"Formulation and Evaluation of Gastro Resistant Extended Release Formulation for Colon Targeted Drug Delivery System"

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Abstract

*Budesonide is a locally-acting glucocorticosteroid with an extensive, primarily hepatic, metabolism after oral administration. Budesonide, a pH- and time-dependent oral formulation of Budesonide, was developed to optimise drug delivery to the ileum and throughout the colon. The objective of the proposed research work has been designed to targeted at the particular action site to overcome the topical actions like inflammatory bowel disease like Crohn's disease, ulcerative colitis and to improved the dissolution rate and enhance the bioavailability. Budesonide capsule was prepared by varying the concentration of plasticizer like ethyl cellulose and evaluated for physico-chemical evaluation parameter such as Description, Identification, %LOD, Assay and In-vitro dissolution studies. The market formulation was formulated and evaluated and was used for comparison. The six formulations, P*1 to P*6 were formulated and among these formulations, P*6 was optimized. The results of all formulation for Description, Identification, %LOD, Assay and In-vitro dissolution were found to be within the standard pharmacopeia limit. Overall, the formulation P*6 containing 21 gm of Aquacoat ECD (Ethyl Cellulose) was found to be promising and it's in vitro dissolution time was found to be 3.8% drug release in 0.1 N HCL, 90.2% drug release in 16 hours in pH 7.5 phosphate buffer and in Cumulative drug released by addition of 0.1N HCL drug released was found to be 94% in 18 hours, % LOD was found to be 1.03% and amount of assay was found to be 101.5% when compared to marketed formulation which show vitro dissolution time of 3.6% drug release in 0.1 N HCL, 90.5% drug release in 16 hours in pH 7.5 phosphate buffer and in Cumulative drug released by addition of 0.1N HCL drug released was found to be 94.16% in 18 hours, % LOD was found to be 1.5% and amount of assay was found to be 102.1% respectively for above parameter. Thus from above result optimized formulation P*6 show better result as compared with marketed formulation. The stability study was also conducted the best formulation, P*6 and it indicates that there was no significant change in any parameters. Hence the formulation P*6 was considered to be highly stable.*

Keywords: Colon targeted, Crohn's disease, % LOD, In-vitro dissolution studies, Stability studies.

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Introduction

The oral route is considered to be most convenient for administration of drugs to patients. Oral administration of conventional dosage forms normally dissolves in the stomach fluid or intestinal fluid and absorb from these regions of the GIT depends upon the physicochemical properties of the drug. It is a serious drawback in conditions where localized delivery of the drugs in the colon is required or in conditions where a drug needs to be protected from the hostile environment of upper GIT. Dosage forms that deliver drugs into the colon rather than upper GIT prefers number of advantages. A traditional oral extended release formulation releases most of the drug at the colon, thus the drug should have absorption window either in the colon or throughout the gastrointestinal tract. Budesonide is a locally-acting glucocorticosteroid with an extensive, primarily hepatic, metabolism after oral administration. It is rapidly absorbed and biotransformed by cytochrome P450 (CYP) 3A to metabolites with negligible glucocorticoid activity. The aim of present study was to formulate extended released capsules of Budesonide for colon targeted drug delivery by using ethyl cellulose. This drug delivery system has been designed to targeted at the particular action site to overcome the topical actions like inflammatory bowel disease like Crohn's disease, ulcerative colitis. To enhance the patient compliance, onset of action, bioavailability, bioassay and bioequivalence of drug. To enhance the amount of assay, In-vitro dissolution rate by using plasticizer ethyl cellulose. To Formulate Extended Release Formulation of Glucosteroids for the treatment of Primary Condition of Crohn's Disease. Optimize the concentration of extended release polymers as well as enteric coating polymer. Should start to release drug at the lower part of the small intestine. Provides drug release about 12 hr including loading dose in 1st part of the large intestine. Should not release the drug in stomach or upper part of the small intestine. Able to reduce in the dose and dosing frequency of the drug.

Materials and Methods

Budesonide was procured by Aarti Industries Ltd (Ahamedabad, India), Sugar pellets (Sugar spheres) was gifted by ocean Pharmacoat Pvt (Ahamedabad, India), Aquacoat ECD-30 was gifted by Signet Chemical Corporation (Ahamedabad, India), Acetyl Tributyl Citrate (Methacrylic Acid Co-Polymer Type A) was gifted by Subhash Chemical Pvt Industries Ltd (India), Instacoat EN-II Type A was gifted by Ideal Curve Pvt Ltd. (India), Tween -80 and Isopropyl Alcohol (IPA) was gifted by cadila Pharmaceutical(In-house Ahamedabad, India).

Preformulation Study(1-2):

It is the first step in rational development of dosage forms of drug substance. Preformulation testing is defined as investigation of physical and chemical properties of a drug substance alone and when combined with Excipients. The overall objective of preformulation testing is to generate information useful to the formulator in developing stable and bioavalaible dosage forms that can be mass-produced. Following preformulation study check on Budesonide extended release capsule.

Organoleptic Properties

This includes recording of color, odor and taste of the new drug using descriptive terminology. Record of color of early batches is very useful in establishing appropriate specifications for later production. Drugs generally have a characteristic odors and tastes. Unpleasant ones are masked later during formulation.

Solubility Study

Solid drugs administered orally can be administered for systemic activity and must dissolve in gastrointestinal fluids prior to their absorption. Hence rate of dissolution of drugs can influence rate and extent of their absorption. Solubility study was performed at 37^{O}C.The Details are given below.

Angle of Repose

The angle of repose of powder blend was determined by the funnel method. The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$\tan \theta = h/r$

Where, h and r are the height and radius of the powder cone.

Bulk Density

Both loose bulk density (LBD) and tapped bulk density (TBD) was determined. A quantity of 2 gm of powder blend from each formula, previously shaken to break any agglomerates formed, was introduced in to 10 ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. LBD and TDB were calculated using the+ following equations.

LBD= Weight of the powder blend/Untapped Volume of the packing
TBD=Weight of the powder blend/Tapped Volume of the packing

Compressibility Index

The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it packed down. The formula for Carr's Index is as below:

Carr's Index (%) = [(TBD-LBD) x100]/TBD

Hausner's Ratio

It is calculated from bulk density and tap density.
Hausner's ratio = Tapped density / Bulk density.

Values less then 1.25 indicate good flow (20% Carr index.) and the value greater then 1.25 indicates poor flow (33% Carr index.). If it is between 1.25-1.5 added glidant normally to improve flows.

Tapped Density (TD)

Weigh accurately 25 g of drug, which was previously passed through 20 # sieve and transfer in 100 ml graduated cylinder. Then mechanically tap the cylinder containing the sample by raising the cylinder and allowing it to drop under its own weight using mechanically tapped density tester that provides a fixed drop of 14± 2 mm at a nominal rate of 300 drops per minute. Tap the cylinder for 500 times initially and measure the tapped volume (V1) to the nearest graduated units, repeat the tapping an additional 750 times and measure the tapped volume (V2) to the nearest graduated units. If the difference between the two volumes is less than 2% then final the volume (V2).Calculate the tapped density in gm/ml by the following formula:

Tapped Density = Weight of powder / Tapped volume

Total Porosity

Total porosity was determined by measuring the volume occupied by a selected weight of a powder (V_{bulk}) and the true volume of the powder blend (The space occupied by the powder exclusive of spaces greater than the intermolecular spaces, V)

Porosity (%) $= V_{bulk}-V/V_{bulk} \times 100$

Diffrential Scanning Colorimetry (DSC)[3]:

The possibility of any interaction between Budesonide, polymers and other excipients was assessed by DSC studies.The thermogram of the samples were obtained at a scanning rate of 10ºC min^{-1} conducted over a range of 0-300ºC under an inert atmosphere flused with nitrogen at a rate of 20 mL min^{-1}.

Identification of Drugs FTIR[4]

The IR spectrum of drugs were recorded in the wave number region of 400-4000 cm^{-1} on a Shimadzu® FTIR spectrophotometer and presented in figure 7.3. The pellets were made with mixing 1gm of drug and 100gm of dried potassium bromide powder. Mixer was then compressed under 10-ton pressure in a hydraulic press to form a transparent pellet. The thin pallet was put on pellet disc to get IR Spectra at the resolution of 2 cm^{-1}. The interpretation of their spectrum bands is given in table 16.

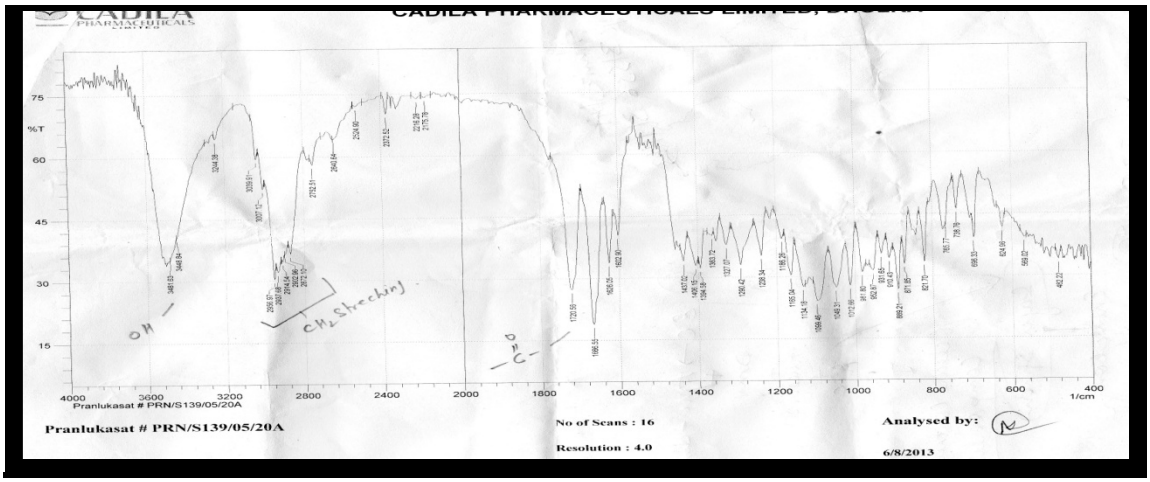


Fig. 1 FTIR spectra of Budesonide

Inference

The procured sample of drug was characterized by FTIR. All the observed data were matched with the reported data. Hence it was inferred that the procured drugs sample were of pure drugs and hence used for further studies.

Identification of Drugs by NMR

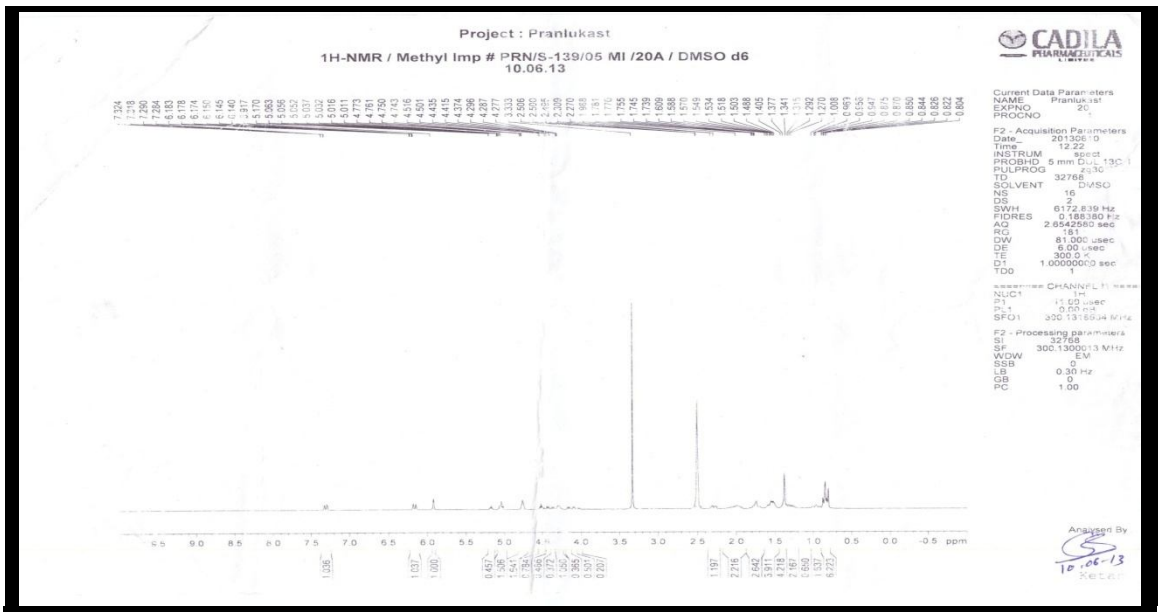


Fig. 2 NMR spectra of Budesonide

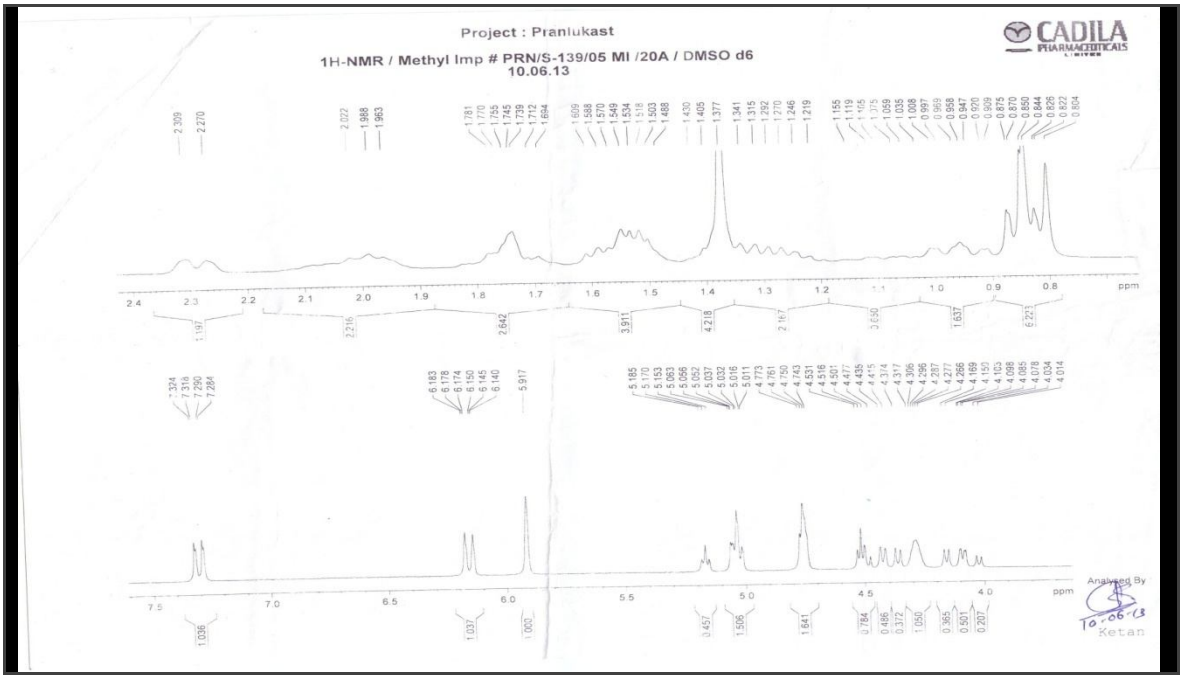


Fig. 3 NMR spectra of Budesonide

Determination of Solubility

Solubility is a useful preformulation parameter mainly for poorly water-soluble drugs. Bioavailability problems are often present when the aqueous solubility of a drug is less than 10 mg/ml over the pH range 1-8.

- **Budesonide:** Freely Soluble in Methylene chloride, Sparingly Soluble in Ethanol (95%).

Drug-Excipients compatibility study

The primary objective of this investigation was to identify a stable storage condition for drug in solid state and identification of compatible excipients for its formulation. The Drug-Excepients compatibility study of Budesonide with different excepients was studied by thermal stability at 40ºC/75% RH in both open and closed vials condition for 1 month. Also samples were exposed to 50ºC and 2-8ºC for 1 month condition and flow of study described in table 17. After one month samples were observed visually for change of color or its appearance in powder form.

Table No 1: Drug-Excipients compatibility protocol

Sr.No.	Condition	Time Point
1.	Initial	On 0th day
2.	40ºC/75% RH (open vials)	15th day
		30th day
3.	40ºC/75% RH (sealed vials)	30th day
4.	50ºC (sealed vials)	15th day
		30th day
5.	2-8ºC (control samples)	30th day

During this period checking for the impurities or any other problem in to A.P.I. are observed and then decide the Excepients for the final Formulation of A.P.I.

Drug-Excipients compatibility study at storage condition: 40ºC/75% RH and 2-8 ºC

Table No 2: Budesonide-Excipient Compatibility Study

Sr.No.	Name of Mixture	Ratio	Observation	
			Initial	After 4 week
1.	Budesonide	1	White colour	NC
2.	Budesonide +Sugar Sphere	1 : 1	White colour	NC
3.	Budesonide +Ethyl Cellulose	1 : 1	White colour	NC
4.	Budesonide + Acetyl Tributyl Citrate	1 : 0.1	White colour	NC
5.	Budesonide +Polysorbate 80	1 : 0.1	White colour	NC
6.	Budesonide+ Instacoat EN II (Eudragit L 100 55)	1 : 1	Yellow colour	NC

NC= No change was found

Process: **Preparation of Polymer-Drug Dispersion for Controlled Released :**

Table No 3: Formulation for Drug Release control suspension			
Ingredients	**Qty. for 3000 capsules**		
	B. No. P 1*	**B. No. P 2***	**B .No. P 3***
Budesonide IP	9	9	9
Aquacoat ECD-30(Ethyl Cellulose)	126*(37.8)	115* (34.5)	105*(31.5)
Acetyl tributyl citrate	2.7	2.7	2.7
Tween-80	0.15	0.15	0.15
Sugar sphere (Pellets)	500	500	500
Sunset yellow	1	1	1
Total	**550.65**	**547.35**	**544.35**
Quantity in gm			

Note: *Aquacoat ECD-30 100 gm contains 30 gm of Ethyl Cellulose.

Enteric Coating Process

Table No 4: Composition for Enteric coating of drug coated pellets			
Ingredients	**Qty. for 3000 capsules**		
	B. No. P 1*	**B. No. P 2***	**B .No. P 3***
Instacoat EN-II	72	73	75
Isopropyl alcohol (IPA)	559	559	559
Purified water	69	69	69
Total	**700**	**701**	**703**
Quantity in gm			

Preparation of Polymer-Drug Dispersion for Controlled Released :

Table No 5: Formulation for Drug Release control suspension			
Ingredients	**Qty. for 3000 capsules**		
	B. No. P 4*	**B. No. P 5***	**B .No. P 6***
Budesonide IP	9	9	9
Aquacoat ECD-30(Ethyl Cellulose)	90*(27)	80*(24)	70*(21)
Acetyl tributyl citrate	2.7	2.7	2.7
Tween-80	0.15	0.15	0.15
Sugar sphere (Pellets)	500	500	500
Sunset yellow	1	1	1
Total fill weight of capsule containing (3mg) of Budesonide	**537.15**	**536.85**	**533.85**
Quantity in gm			

Note: * Aquacoat ECD-30 100 gm contains 30 gm of Ethyl Cellulose.

Enteric Coating Process:

Table No 6: Formulation for Enteric coating of drug			
Ingredients	**Qty. for 3000 capsules**		
	B. No. P 4*	**B. No. P 5***	**B .No. P 6***
Instacoat EN-II	72	72	72
Isopropyl alcohol (IPA)	559	559	559
Purified water	69	69	69
Total	**700**	**700**	**700**
Quantity in gm			

Calculation of Amount of Assay:

$$\textbf{Assay of Budesonide (\%)} = \frac{Au}{As} \times \frac{W1}{50} \times \frac{3}{20} \times \frac{200}{5} \times \frac{1}{LC} \times \frac{P}{100} \times 100$$

Where,

Au = Average area of sum of Budesonide Epimers peak obtained from the duplicate injections of the assay preparation.

As = Average area of sum of Budesonide Epimers peak obtained from the five replicate injections of the standard preparation.

W1 =Weight of Budesonide standard in mg.

LC = Label claim in mg.

P = Potency of Budesonide standard in percentage basis.

In vitro dissolution studies:

Dissolution parameter

Status	Specifications
Dosage Form	Capsules (controlled released formulation)
USP Apparatus	Type II (Paddle)
Speed (RPM)	75
Dissolution Medium	Acid Stage: 0.1 N HC1 Buffer Stage: Sodium Phosphate buffer pH=7.5
Volume (ml)	Acid Stage : 1000 ml, 0.1 N HC1 Buffer Stage:1000 ml , Sodium Phosphate buffer pH=7.5
Recommended Sample Timings	Acid Stage : 2 hours. Buffer Stage: 1,2,4,6,8,10,14 and 16 hours.

Evaluation of Budesonide Capsule

Pre-Encapsulation parameters

Pre-encapsulation parameters like bulk density, tapped density, Carr's index, Hausner's ratio and Angle of repose for powder blend/granules were checked as described in chapter 7 Pre- formulation studies.

Post- Encapsulation parameters

1. Appearance

The pellets should be free from twins, and lumps. The size of the pellets should be uniform.

2. Friability Test

Friability Test for Pellets[5]

There is no standard method established for evaluating friability of pellets. The friability of pellets was determined using a rotating drum like apparatus (Roche friabilator). But due to the low weight of pellets the mechanical stress applied is less. This can be corrected by adding glass or steel balls to increase stress. The best method for testing the friability of pellets was the **AIR STREAM** method. In this method the fines were removed through sieving and approximately 8g (m1) of pellets were filled in glass apparatus. The apparatus was closed using a sieve lid and the pellets were subjected to air stream. After 16 min the pellets were removed and reweighed (m2). Each batch was tested 3 times (n).The friability was calculated as percentage weight loss according to the equation:

F= [(m1-m2)/m1] x100%

STABILITY STUDY[6-8] :

Tablets of the final batch were packed in High-Density Polyethylene Containers (HDPE, 60CC) and were subjected to accelerated stability studies.

(400±20C/75±5%RH – 1Month)

The effects of temperature and humidity with time on the physical and chemical characteristics of the tablet were evaluated for assessing the stability of the prepared formulation. After each time period, the samples were tested for Appearance, Dissolution, Assay and Impurities.

Results and Discussion

Characterization of Budesonide

FTIR studies

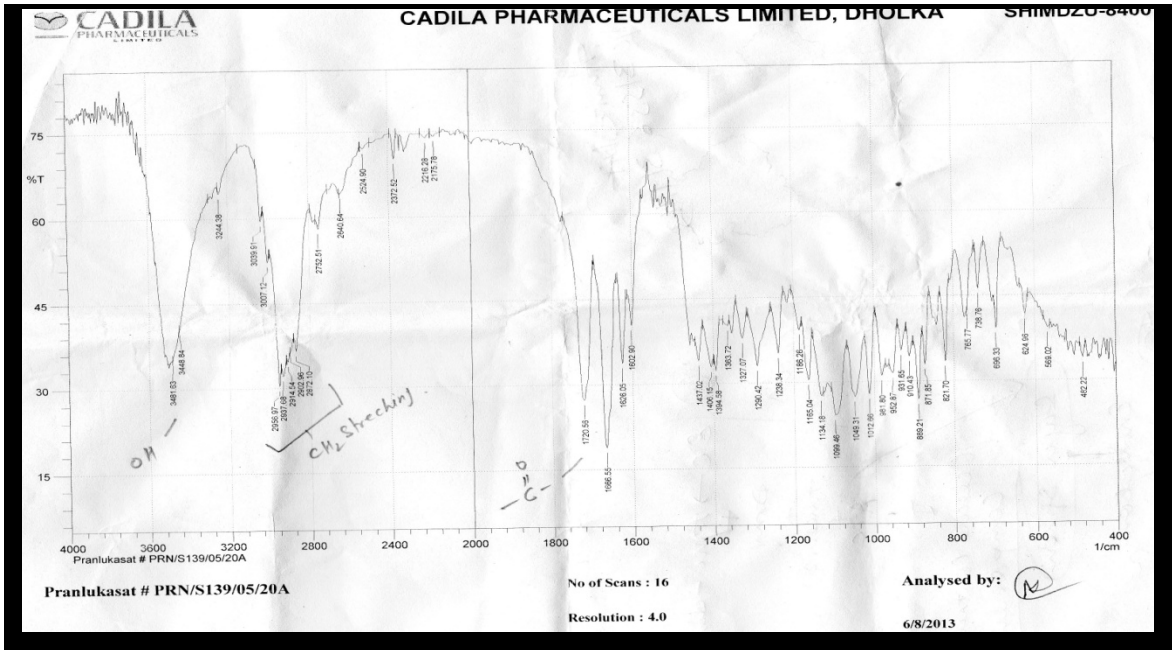


Figure 4 FTIR spectra of Budesonide

Inference

IR spectrum of Budesonide drug sample was taken shown in Fig.9.1. Interpretation of Budesonide IR spectra was shown in Table No.16. IR spectra showed no evidence of the interaction between the drug and the excipients studies.

DSC studies

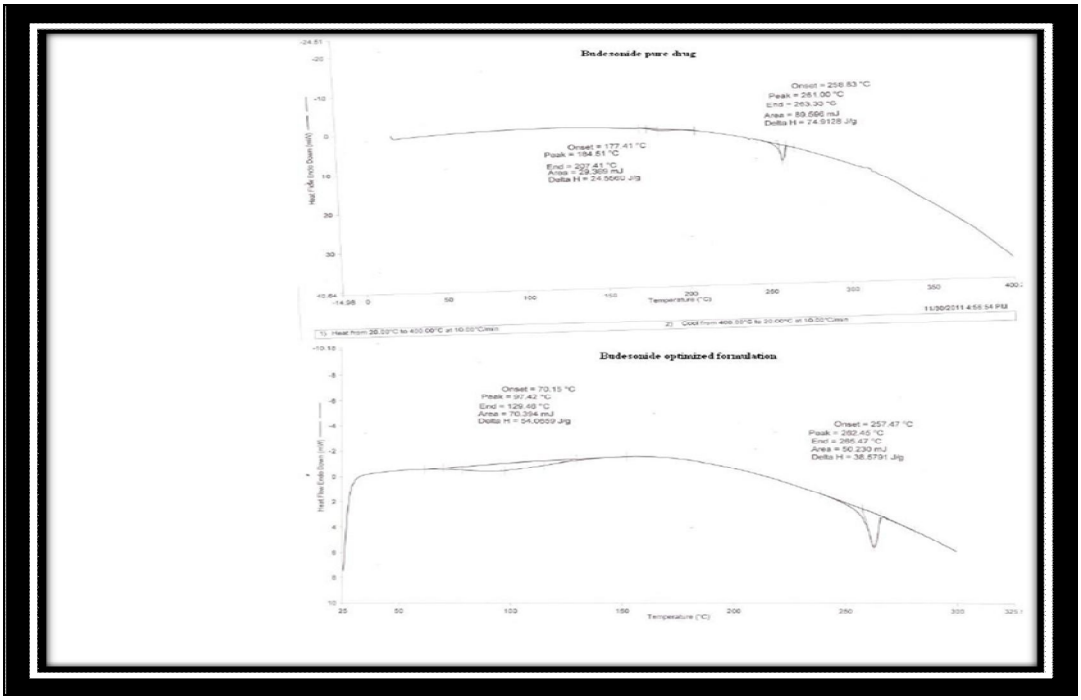


Figure.No:5 DSC thermogram of Budesonide (B1) and (b) Optimized formulation (B2)

Inference

The drug Budesonide was subjected for DSC. The DSC thermogram shows a sharp endothermic peak at 261ºC for Budesonide. While in final optimum formulation containing drug and polymer, the endothermic peak was observed at 262.45 ºC which is same as close to pure drug. Evaluation and interpretation of the thermogram revealed no interaction between drug and the polymer in the optimized formulation.

Standard Calibration Curve of Budesonide

Table No 7: Data for standard calibration curve in 7.5 phosphate buffer

Sr. No	Concentration (µg/ ml)	Absorbance
1	1	0.096
2	2	0.182
3	3	0.262
4	4	0.368
5	5	0.461
6	6	0.529
7	7	0.613
8	8	0.704
9	9	0.782
10	10	0.862

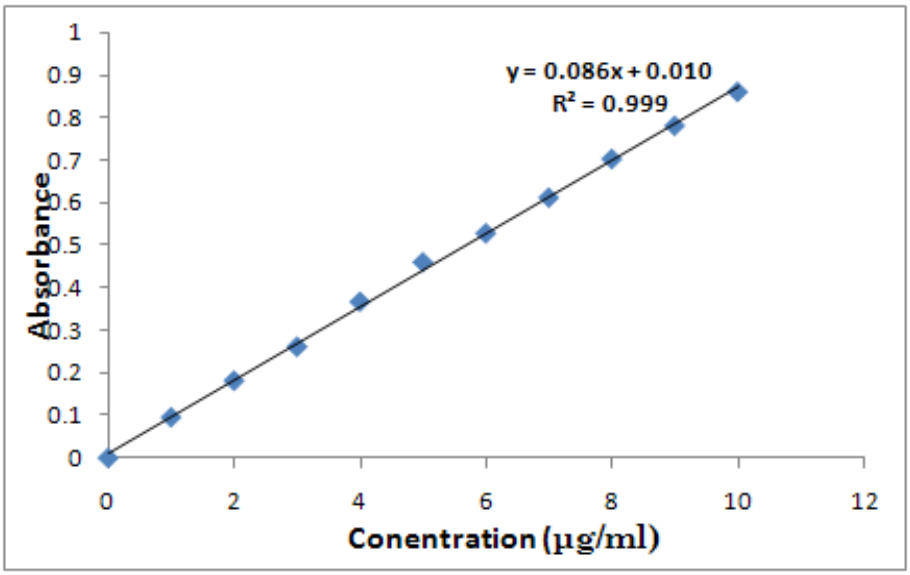


Figure.No: 6 Calibration plot of Budesonide in 7.5 phosphate buffer

Beer-Lembart's law was obeyed over the range and data was found to fit the equation Slope = 0.086

$R^2 = 0.999$
Where,
x=concentration in µg/ml
y=Absorbance

Conclusion

The standard curve prepared shown very linearity hence it was used for further analysis.

Dissolution Profile:

Table No 8: % Drug released of Marketed product

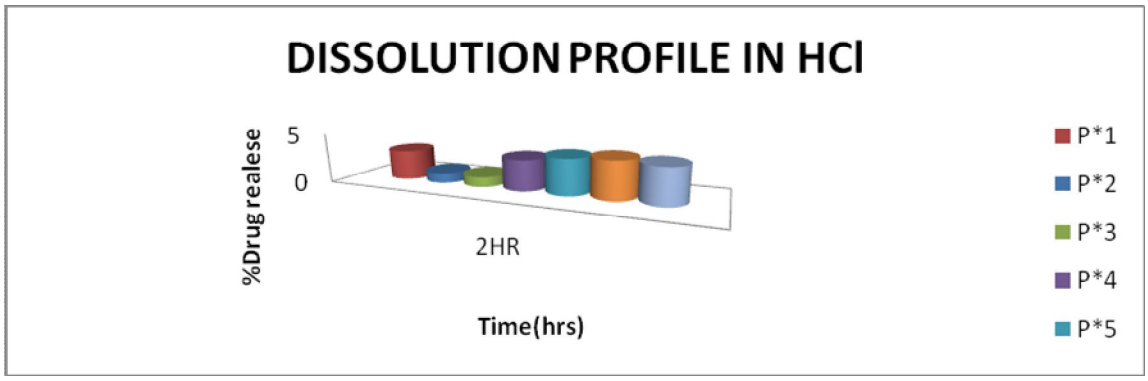
Media	Time point	Unit-1	Unit-2	Unit-3	Unit-4	Unit-5	Unit-6	%Mean	RSD %
0.1N HCL	2HR	3.8	3.7	3.6	3.4	3.6	3.5	**3.6**	3.9
Phosphate Buffer pH 7.5	1HR	19.4	21.6	22	22.5	22.2	21.9	**21.6**	5.2
	2HR	33.1	33.7	33.8	34.2	33.7	33.1	**33.6**	1.3
	4HR	49.7	49.9	50.4	51.4	50.7	49.2	**50.2**	1.6
	6HR	61.7	61.5	61.0	62.4	61.5	61.2	**61.6**	0.8
	8HR	69.0	69.6	68.9	68.6	68.6	66.9	**68.6**	1.3
	10HR	75.8	75.5	75.9	74.9	74.9	75.8	**75.4**	1.8
	14HR	80.9	80.7	79.9	80.8	80.6	80.1	**80.5**	1.3
	16HR	90.8	90.9	90.6	90.2	90.4	90.5	**90.5**	1.5
% Cumulative drug released by addition of 0.1N HCL drug released									
Phosphate buffer pH 7.5	3HR	23.2	25.3	25.6	25.9	25.8	25.4	**25.2**	4.0
	4HR	36.9	37.4	37.4	37.6	37.3	36.6	**37.2**	1.0
	6HR	53.5	53.6	54	54.8	54.3	52.7	**53.8**	1.3
	8HR	65.5	65.2	64.6	65.8	65.1	64.7	**65.2**	0.7
	10HR	72.8	73.3	72.5	72	72.2	70.4	**72.2**	1.4
	12HR	79.6	79.2	79.5	78.3	78.5	79.3	**79.06**	1.3
	16HR	84.7	84.4	83.5	84.2	84.2	83.6	**84.1**	1.2
	18HR	94.6	94.6	94.2	93.6	94.0	94.0	**94.16**	0.8

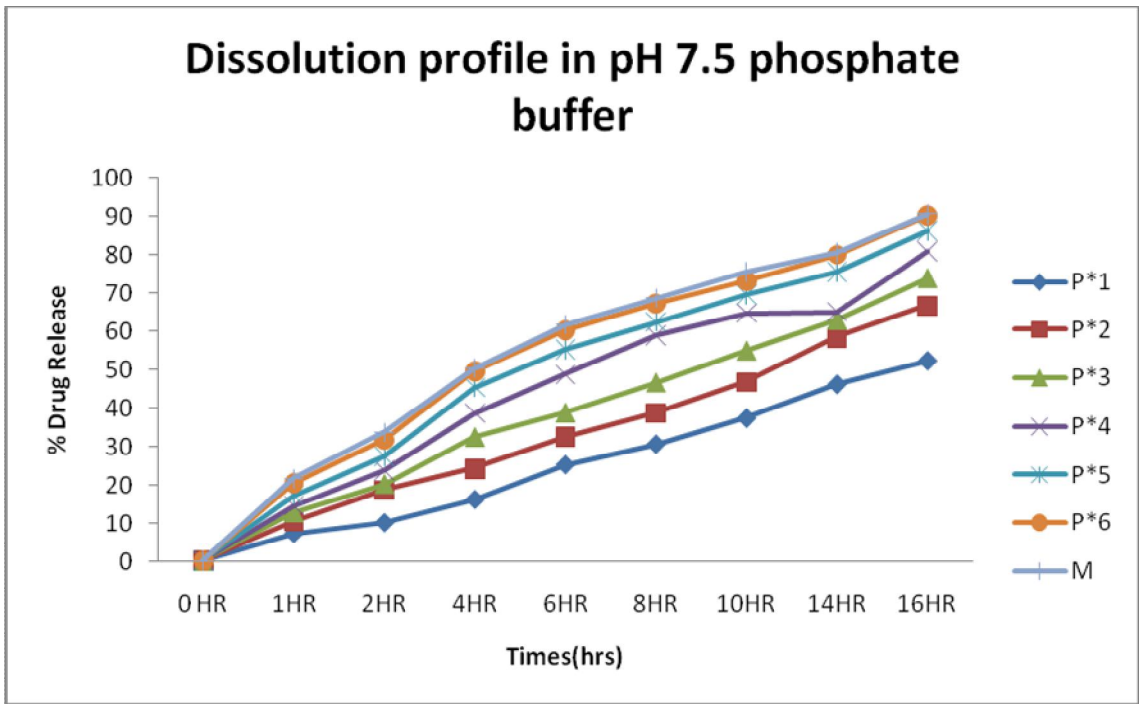
Comparison of present formulation with marketed formulation:

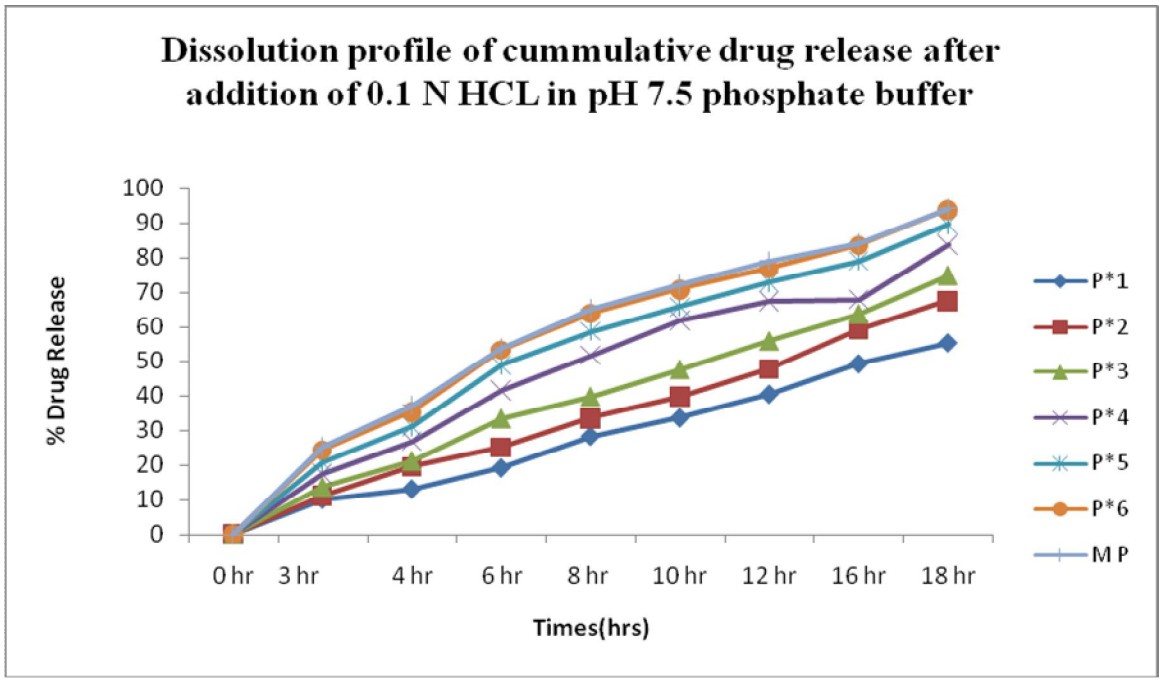
Table No 9: % Drug released of present formulation with comparison to Marketed product

Media	Time point	Batch. No.P1*	Batch. No.P2*	Batch. No.P3*	Batch. No.P4*	Batch. No.P5*	Batch. No.P6*	%Mean of marketed sample
0.1N HCL	2HR	3.0	1.0	1.0	3.1	3.6	3.8	**3.6**
Phosphate Buffer pH 7.5	1HR	7.2	10.2	12.7	14.5	17.2	20.5	**21.6**
	2HR	10.1	18.6	20.2	23.8	27.5	31.6	**33.6**
	4HR	16.2	24.2	32.4	38.5	45.2	49.5	**50.2**
	6HR	25.3	32.5	38.7	48.6	55.2	60.2	**61.6**
	8HR	30.6	38.7	46.5	58.8	62.3	67.2	**68.6**
	10HR	37.4	46.8	54.8	64.5	69.5	73.2	**75.4**
	14HR	46.2	58.2	62.7	64.9	75.5	79.9	**80.5**
	16HR	52.3	66.7	73.8	80.8	86.2	90.2	**90.5**
% Cumulative drug released by addition of 0.1N HCL drug released								
Phosphate buffer pH 7.5	3HR	10.2	11.2	13.7	17.6	20.8	24.3	**25.2**
	4HR	13.1	19.6	21.2	26.9	31.1	35.4	**37.2**
	6HR	19.2	25.2	33.4	41.6	48.8	53.3	**53.8**
	8HR	28.3	33.5	39.7	51.7	58.8	64.0	**65.2**
	10HR	33.6	39.7	47.5	61.9	65.9	71.0	**72.2**
	12HR	40.4	47.8	55.8	67.6	73.1	77.0	**79.06**
	16HR	49.2	59.2	63.7	68.0	79.1	83.7	**84.1**
	18HR	55.3	67.7	74.8	83.9	89.8	94.0	**94.16**
Assay%		101%	100%	99.8%	102.2%	103%	101.5%	**102.1%**

Comparison of present formulation with marketed sample







Conclusion

In vitro dissolution studies on the promising formulation (P*1-P*6) and marketed formulation(M) were carried out in 0.1 N HCL and pH 7.5 phosphate buffer The above all formulation has shown better release characteristics for all batches as comparison with marketed formulation. However the optimized batch P*6 has shown nearly greater result as comparison with other formulation with the marketed formulation.

Stability studies at 40oC/75% RH

Table No 10: Stability studies of final optimized Batch.No. P*6

Sr. No.	Test to be performed	Specification	Final optimized Batch No. P6*	
			Initial	**1 month**
1.	Description	Cream coloured cap and body capsule size"2"	Cream coloured cap and body capsule size"2"	Cream coloured cap and body capsule size"2"
2.	**Assay**	90 to110%	101.5%	100.5%
3.	**Dissolution**	For information only (As compare to Reference product)		
	(1) 0.1N HCL -2HR	3.6	3.8	4.4
	(2) Phosphate buffer (pH 7.5+0.1N HCL) % cumulative Drug released			
	3hr			
	4hr	25.2	24.3	25.0
	6hr	37.2	35.4	36.4
	8hr	53.2	53.3	54.0
	10hr	65.2	64.0	63.2
	12hr	72.2	71.0	70.1
	16hr	79.06	77.0	75.3
	18hr	84.1	83.7	82.8
		94.16	94.0	93.2
4.	%Loss on drying	NMT 1.5%	1.0%	1.03%
5.	Related Substance			
	Single max	NMT 0.5%	0.2%	0.26%
	Total impurity	NMT 1.5%	0.93%	1.1%

Discussion

From Table 26, it was observed that present formulation (Batch No.P*6) did not show any appreciable change in parameters like description,% LOD, dissolution, assay and amount of related substance after 1 month accelerated stability studies.

Conclusion

Prepared formulation of Budesonide capsule was found to be stable.

Table No 11: Physical Evaluation of Budesonide

Physical Parameters	Budesonide
Bulk density (g/ml)	0.218
Tapped density (g/ml)	0.321
Carr's Index (%)	32
Hausner's ratio	1.47
Angle of Repose	38.50

Result

As per above data the drug has poor flow properties.

Conclusion

As per flow ability scale, the drug has poor characteristics to flow. The excipients may effect on the flow of blend and thus Pelletization technique was chosen so that minimum amount of drug react with excipients for better flow properties.

Summary and Conclusion

Budesonide is a locally-acting glucocorticosteroid with an extensive, primarily hepatic, metabolism after oral administration. Budesonide, a pH- and time-dependent oral formulation of Budesonide, was developed to optimise drug delivery to the ileum and throughout the colon. Pharmaco-scintigraphic studies have confirmed that the Entocort EC formulation delays budesonide absorption and prolongs the rate of elimination but maintains complete absorption.

The oral route is considered to be most convenient for administration of drugs to patients. Oral administration of conventional dosage forms normally dissolves in the stomach fluid or intestinal fluid and absorb from these regions of the GIT depends upon the physicochemical properties of the drug. It is a serious drawback in conditions where localized delivery of the drugs in the colon is required or in conditions where a drug needs to be protected from the hostile environment of upper GIT. Dosage forms that deliver drugs into the colon rather than upper GIT prefers number of advantages. A traditional oral sustained release formulation releases most of the drug at the colon, thus the drug should have absorption window either in the colon or throughout the gastrointestinal tract.

The drug excipients studies were carried out to FT-IR analysis, it showed that there was no interaction between drug and excipients chosen for formulation. The drug Budesonide was subjected for DSC. The melting process of Budesonide pure drug was started at 258.83ºC and sharp peak was obtained at 261ºC**.** This short melting process suggests that the drug is in pure form. When the optimized formulation was subject for DSC, sharp peak of Budesonide was disappeared. The melting point was started at 70.15 ºC and the broad peak was obtained at 97.42 ºC. This narrow range of melting process suggested that there was reaction between pure drug and optimized formulation of Budesonide.

The results of all formulation for Description, Identification, %LOD, Assay and In-vitro dissolution were found to be within the standard pharmacopeia limit. Overall, the formulation P*6 containing 21 gm of Aquacoat ECD (Ethyl Cellulose) was found to be promising and it's in vitro dissolution time was found to be 3.8% drug release in 0.1 N HCL, 90.2% drug release in 16 hours in pH 7.5 phosphate buffer and in Cumulative drug released by addition of 0.1N HCL drug released was found to be 94% in 18 hours, % LOD was found to be 1.03% and amount of assay was found to be 101.5% when compared to marketed formulation which show vitro dissolution time of 3.6% drug release in 0.1 N HCL, 90.5% drug release in 16 hours in pH 7.5 phosphate buffer and in Cumulative drug released by addition of 0.1N HCL drug released was found to be 94.16% in 18 hours, % LOD was found to be 1.5% and amount of assay was found to be 102.1% respectively for above parameter.

Thus from above result optimized formulation P*6 show better result as compared with marketed formulation.

The stability studies were performed. Formulation P*6 was selected it was observed that present formulation (Batch No.P*6) did not show any appreciable change in parameters like description,% LOD, dissolution, assay and amount of related substance after 1 month accelerated stability studies. Hence it was concluded that prepared formulation of Budesonide capsule was found to be stable.

The pellets were found to be free from twins and clumps with optimum granule size. The pellets prepared by using 21 gm of Aquacoat ECD (Ethyl Cellulose) were found to be more promising and it's in vitro dissolution profile and amount of assay was found to be more promising results as compared to the marketed product. Thus it was concluded that amount of drug release and in vitro dissolution profile depend upon the ethyl cellulose concentration and thus by lowering the ethyl cellulose concentration the in vitro dissolution profile and the amount of drug release can be enchanced for better bioavalibility and bioassay of drug and thus the drug have better pharmacological activity in the targeted site. Thus it was concluded that Budesonide pellets can be formulated by using lesser amount of ethyl cellulose concentration for better bioavalibility of drug.

Acknowledgements

Authors are thankful to Prof (Dr.).B.Jaykar, Principal Vinayaka Mission's College of Pharmacy, Salem, Tamil nadu and providing all the facilities for this research project.

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ICH Guideline Published by Europian Medicines agency CAMP /ICH/ 2736/99 August 2003. http://www.ichguidelines.com