots the logarithm of time (T) against the cumulative percentage of medication released.

RESULTS AND DISCUSSION

Drug polymer interaction (FTIR) study

The existence of all typical BHC peaks in the combination spectrum, which were identified from the spectra of BHC, BHC in combination with polymer, BHC granules, and pure drug, demonstrated the drug and polymer's compatibility. Infrared spectra are shown in Figures 1-4. There were no variations between the BHC's FTIR patterns, the physical mixing of BHC and polymer, and the blank polymers. Drugs and excipients are represented spectrally in Figure 1.

Solubility study

BHC was freely soluble in water and methanol.

Micromeritic properties

Flow property study

The formulated blends were assessed for their flow properties, and the results are given in the below Table 4.

Carr's index and Hausner's ratio, which assess compressibility, were found to range from 14.09% to 19.51% and from 1.14 to 1.25, respectively. The angle of repose was determined using a funnel, with the angle measured between 25.19 and 28.21°. The bulk density and tapped density were measured using a measuring cylinder, revealing powder volumes between 0.281 and 0.335 g/cc for bulk density and between 0.423 and 0.344 g/cc for tapped density.

Evaluation of formaldehyde treated capsules

Prior to and following formaldehyde treatment, the average capsule body length was determined to be 16.39 mm and 15.35 mm, respectively. Similarly, the average capsule body width was discovered to be 6.45 mm and 6.04 mm for each period. The length and width of the capsule bodies significantly decreased after being treated with formaldehyde.

Solubility studies for treated capsules

During solubility tests conducted over a full day, the body and cap of the conventional capsules dissolved in about 15 min. On the other hand, the body of the formaldehyde-treated capsules remained intact for almost 24 hr, whereas just the cap dissolved in 15 min.

Qualitative test for free formaldehyde

The level of free formaldehyde in the formaldehyde capsules was determined through testing. Notably, the sample solution had the same colour intensity as the standard solution, indicating that each of the 25 capsule bodies contained less than 20 µg of free formaldehyde.

Drug content

Drug content estimation was carried out using specified 6.8 pH buffer and water and the % drug content of all the formulations

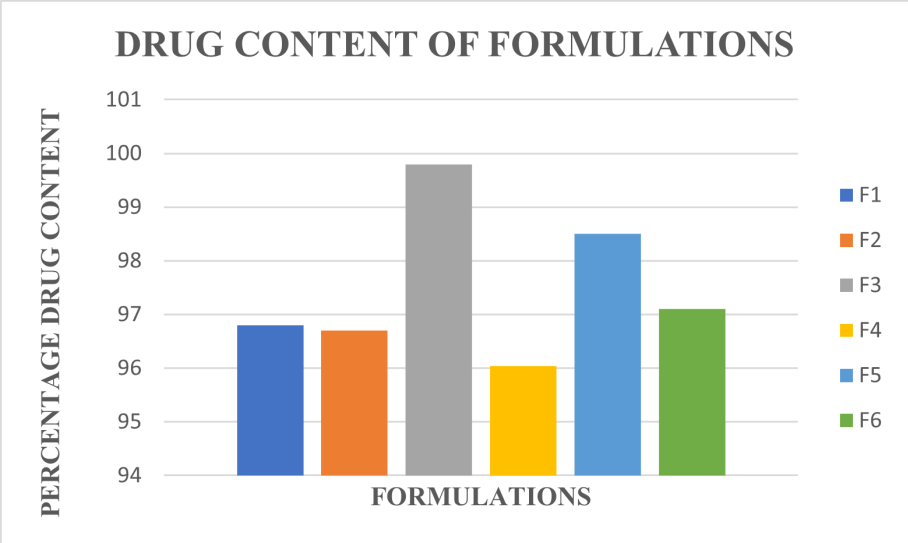

Figure 2: Graph of the percentage drug content in each formulation.

ranges from 96.04 -99.80% were formulation F3 shows the highest % of drug release that is 99.80%. Graph of the percentage drug content in each formulation is shown in Figure 2.

In vitro dissolution profile of BHC granules

In vitro release of BHC granules in Formulation F1 and F2 has shown a drug release of 97.93% in 45 min and 96.15% in 30 min which was having 15 and 30 mg of cross carmellose sodium as super disintegrant. Where F3 and F4 has shown 84.37% in 30 min and 93.37% release at 45 min which was having 15 and 30 mg of sodium starch glycolate as super disintegrant. F5 and F6 has shown 97.75% in 30 min and 95.65% at 15 min respectively containing 15 and 30 mg of crospovidone as super disintegrant. Dissolution profile of BHC granules with change in super disintegrant is shown in Figure 3.

Evaluation parameters for hydrogel plug

Thickness, diameter and hardness

The thickness of the hydrogel plug, measured using a vernier calliper, ranged from 2.75 to 4.4 mm. The diameter of the plug was between 6.00 and 6.06 mm. The hardness, determined using a Monsanto hardness tester, was found to be in the range of 4.80 to 5.00 Kg/cm^2. Data of Thickness, diameter and hardness of hydrogel plug is discussed in Table 5.

In vitro drug release data of BHC Pulsin Cap

Formulation F6-P1 was filled in treated capsule with the plug containing 100 mg of HPMC E-15 were it shows only 2 hr of lag time with maximum drug release of 97.07% at 6th hr, formulation F6-P2 was filled in the treated capsules with the plug containing 100 mg ethyl cellulose which shows 2 hr of lag time with maximum drug release of 98.85% at 8th hr, formulation F6-P3 was filled in the treated capsules with the plug containing xanthan gum 50 mg and in combination with lactose 50 mg which shows 2 hr of lag time with maximum drug release of 99.01% at 5th hr, formulation F6-P4 was filled in the treated capsules with the plug containing guar gum 50 mg and in combination with lactose 50 mg which shows 3 hr of lag time with maximum drug release of 56.79% at 12th hr and formulation F6-P5 was filled in the treated capsules with the plug containing karaya gum 50 mg and in combination

Table 4: Data for flow property study of BHC granules.

Formulations	*Angle of repose (ep	Hausner's ratio	Carr's index (%)	Tapped density (g/cc)	Bulk density (g/cc)
F1	26.12±1.12	1.14	17.65	0.415	0.335
F2	26.18±1.12	1.17	14.09	0.372	0.321
F3	25.19±1.11	1.18	17.79	0.344	0.281
F4	28.15±1.46	1.21	18.84	0.378	0.331
F5	27.19±1.15	1.19	17.54	0.423	0.313
F6	28.21±1.83	1.25	19.51	0.412	0.318

*Mean±Standard Deviation (*n*=3).

Table 5: Data of Thickness, diameter and hardness of hydrogel plug, Mean±SD (*n*=3).

Formulation	Thickness in mm	Diameter in mm	Hardness (Kg/cm2)
F6-P1	3.00±0.14	6.06±0.04	5.00±0.17
F6-P2	2.75±0.21	6.00±0.112	4.80±0.14
F6-P3	2.95±0.14	6.05±0.13	4.90±0.19
F6-P4	3.00±0.06	6.00±0.121	4.80±0.17
F6-P5	4.4±0.01	6.01±0.15	4.90±0.16

Table 6: Regression co-efficient (r^2) values and diffusion exponent (*n*) of Peppas model.

Formulations	First order	Zero order	Higuchi Matrix	Peppas model	
				r^2 value	'n' value
F6-P1	0.9979	0.8189	0.8556	0.8891	2.0103
F6-P2	0.7938	0.6980	0.6443	0.8966	2.1579
F6-P3	0.7590	0.7902	0.7597	0.7280	2.2197
F6-P4	0.9865	0.9929	0.9877	0.9695	1.8511
F6-P5	0.7039	0.8272	0.8093	0.7906	2.1539

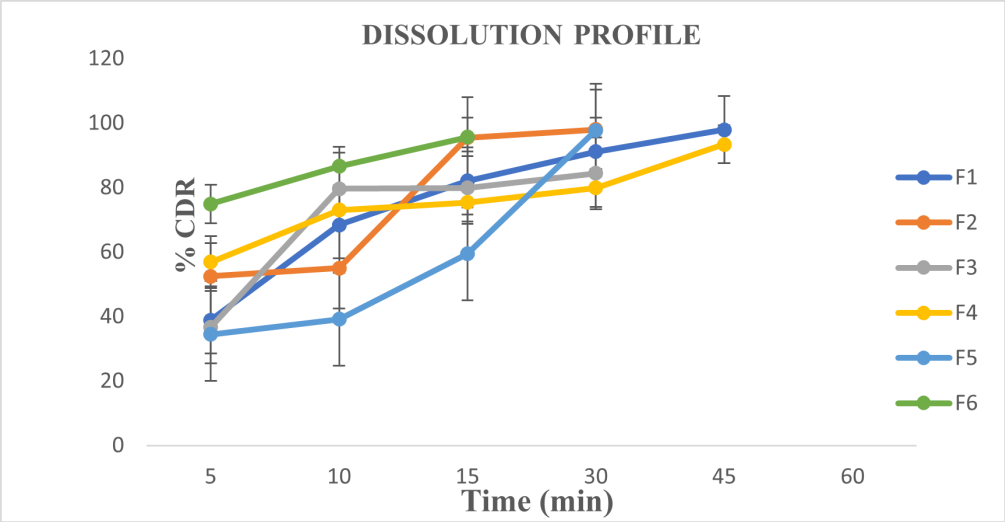

Figure 3: Dissolution profile of BHC granules with change in super disintegrant.

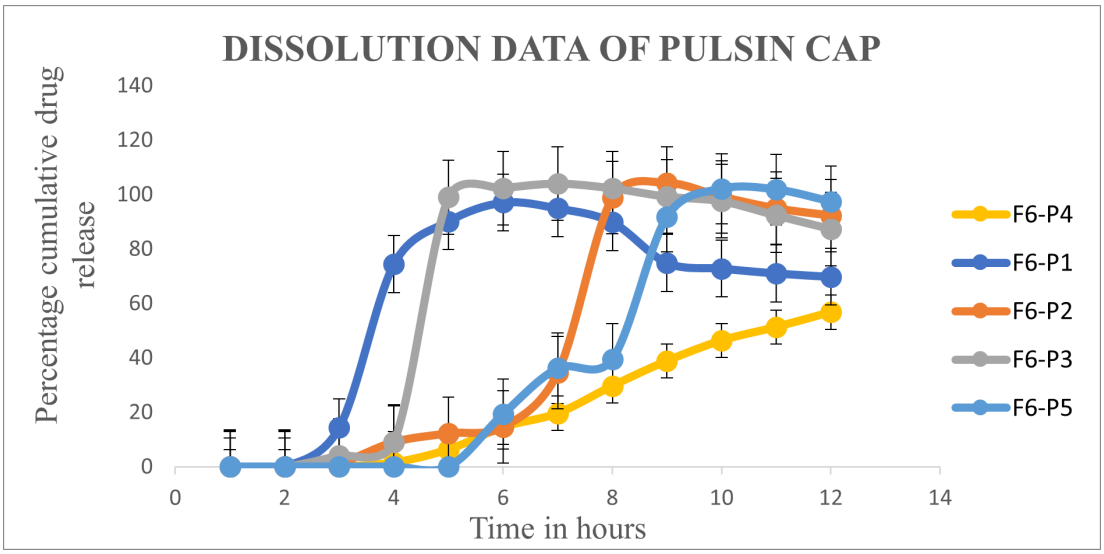

Figure 4: Dissolution profile of BHC pulsin cap.

with lactose 50 mg which shows 5 hr of lag time with maximum drug release of 91.87% at 9th hr hence this formulation F6-P5 was best suited for the conduct of release kinetics studies. Dissolution profile of BHC pulsin cap is shown in Figure 4.

Release kinetics of BHC modified pulsin cap formulations (F6-P5)

Table 6 presents the regression coefficients of determination (r^2) and slopes. The cumulative percentage of drug release data from the BHC pulsin cap was analyzed using Higuchi's square root of time, zero-order, first-order, and Korsmeyer-Peppas equations to better understand the drug release process. The coefficients of determination indicated that F6-P1 exhibited first-order kinetics, F6-P2 followed Peppas release kinetics, while F6-P3, F6-P4, and F6-P5 demonstrated zero-order kinetics. The release mechanism for formulations F6-P1 through F6-P5 was governed by the Super Case II transport mechanism, as suggested by the values of n obtained from the Korsmeyer-Peppas plot, which ranged from 1.851 to 2.219.

CONCLUSION

To enhance asthma treatment, a pulsatile drug delivery system incorporating BHC granules was developed and evaluated in this study. Delivering BHC via the Gastrointestinal (GI) tract may effectively prevent asthma symptoms while minimizing unwanted systemic side effects, potentially reducing the overall dosage required. Within 15 min, the F6 formulation, which includes 30 mg of crospovidone as a super disintegrant, reaches a 95.65% release rate. Consequently, a desired lag period of 5 hr has been attained by the F6-P5 formulation. F6 formulated granules are enclosed in a cross-linked gelatin capsule with a hydrogel plug that contains 50 mg of lactose and 50 mg of karaya gum. The formulations F6-P4, F6-P1, F6-P2, and F6-P3 have all shown a 2-hr lag time.

ACKNOWLEDGEMENT

I would like to thank the management of Sree Siddaganga College of Pharmacy for facilitating my study and extending their full technical support and co-operation.

ABBREVIATIONS

NDDS: Novel Drug Delivery System; **ChrDDS:** Chronotherapeutic Drug Delivery System; **PDDS:** Pulsatile Drug Delivery Systems; **BHR:** Bronchial Hyper-Reactivity; **PEF:** Peak Expiratory Flow; **FT-IR:** Fourier-Transform Infrared; **ICH:** International Council for Harmonisation; **BHC:** Bambuterol Hydrochloride; **HPMC:** Hydroxypropyl Methylcellulose; **Conc. HCl:** Concentrated Hydrochloric Acid; **FTIR:** Fourier-Transformation Infrared; **KBr:** Potassium Bromide; **UV:** Ultraviolet; **NaOH:** Sodium Hydroxide; **USP:** United States Pharmacopeia; **Db:** Bulk Density; **Dt:** Tapped Density; **LBD:** Loose Bulk Density; **TBD:** Tapped Bulk Density; **TPD:** Tapped Density; **rpm:** Revolutions Per Minute; **hr:** Hour; **min:** Minute; **mg:** Milligram; **mL:** Millilitre; **µg:** Microgram; **°C:** Degree Celsius; **cm^2:** Square Centimetre; **g/cc:** Gram per Cubic Centimetre; **r^2:** Regression Coefficient of Determination.

CONFLICT OF INTEREST

The authors declare there is no conflict of interest.

AUTHOR'S CONTRIBUTIONS

Sanjay J: Conceptualization, Methodology, Data curation, Writing-Original draft preparation. Manjunath K: Conceptualization, validation, formal analysis, investigation, Reviewing and Editing, Abdul Waris Khan: Conceptualization, validation, formal analysis, visualization and supervision, project administration.

SUMMARY

- The research focuses on developing a pulsincap formulation to target the Gastrointestinal Tract (GIT) for delivering bambuterol, a drug used to treat asthma.
- FTIR spectra analysis confirmed no interaction between the polymer and Bambuterol Hydrochloride (BHC), while preformulation studies indicated good flow properties of the granules.
- *In vitro* drug release study demonstrated a quick release of BHC, with formulation F6 showing a 95.65% release within 15 min due to the concentration of super disintegrants.
- The modified pulsincap formulation exhibited a 5-hr lag time before releasing BHC, with 91.87% of the drug released by the 9th hr, indicating effective targeting to the GIT.

Gastro-Retentive Drug Delivery Systems (GRDDSs) offer an innovative approach to drug delivery by retaining dosage forms in the stomach, enabling controlled release of drugs with an absorption window, such as BHC in Pulsatile Drug Delivery Systems (PDDS) for asthma. These systems are particularly suited for drugs absorbed in the upper GIT or those prone to degradation in alkaline pH. This study utilized super disintegrants (crospovidone, croscarmellose sodium, sodium starch glycolate) and polymers (ethyl cellulose, HPMC E15, xanthan gum, guar gum, karaya gum) to achieve a 5-hr lag time. FTIR preformulation studies confirmed the compatibility of BHC with the polymers. Gelatin capsules were crosslinked with formaldehyde, filled with BHC granules prepared using isopropyl alcohol and super disintegrants, and sealed with hydrogel plugs for targeted drug release. Dissolution studies showed no release of BHC in acidic pH (1.2) for 2 hr, followed by controlled release in intestinal pH (6.8) over 10 hr. Increasing super disintegrant concentrations enhanced drug release rates, with the order of effectiveness being crospovidone > croscarmellose sodium > sodium starch glycolate. The combination of karaya gum and lactose in the hydrogel plugs successfully extended the lag time, with the F6-P5 formulation demonstrating optimal results, achieving a 5-hr lag time and rapid drug release thereafter.

REFERENCES

1. Chandani G, Ganesh B, Preeti K. THE PHARMA INNOVATION A Comprehensive Review of Pulsatile Drug Delivery System. 2012;1(7).
2. Sharma S, Pawar A. Low density multiparticulate system for pulsatile release of meloxicam. Int J Pharm. 2006;313(1-2):150-8.
3. Jain D, Raturi R, Jain V, Bansal P, Singh R. Recent technologies in pulsatile drug delivery systems. Biomatter. 2011;1(1):57-65.
4. Lambrecht BN, Hammad H. The immunology of asthma. Nat Immunol. 2015;16(1):45-56.
5. Sitar DS. of Bambuterol. 1996;31(4):246-56.
6. Petrie GR, Chookang JY, Hassan WU, Morrison JF, O'Reilly JF, Pearson SB, *et al.* Bambuterol: Effective in nocturnal asthma. Respir Med. 1993;87(8):581-5.
7. Mallikarjuna Gouda M, Ramakrishna Shabaraya A, Shantakumar SM, Somashekar Shyale S, Kumar PR. Development and validation of selective uv spectrophotometric analytical method for budesonide pure sample. J Appl Pharm Sci. 2011;1(7):158-61.
8. Experiments RM and P optimization using designed, 2002 undefined. Response Surface Methodology (RSM). cir.nii.ac.jp [Internet]. [cited 2024 Jul 25]; Available from : https://cir.nii.ac.jp/crid/1571698601098166912
9. Mastiholimath V, Dandagi P, … SJI journal of, 2007 undefined. Time and pH dependent colon specific, pulsatile delivery of theophylline for nocturnal asthma. ElsevierVS Mastiholimath, PM Dandagi, SS Jain, AP Gadad, AR KulkarniInternational journal of pharmaceutics, 2007•Elsevier [Internet]. [cited 2024 Jul 25]; Available from: https://www.sciencedirect.com/science/article/pii/S0378517306006375
10. Abraham S, pharmaceutical MSI journal of, 2007 undefined. Development of Modified Pulsincap Drug Delivery System of Metronidazole for Drug Targeting. search.ebscohost.comS Abraham, MS SrinathIndian journal of pharmaceutical sciences, 2007•search.ebscohost.com [Internet]. [cited 2024 Jul 25]; Available from: https://search.ebscohost.com/login.aspx?direct=true&profile=ehost&scope=site&authtype=crawler&jrnl=0250474X&AN=25056620&h=Q3oNazFPS9HY6LINbAmn0%2B5xr22VYxo2spKBi243BfSmp52WMkspvuOH8ZfADaTvezLY5lvz6%2BbhUbPyRfBylw%3D%3D&crl=c
11. Ishrath A, Devadas V, Res MAPT, 2019 undefined. Formulation, Development and characterization of Diltiazem Pulsin Cap for pulsatile dru delivery. ajptr.comA Ishrath, V Devadas, MM AhmedPharm Tech Res, 2019•ajptr.com [Internet]. [cited 2024 Jul 25]; Available from: http://ajptr.com/assets/upload/publish_article/AJPTR_95009.pdf

Cite this article: Jayaram S, Kopparam M, Khan AW. Design and Development of Pulsatile Drug Delivery System of Bambuterol for Asthma Treatment. Indian J of Pharmaceutical Education and Research. 2026;60(4):1416-24.