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DEVELOPMENT AND EVALUATION OF COLON TARGETED DRUG DELIVERY SYSTEM

Ketakee A. Nichat, Nishan N. Bobade, Chitralekha G. Therkar, Kajal S. Jumde, Mohd. Vaqqas Quraishi

Department of Pharmaceutics

Vidyabharti College of Pharmacy, C. K. Naidu Road , Camp , Amravati, Maharashtra , INDIA 444602

Abstract

In the present investigation, an attempt was made to formulate the time and pH dependent drug delivery system, reduce the frequency of dose administeration, and prevent ulcerative colitis by developing sustained delayed release tablets using a combination of Eudragit S-100 and L-100 as enteric coating. The core tablets of Celecoxib were prepared using the direct compresion method. The aim of the present study is to develop colon specific drug delivery of Celecoxib sustained release enteric coated tablet for ulcerative colitis using HPMC K-4M as a semisynthetic polymer. The impact of polymer concentration and superdisintegrant concentration was also studied. In-vitro drug release research was performed on the enteric coated Celecoxib tablet using simulated gastric fluid (0.1N HCl) for 2 hours, simulated intestinal fluid (pH 7.4) for 3 hours, and the simulated colonic fluid (pH 6.8) for 7 hours as a dissolution fluid. The study showed that the coating had a significant impact on the lag time before medication release. In the treatment of colonic illness and the oral administration of medications that are unstable and vulnerable to enzymatic degradation in the upper GI tract, colon drug delivery is advantageous. The results also showed that a mixture of Eudragit S-100 and L-100 may be used to coat tablets for medication delivery to the colon.

Key Words : Colon drug delivery system , Targeted System, Enteric coated tablet , Time and pH dependent system.

INTRODUCTION :

CTDDS suggests that targeted delivery of medication into the lower puke, that happens primarily within the gut (i.e. colon). Pharmaceutical scientists have extensively investigated the world of the colonic region for targeted drug delivery within the past 20 years. Colon targeting depends on exploiting a novel feature of a particular web site and protective the drug till it reaches the positioning. Targeted drug delivery to the colon is extremely fascinating for native treatment of a range of viscus unwellnesss like inflammatory viscus disease, amebiosis, colonic cancer, and for native treatment of native colonic pathologies, in addition as general delivery of macromolecule and amide medication. the arrival of slow unharness technologies will increase the probabilities for a

drug to be discharged within the colon, and so this organ has a very important role to play in drug absorption from oral sustained unharness formulations. [2]

Various approches have been used For oral drug(s) delivery to the colon, several approaches have been used, including time-dependent delivery, pH-dependent systems, and bacteria-dependent delivery. The pH-dependent systems exploit the generally accepted view that the pH of the human gastrointestinal (GI) tract increases progressively from the stomach (pH 2-3), small intestine (pH 6.5-7) and colon (7.0-8.0). Taking advantage of the highest pH value of the colon content, the dosage form containing the active drug in the core is coated with pH dependent material which dissolves at the pH of the colon. [3,4] But recent studies using sensitive and reliable equipment contradict the traditional view and provide evidence of a fall in pil in the Gi region between ileum and colon. Apparently, the colon has a lower pH value (6.5-7) than the small intestine (70-7.8), and the jejunal region of some individuals has a higher pH range (6.1–7.4) than the small intestine or colon of other individuals.[3]

Ulcerative colitis is that the anti-inflammatory unwellness of the colonic tissue layer that is restricted to intestine und is typically treated with salicylates of glucocorticoids. However, during times of remission Celebrex is that the drug of alternative. during this case it's fascinating to localize the discharge of mesalamine to the afflicted website within the colon. so Celebrex was used as a model drug within the gift study. Celebrex is associate anti-inflammatory drug, for oral adminsteration within the treatment of diseases of colon (ulcerative redness, crohn's disease: carcinomas and infections) whereby high native concentration may be achieved whereas minimizing facet effects that occur attributable to unharness of medication within the higher bum or reserve general absorption.[5]

The aim of the present research work was to develop sustained release tablet formulation of Celecoxxib targeted to colon by using various polymers. Celecoxib is a selective cyclooxygenase-2 inhibitor with pH-dependent solubility. pH modifying agents (buffering agents) were used.Celecoxib enteric coating tablets containing several retarding agents, were used in order to extend the release of drug over the desired period of time.[6,7]

MATERIALS AND METHODS

MATERIALS

Celecoxib was obtained as a gift sample from Amoli Organics Pvt. Ltd., Mumbai., HPMC K4 were obtained as a gift sample from Colorcon Asia Pvt. Ltd., Goa., Eudragit S100 and Eudragit L100 was obtained as a gift sample from Evonik Degussa India Pvt. Ltd., Mumbai., Guar Gum, Starch, Magnesium Sterate, Talc was obtained from S.D Fine Chem. Mumbai.. All reagent and solvent used were of analytical grade satisfying pharmacopieal standard.

Table No 1 . Preparation Of Core Tablet Using Polymer Drug Retardant

Ingredients	Quantity Taken (mg)								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Celecoxib	100	100	100	100	100	100	100	100	100
Gaur Gum	10	20	30	10	20	30	10	20	30
HPMC K4M	20	20	20	40	40	40	60	60	60
Starch	64	54	44	44	34	24	24	14	4
Talc	4	4	4	4	4	4	4	4	4
Mgnesium Sterate	2	2	2	2	2	2	2	2	2
Total	200	200	200	200	200	200	200	200	200

METHODS

1.Pre -formulation study[8,9,10]

1.Oraganoleptic properties

About 1.0 g of drug sample was placed in watch glass and was observed for appearance, colour, any peculiar odour and taste.

2. Determination of melting range

Glass capillary metrhod was used to determine the melting point. Drug filled capillary was tied with a thermometer and immersed liquid paraffin containing in Thiele's tube. It was heated uniformly and the temperature at which the drug just begain to melt and the one at which it melted completely were recorded. Reading were recorded in tr iplicate and mean value has been reported.

3.Solubility study

The solubility study of drug was carried out to select the solvent in which the drug is soluble. In each selected solvent viz. water and ethanol accurately about 10 mg of drug was placed and solubility was visually observed

2. Pre- Compressional studies[9,10 ,11]

2.1 Flow properties of powder

Bulk Density : Apparent bulk density was determined by placing a powder into cylinder and measuring the volume and weight as it. It was calculated by using formula given by.

Bulk density = mass / volume

Tapped Density : Weighing a sample of powder was transferred to a cylinder and was tapped for a mixed number of taped (100) Tapped density was calculated by formula given by .

Tapped density = weight of powder / tapped volume

Hausner's Ratio : The hausner's ratio is a number that is correlated to the flowability of a powder material . ait is clacualted by formula given by.

Hausner's ratio = Tapped density / Bulk density

Compressibility Index : It is a sample test to evaluate bulk density and tapped density of powder and the rate of which it is packed down . the formula of Carr's Index was given by.

Carr's inde (%) = [Tapped density – Bulk density] x 100 / Tapped density

Angle of Repose: The angle of repose of blend was determined by the fixed funnel method. The accurately weighed granules were taken in the funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the blend. The blend was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the formula given in equation

$$Tan\,\theta = h / r$$

Where , h and r the hight and radius of the powder cone.

3. Post Compressional Studies[9,10]

Shape and Appearance : Tablets were examined under a fen's for the shape of the tablet, and colour was observed by keeping the tablets in light.

Hardness : Monsanto hardness tester was used for the determination of the hardness The tablet to be tested was held between a fixed and a moving jaw and reading of the indicator was adjusted zero. The force applied to the edge of the tablet was gradually increased by moving the screw knoh forward until the tablet broke. The reading was noted from the scale which indientes the pressure required in kg or b to break tablets.

Thickness : The crown-to-crown thickness of ten tablets from each batch was determined using vernier caliper. The thickness variation limits allowed are 5% of the size of the tablet.

Weight Variations : Weight variation study was carried out as per USP. Twenty tablets were randomly selected from each batch weighed individually. The average weight and standard deviation was calculated.

Friability: Roche friabilator (Electrolab Mumbai) was used for testing the friability of prepared tablets. Twenty tablets were weighed accurately and placed in the friabilator and rotated at 25 rpm for a period of 4 min. Tablets were dedusted using soft muslin cloth and weighed again. Percentage weight loss was determined by using following formula.

% Friability= [(Initial weight-Final weight)/ Initial weight] X 100

Uniformity of Drug Content:

For determination of drug content, five tablets from each formulation were triturated using mortar and pestle. An accurately weighed powder equivalent to 200 mg of drug was taken in 100 ml volumetric flask and diluted with sufficient amount of phosphate buffer of pH 6.8 up to mark. Then the sample was sonicated for 1 hr and filtered. An aliquot of the filtrate was diluted suitably and analyzed spectrophotometrically at 251-270 nm against blank. The test was done in triplicate and average drug content was estimated.

PREPARATION OF COATING SOLUTION

The core tablet was coated with polymer Eudragit L100 and Eudragit S100 in various concentrations: 1:1, 2:1, and 1:2. The coating formula was applied to core tablet batches using the formulation described in table no. 2 respectively.

Table No 2: Coating Formula

	Coated of F8 formula								
Ingredients	**EC1**	**EC2**	**EC3**	**EC4**	**EC5**	**EC6**	**EC7**	**EC8**	**EC9**
Eudragit S 100	10 g	10 g	10 g	20 g	20 g	20 g	10 g	10 g	10 g
Eudragit L 100	10 g	10 g	10 g	10 g	10 g	10 g	20 g	20 g	20 g
Dibutyl phthalate	2.5 ml	2.5 ml	2.5 ml	2.5 ml	2.5 ml	2.5 ml	2.5 ml	2.5 ml	2.5 ml
Acetone	200 ml	200 ml	200 ml	200 ml	200 ml	200 ml	200 ml	200 ml	200 ml
Isopropyl alcohol	200 ml	200 ml	200 ml	200 ml	200 ml	200 ml	200 ml	200 ml	200 ml
% coating	5%	10%	15%	5%	10%	15%	5%	10%	15%

Therefore 5% coating means 5% weight gain on core tablet, 10 % coating means 10% weight gain on core tablet and 15% coating means 15% weight gain on core tablet.

EVALUATION OF ENTERIC COATED TABLETS[11,12]

Hardness Test

The hardness of the coated tablets was measured using same procedure as described earlier with the help of Monsanto hardness tester. The hardness of various formulations was shown in table

Weight Variation Test

The weight variation test was carried out for the coated tablets using the same procedure as described earlier and the results were reported in the table

***In-vitro* Disintegration Test of Coated Tablets**

Tablet disintegration was carried by placing one tablet in each tube of the basket and top portion of the each tube was closed with disc. Tablets were firstly tested in 0.1N HCl for 2 h (simulated gastric transit time) to see the damage to the coat. Afterwards, tablets were tested in the phosphate buffer pH 6.8 (simulated colonic pH) till the coating dissolved. Temperature in each case was kept at 37±0.5°C. Disintegration time was reported in min. The time taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured. The experiment was carried out in triplicate.

Lag Time Profile :

Time dependent system are formulated to undergose lag time predetermined span of time of on release, followed by a rapid and complete release of loaded drug . Lag time is the required to transit from the month to the colon.

***In-vitro* Dissolution Profile of Celecoxib Coated Tablets:**

In vitro drug release studies for the prepared tablets were conducted for a period of 12 hours using USP type-II (Paddle) dissolution apparatus (Electro lab, Mumbai.) at 37.5 ^{0}C and 75 rpm speed using pH 1.2 buffer for initial 2 h, phosphate buffer of pH 7.4 up to 3 h as and phosphate buffer of pH 6.8 for 7 h as dissolution medium. At predetermined interval of time, 10 ml of sample was withdrawn from the dissolution medium and replaced with fresh medium to maintain the volume constant. After filtration and appropriate dilution, the sample solutions were analyzed at 255 nm (acidic media) and 252nm (basic media) for Celecoxib by a UV-visible spectrophotometer. The amount of drug present in the samples was calculated and the results were reported in table.

STABILITY STUDY [13]

The selected batch (F8) was kept at room tempreature with at 40°C ± 2°C / 75 ± 5% RH and the samples were withdrawn at 4 week for physical and *in-vitro* evaluation of drug release.

RESULT and DISCUSSION

Table No 3 : Pre -formulation Parameter :

Sr.no	Test	Specification	Results
1	Colour	White or almost white crystalline powder or amorphous powder	White crystalline powder
2	Solubitity	Freely soluble to soluble in anhydrous ethanol. Soluble in dichloromethane and practically insoluble in water	Soluble in anhydrous ethanol, soluble in dichloromethane and practically insoluble in water
3	Melting point	158 – 164^{0}C	161^{0}C + 0.

All values are expressed as mean ± standard deviation, n=3

Evalution of Core Tablet :

Table No 4 : Flow properties of powder

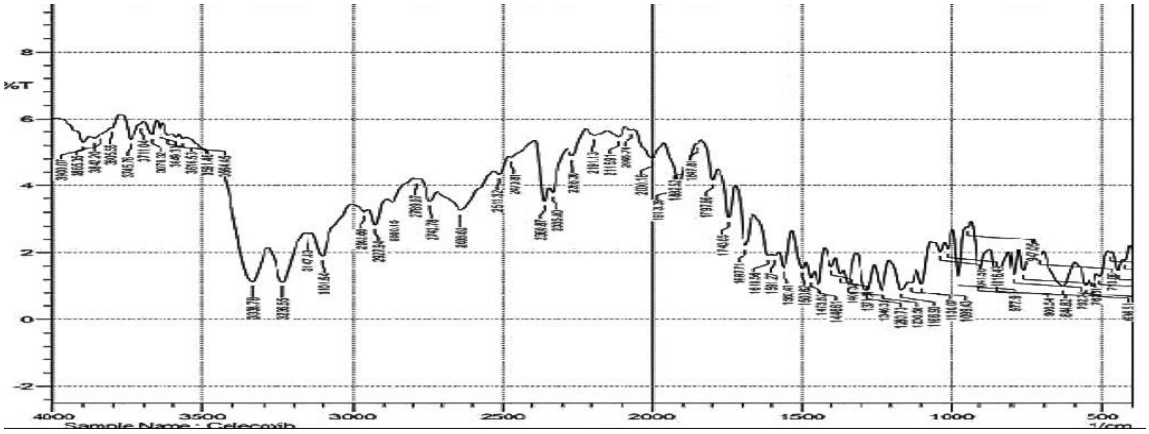
Sr. No	Formulation	Bulk density (g/ml)	Tapped density (g/ml)	Angle of Repose (%)	Compressibility index %	Hausner's ratio
1	F1	0.362 ± 0.02	0.411 ± 0.03	27^0.14 ± 0.51	11.92 ± 0.12	1.13 ± 0.02
2	F2	0.355 ± 0.01	0.408 ± 0.01	29^0.36 ± 0.61	12.99 ± 0.22	1.14 ± 0.07
3	F3	0.361 ± 0.03	0.410 ± 0.04	28^0.12 ± 0.22	11.85 ± 0.16	1.13 ± 0.04
4	F4	0.372 ± 0.04	0.415 ± 0.03	20^0.11 ± 0.11	10.36 ± 0.17	1.11 ± 0.10
5	F5	0.345 ± 0.01	0.411 ± 0.01	22^0.72 ± 0.25	16.05 ± 0.13	1.19 ± 0.11
6	F6	0.353 ± 0.02	0.412 ± 0.02	27^0.11 ± 0.45	14.32 ± 0.21	1.16 ± 0.05
7	F7	0.367 ± 0.03	0.407 ± 0.01	29^0.88 ± 0.23	9.82 ± 0.14	1.10 ± 0.08
8	F8	0.357 ± 0.01	0.413± 0.02	25^0.56 ± 0.69	13.55 ± 0.11	1.15 ± 0.06
9	F9	0.331 ± 0.02	0.397 ± 0.03	26^0.77 ± 0.11	16.62 ± 0.17	1.19 ± 0.11

All values are expressed as mean ± standard deviation, n=3

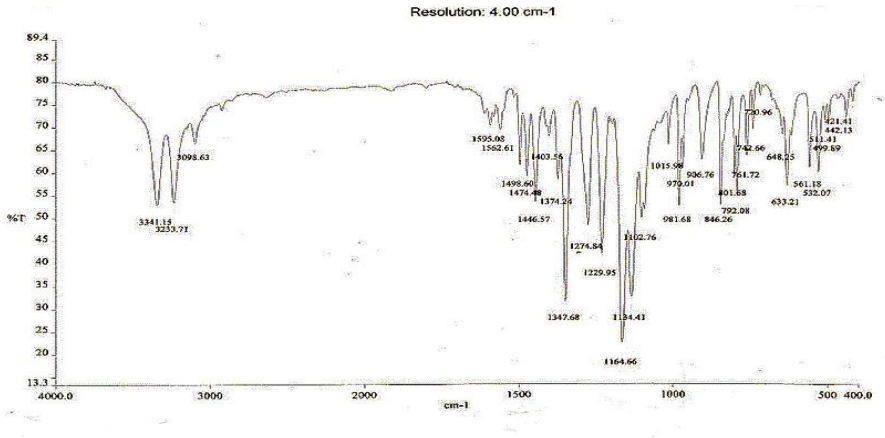
Tablets showed standard concave surfaces with a circular shape. The tablets were light off white in color. From the results of bulk density, tapped density, angle of repose, carr's index, and hausner's ratio, it was concluded that except for formulation F8, all the formulations possess poor flowability of powder. Formulations F8 had a passable flow of powder. From the results of angle of repose, it was concluded that except for the powder of F8, all other formulations possess poor flow. F8 had acceptable flow.

IR SPECTRAL ANALYSIS:

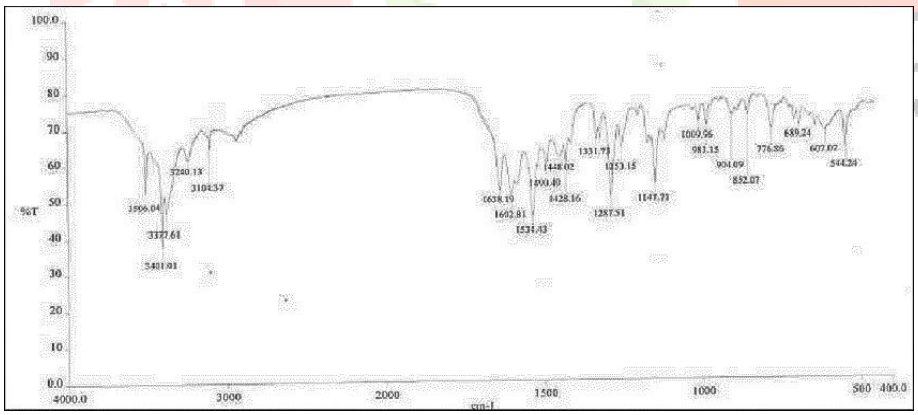
The FTIR studies of the IR absorption spectrum of the pure drug were taken in the range of 4000–450 cm using the KBr pellet method. The major peaks were reported for evaluation of purity. Observed peaks are similar to reported peaks of Celecoxib and Celecoxib with excipients. The results are shown below.



A



B



C

Graph A : FTIR of Celecoxib

Graph B: FTIR of Celecoxib + HPMC K4M

Graph C: FTIR of Celecoxib + Guar Gum

The FTIR graph concluded that the excipients with pure drug of celecoxib do no interacted to each other.

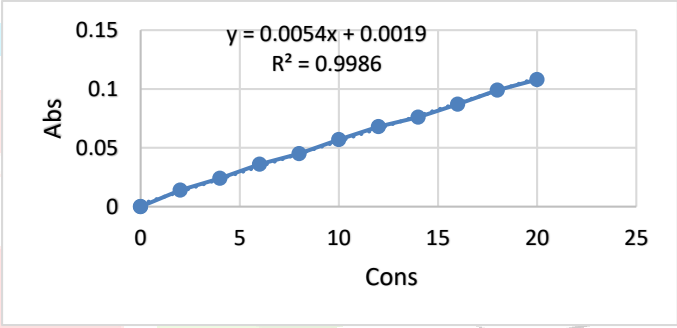
STANDARED CALIBRATION CURVE :

Standard Calibration Curve of Celecoxib in 0.1 N HCL at 252 nm, pH 6.8 at 252 nm, pH at 7.4 nm at 255nm.

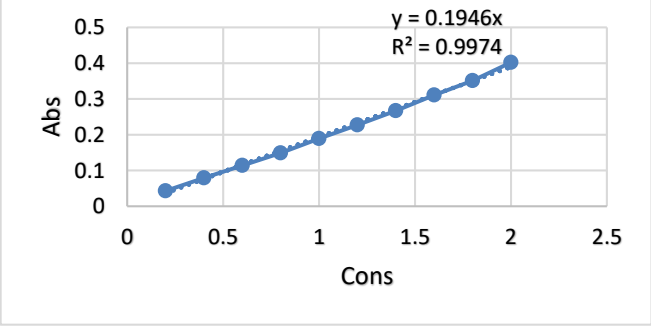
Table No 5 : Calibration curve

Sr. No.	Conentration	Absorbance		
		0.1N HCL	pH 6.8	pH 7.4
1	00	00 ± 0.02	00 ± 0.09	00 ± 0.03
2	2	0.014 ± 0.23	0.043 ± 0.03	0.031 ± 0.05
3	4	0.024 ± 0.015	0.079 ± 0.05	0.049 ± 0.04
4	6	0.036± 0.11	0.114 ± 0.06	0.068 ± 0.12
5	8	0.045 ± 0.2	0.149 ± 0.02	0.089 ± 0.06
6	10	0.057 ± 0.031	0.189 ± 0.11	0.111 ± 0.03
7	12	0.068 ± 0.09	0.227 ± 0.08	0.129 ± 0.02
8	14	0.076 ± 0.12	0.267 ± 0.14	0.156 ± 0.01
9	16	0.087 ± 0.14	0.311 ± 0.02	0.178 ± 0.03
10	18	0.099 ± 0.08	0.351 ± 0.04	0.205 ± 0.05
11	20	0.108 ± 0.03	0.402 ± 0.03	0.227 ± 0.02

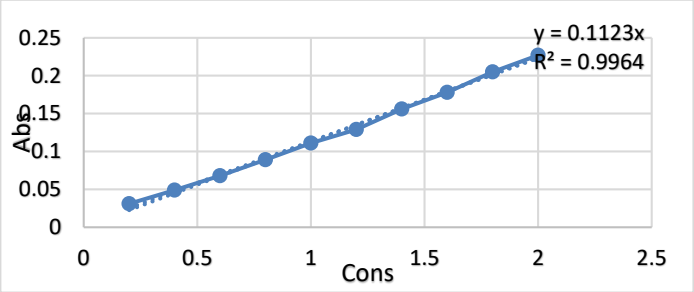
All values are expressed as mean ± standard deviation, n=3



Graph 1 : Calibration Curve of Celecoxib in 0.1 N HCL



Graph 2 : Calibration Curve of Celecoxib in pH 6.8



Graph 3 : Calibration Curve of Celecoxib in pH 7.4

The standard calibration curve was prepared and put into the various phosphate buffers (pH). The above cure were done to determine the linearity and interpret the absorption of drugs, respectively.

Table No 6 : EVALUATION OF CORE TABLET PRODUCT (UNCOATED)

Parametes	**Formulation**								
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**	**F9**
Average weight (mg)	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passses
Thickness (mm)	2.48 ± 0.16	2.39 ± 0.11	2.55 ± 0.23	2.99 ± 0.12	3.1 ± 0.23	2.21 ± 0.54	2.65 ± 0.12	2.58 ± 0.58	2.54 ± 0.15
Hardness (kg/cm^2)	5.2 ± 0.15	5.5 ± 0.13	5.1 ± 0.23	5.02 ± 0.11	5.23 ± 0.21	5.21 ± 0.09	5.5 ± 0.12	5.1 ± 0.31	5.6 ± 0.12
Friability %	0.36 % ± 0.02	0.38 % ± 0.05	0.35% ± 0.03	0.38% ± 0.03	0.31% ± 0.01	0.39% ±0.04	0.36% ± 0.05	0.35% ±0.02	0.4% ± 0.05
Disintegration time (min)	190.49 ± 0.02	205.67 ±0.1	180.76 ± 0.15	197.43 ± 0.11	195.18 ± 0.05	210.23± 0.15	205.45 ± 0.03	186.51± 0.06	211.64 ± 0.16
Drug Content %	94.51% ± 0.05	93.26% ±0.04	97.50% ± 0.03	97.03% ± 0.06	97.23% ± 0.04	97.65% ± 0.01.	95.22% ± 0.02	98.22% ± 0.03	96.23% ± 0.01

All values are expressed as mean ± standard deviation, n=3

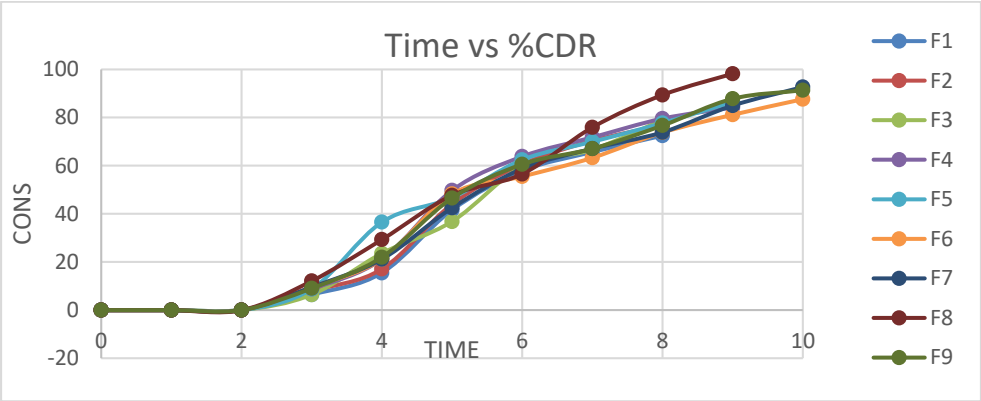
The tablets are evaluated for different parameters of formulation from F1 to F9 batches, The F8 batch given the Disintegration time, Drug Content % was show satisfied result

Table No 7 *:IN-VITRO* DISSOLUTION PROFILE OF UNCOTED TABLET.

Dissolutios Media	Samplig Time	Cumulative % Drug Release in Different Trial								
		F1	F2	F3	F4	F5	F6	F7	F8	F9
Simulated gastric fluid(0.1 HCL)	0	0	0	0	0	0	0	0	0	0
	1	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0
Simulated pH 7.4	3	6.411± 0.23	8.0142 ±0.05	6.4113 ±0.05	8.815±0 .02	8.815±0 .03	9.617±0 .04	9.6170± 0.32	12.101± 0.21	9.056±0 .11
	4	15.467 ±0.2	17.105 ±0.05	23.570 ±0.21	21.166± 0.15	36.562± 0.11	30.899± 0.23	21.175± 0.05	29.305± 0.12	21.979± 0.32
	5	41.567 ±0.05	44.033 8±0.22	36.794 3±0.12	49.7595 ±0.03	46.6874 ±0.12	48.2546 ±0.36	42.475± 0.15	47.693± 0.25	46.529± 0.54
Simulated pH 6.8	6	57.810 ±0.04	60.585 8±0.23	59.660 8±0.5	63.8232 ±0.23	62.4357 ±0.05	55.4984 ±0.06	58.735± 0.12	56.521± 0.22	60.585± 0.15
	7	65.642 ±0.24	70.349 4±0.15	66.598 ±0.2	71.7882 ±0.36	69.9023 ±0.09	63.2785 ±0.05	67.055± 0.21	75.897± 0.5	67.076± 0.65
	8	72.435 ±0.06	76.726 6±0.09	79.013 ±0.9	79.5837 ±0.02	77.6772 ±0.03	73.7872 ±0.04	73.864± 0.52	89.356± 0.52	76.690± 0.11
	9				84.1829 ±0.04	86.4645 ±0.06	81.1305 ±0.11	84.948± 0.23	98.153± 0.09	87.805± 0.08
	10						87.6104 ±0.51	92.648± 0.2		91.357± 0.03

All values are expressed as mean ± standard deviation, n=3

The core tablet formulation of different batches from F1 to F9 was evaluated by the dissolution test appratus. The drug was released up to 9 hr in 98.1531 % CDR of formula F8 was satisfied.



Graph 4 : % cumulative drug release

Table No 8 : EVALUATION PARAMETERS OF CELECOXIB ENTERIC COATED TABLETS

Parametes	**Enteric Coated Formulation**								
	EC1	**EC2**	**EC3**	**EC4**	**EC5**	**EC6**	**EC7**	**EC8**	**EC9**
Average weight (mg)	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passes	Passses
Thickness (mm)	2.48 ± 0.16	2.39 ± 0.11	2.55 ± 0.23	2.99 ± 0.12	3.1 ± 0.23	2.21 ± 0.54	2.65 ± 0.12	2.58 ± 0.58	2.54 ± 0.15
Hardness (kg/cm^2)	5.2 ± 0.15	5.5 ± 0.13	5.1 ± 0.23	5.02 ± 0.11	5.23 ± 0.21	5.21 ± 0.09	5.5 ± 0.12	5.1 ± 0.31	5.6 ± 0.12
Friability %	0.36 % ± 0.02	0.38 % ± 0.05	0.35% ± 0.03	0.38% ± 0.03	0.31% ± 0.01	0.39% ±0.04	0.36% ± 0.05	0.35% ±0.02	0.4% ± 0.05
Disintegration time (min)	225.89 ± 0.02	223.67 ±0.1	216.76 ± 0.15	227.43 ± 0.11	231.18 ± 0.05	230.82± 0.15	235.45 ± 0.03	218.65± 0.06	235.64 ± 0.16
Drug Content %	94.51% ± 0.05	93.26% ±0.04	97.50% ± 0.03	98.23% ± 0.06	97.23% ± 0.04	97.65% ± 0.01.	95.22% ± 0.02	98.22% ± 0.03	96.23% ± 0.01

All values are expressed as mean ± standard deviation, n=3

The Enteric coated tablet was evaluated by diffetent parameters from the batches of EC1 to EC9,

Table No 9 *: IN VITRO* DISSOLUTION PROFILE OF ENTERIC COATED TABLET

Dissolutios Media	Samplig Time	Cumulative % Drug Release in Different Trial								
		EC1	EC2	EC3	EC4	EC5	EC6	EC7	EC8	EC9
Simulated gastric fluid (0.1 HCL)	0	0	0	0	0	0	0	0	0	0
	1	0	0	0	0	0	0	0	0	0
	2	0	0	0	0	0	0	0	0	0
Simulated pH 7.4	3	4.808±0.02	7.2128±0.03	5.6099±0.05	6.411±0.023	8.815±0.02	12.021±0.03	8.014±0.02	12.101±0.05	9.617±0.05
	4	12.2083 ±0.02	12.2350 ±0.01	13.8379 ±0.03	17.0881 ±0.05	21.1665 ±0.6	29.3054 ±0.01	20.3472 ±0.01	29.3054 ±0.06	21.985±0.01
	5	35.4496 ±0.02	39.9198 ±0.01	36.6785 ±0.03	41.5850 ±0.02	47.3285 ±0.01	52.3152 ±0.03	41.6384 ±0.6	45.6936 ±0.05	47.3463±0.5
Simulated pH 6.8	6	57.6291 ±0.05	60.0385 ±0.03	60.4705 ±0.05	61.9713 ±0.05	57.4286 ±0.02	56.6715 ±0.06	59.2190 ±0.05	56.5215 ±0.05	61.1875±0.05
	7	63.8676 ±0.36	63.3144 ±0.02	65.3369 ±0.03	70.3494 ±0.01	63.7512 ±0.05	61.8705 ±0.06	65.6423 ±0.04	70.8016 ±0.02	66.5981±0.04
	8	71.1029 ±0.03	69.6145 ±0.15	77.2639 ±0.36	77.1942 ±0.06	70.9917 ±0.06	72.3638 ±0.04	73.3710 ±0.01	86.2692 ±0.06	77.1428±0.05
	9		75.5087 ±0.65		81.3001 ±0.08	78.3042 ±0.05	80.6269 ±0.08	84.4501 ±0.02	92.7646 ±0.05	86.8602±0.01
	10					86.623±0.05	83.828±0.05	90.966±0.02	97.839±0.3	93.401±0.02

All values are expressed as mean ± standard deviation, n=3

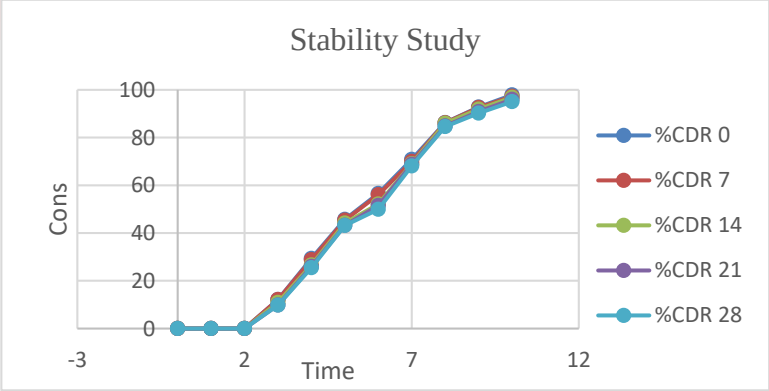
The results obtained in the *in-vitro* drug release study are tabulated. The cumulative percentage of Celecoxib released as a function of time for all the formulations are shown in graph . Coating of tablets with Eudragit L-100: Eudragit S-100 in combination showed the lag time of nearly before burst effect. From the result, concluded that the combination of Eudragit L-100: Eudragit S-100 can be successfully utilized to create desired release profile similar to the targeted release profile in future study. From the results, we have seen that 10% enteric coating gave us more appropriate results as the release of drug at pH 7.4 was less and the drug release at pH 6.8 was more, i.e the drug release was more in the colonic region.

Stability study :

Table No 10 : Drug release profile of formulation F8 for stability study

Sr. No	Days Time (min)	0 %CDR	7 %CDR	14 %CDR	21 %CDR	28 %CDR
1	0	0	0	0	0	0
2	1	0	0	0	0	0
3	2	0	0	0	0	0
4	3	12.101±0.05	12.091±0.14	10.912±0.06	9.851±0.06	9.791±0.09
5	4	29.305±0.06	28.831±0.02	26.571±0.05	26.008±0.02	25.451±0.08
6	5	45.693±0.05	45.367±0.10	44.136±0.05	43.194±0.14	43.121±0.12
7	6	56.521±0.05	56.023±0.14	52.107±0.10	51.549±0.09	49.923±0.08
8	7	70.801±0.02	69.936±0.06	69.023±0.11	68.762±0.10	68.054±0.04
9	8	86.269±0.06	86.201±0.02	85.975±0.12	84.856±0.12	84.556±0.07
10	9	92.764±0.05	92.151±0.08	91.901±0.09	90.886±0.10	90.221±0.15
11	10	97.839±0.3	97.229±0.12	96.865±0.08	95.992±0.01	95.011±0.02

All values are expressed as mean ± standard deviation, n=3



Graph 5 : Stability study of tablet

Table No 11 : Stability study at 40°C ± 2°C / 75 ± 5% RH

Stability study	% Drug Content	Lag Time (min)	Apperence
0 Days	98.15 ± 0.03	192 ± 0.643	No Change
1 Weeks	98.11 ± 0.03	192 ± 0.643	No Change
2 Weeks	97.15 ± 0.03	192 ± 0.643	No Change
3 Weeks	97.15 ± 0.03	192 ± 0.643	No Change
4 Weeks	97.14 ± 0.03	192 ± 0.643	No Change

It was concluded that F8 were having sufficient lag time of 192 ± 0.643 . The greater the lag time, more will be the time taken by the dosage form to release the drug.

The selected formulation (EC8) was found to be stable upon storage for 4 week. No change was observed in the appearance, hardness and average weight of the tablet. Also no significant change was observed in the *in-vitro* release of the drug.

CONCLUSION

From the above results we can conclude that Celecoxib enteric coated tablet formulations prepared with Gaur Gum , HPMC K4M, showed acceptable properties like friability, weight variation, hardness etc and *in-vitro* drug release which remained unchanged upon storage for 4 week. Eudragit L100 and S 100 was the most susccesfuly coating polymer. Celecoxib tablets with the formulation code EC8 proved to be the formula of choice, While coating ratio 1:1 was selescted for coating, using the 8% enteric coating, more drug was degraded in the small intestine. Also, using the 12% coating, the release of drug in the pH 6.8 (colonic pH) was very less as compared to the 8% and 10% enteric coating. So, the optimized formula of coating consisted of 10% coating of tablets. since it showed the highest drug release and lag time. So, Celecoxib tablets can be used in sustained delayed drug delivery in treatment of ulcerative colitis so as to reduce the side effects of drug in stomach and also to reduce the dosing frequency of the drug.

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