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In vitro – In vivo evaluation of aceclofenac colon drug delivery system

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Abstract
In the present study, drugs were targeted to colon by using combination of pH reliant polymers used to make Aceclofenac pellets coated with multiple layers of swelling polymer and time dependent polymer. The drug solubility was maximum at alkaline or weak acidic than strong acidic conditions for Aceclofenac. Multiparticulate approach to achieve colon targeted Aceclofenac pellets containing Hydroxypropyl cellulose as swelling layer to retard the drug release in a sustained manner and Ethylcellulose as time dependent outer coating, to protect the upper GI environment conditions. Both polymers were coated on the drug absorbed beads in conventional coating pan. Furthermore, *in-vivo* gastrointestinal transit of drug irrespective of their type of polymer used to delay the released at pre-designed time intervals. Also physical presence and quantitative analysis of drug pellets at small intestine colon are estimated. Presume that the drug is well scattered and absorbed at intestine and colonic areas from the measured length and amount of drug analysed. It was studied for combinations of polymers could achieve budding applications as a colon–specific drug delivery device with added gain for scale up.

Keywords: aceclofenac, hydroxypropyl cellulose, EC, colon drug delivery

1. Introduction
Colon is the best site for those drugs which are prone to degrade by physiological enzymes on stomach or intestine. Formulation which designed to act locally for the treatment of colorectal cancer, Crohn's disease and ulcerative colitis would be more proficient. Drugs that were originated from protein or peptides degraded upon exposure to acidic conditions of upper GIT. Drugs that were delivered through anal were interchanged to colon route due to ability of extended hold time [1-2].

Aim of present work was design and develop consistent and optimized formulations of Aceclofenac multiparticulate targeted drug delivery to colon with the following objectives. The first purpose of the study was developing multiparticulate CDDS by means of swelling and time dependent polymers such as hydroxypropyl cellulose (HPC) and ethyl cellulose (EC) embedded on Aceclofenac to let loose the drug at colon in a sustained manner.

The optimized formulation was selected and studied for stability followed by *in vivo* studies were done.

2. Materials and methods
2.1 Materials
Aceclofenac was procured from Rachita Pharma. Ltd, HPC, EC were procured from Signet chemicals, HPMC from Colourcon Asia Pvt. Ltd, All other chemicals were of analytical grade

2.2 Preparation of Aceclofenac colon targeted delayed release pellets
The Aceclofenac colon targeted release pellets formulation involves three different steps which includes drug absorption to sugar spheres by dissolving Aceclofenac and HPMC E5 in acetone. Hydroxypropyl Cellulose was used in swelling polymer covering of drug pellets and functional coating with ethyl cellulose 7cps at different concentrations as mentioned in the composition of formulation's are as described in table 1. The processes are carried out for three stages at pan coating equipment shown in table 2.

2.2.1 Step -1 Drug layering Process
Drug wrapped sugar spheres were prepared by taking sugar pellets of 30-35# fractions pre-warmed at 35^0C in a pan (ideal cures convectional coater). Aceclofenac and 1.5% (w/v) HPMC E5 dissolved in acetone were squirted with the help of spray gun. Drug was absorbed on to the core pellets; bed temperature and airflow were fabricated appropriately to keep away from overheating. It may cause loosing of drug from beads on repeating pan rotation. Drug layering process by conventional pan coating was adopted based on the scientific literature for the preparation of ketopfroen pellets by powder layering technology [3].

2.2.2 Step -2 Coating of swelling layer
HPC along with PEG 6000 as plasticizer at different concentrations in aqueous conditions using coating pan layered drug beads to reach required weight gain. The process parameters kept in controlled range for producing consistent formulations and reducing variability in dissolution profile.

2.2.3 Step-3 Coating with Ethyl cellulose
The swelling layer was covered by various conc. of ethyl cellulose 7cps. Measured quantity of EC, polyethylene glycol 6000 2.55 % w/v in water were was liquefy in isopropyl

alcohol to get clear solution and sprayed onto the encumbered beads in anticipation of longing coating intensity achieved. Surface temperature and air flow were adjusted to reduce friability of pellets, the beads finally cured for 12 hour at 40^0C on hot air oven.

Table 1: Compositions of Aceclofenac colon targeted delayed release pellets

Ingredient	Amount
Drug loading	
sugar pellets	80-150 gm
Aceclofenac	25-35g
HPMC E5	0.5 -2g
Swelling polymer coating	
HPC	3-10%
Enteric polymer coating	
EC 7cps	10-20%
PEG 6000	2-3%

Table 2: Process parameters for coating (Ideal cure coating machine)

Stage → Parameter ↓	Drug loading	Functional layer I	Functional layer II
Pan size	6 inch	6 inch	6 inch
In let temp	50^0C + 5^0 C	65+ 5^0C	65+ 5^0C
Bed temp	30^0 C+ 3^0 C	45^0 C + 3^0 C	35^0 C + 3^0 C
Pan speed	5 – 20 rpm	5 – 25 rpm	10 – 40 rpm
Spray rate	1– 5 gm/min	1– 5 gm/min	2 – 10 gm/min
Atomization pressure	1-3 bar	1-3bar	1-3 bar

3. Pre-formulation studies of aceclofenac

Pre-formulation studies were carried out to understand pH dependent solubility, active pharmaceutical ingredient and polymers compatibility in the formulation.

3.1 pH solubility profile

Aceclofenac was subjected to pH dependent solubility studies.

1. 0.01N HCl
2. pH 4.5 Acetate buffer
3. pH 6.8 phosphate buffer
4. pH 7.2 phosphate buffer
5. Purified Water

1.0 gm quantity of drug was weighed and relocates to individual 25 ml glass container then different pH solutions were added and mix well then quantity was made; samples were set aside in steady water bath shaker at temperature of 37 °C and removed behind twenty four hour from bath. Solution equilibrated for 1 hour then filtered. The dissolved portion was measured using HPLC method for Aceclofenac respectively after suitable dilutions [4].

3.2 Compatibility Studies

Aceclofenac alone and physical mixture with excipients prepared as per the composition ratio's given in table 3 and stored in glass vials. These vials are exposed to various environmental stress conditions like temperature and humidity, results material undergoes interaction at molecular level and/ a physical transformation such as phase transitions and melting point change due to interaction between materials, which can be detected by infrared spectral analysis and differential scanning calorimeter [5].

3.2.1 Differential Scanning Calorimeter (DSC)

The API and polymers were subjected to compatibility, to understand when blended any transform arise in melting point of the drug. It was conducted at a rate of 6°C min^{-1} from 26°C to 305°C temperature series under nitrogen flow of 30 ml min-1 using DSC.

3.2.2 Fourier Transform Infra-Red (FT-IR) spectral analysis

Spectrum analysis performed in mixture at range of 405 to 4005 cm^{-1} and the decree was 1.5 cm^{-1} using FTIR spectrophotometer.

Table 3: Physical mix of Aceclofenac for compatibility studies

S. No	Name of the Binary Mixture	Composition Ratio
1	Aceclofenac	Not Applicable
2	Aceclofenac + Sugar Sphere	1 : 5
3	Aceclofenac + Hydroxypropyl Cellulose (Klucel LF)	1 : 1
4	Aceclofenac + Ethyl cellulose 7 cps	1 : 1
5	Aceclofenac + Polyethylglycol 6000	1 : 0.5
6	Aceclofenac + Hypromellose (Methocel E5)	1 : 0.5
7	Aceclofenac + Hypromellose + Ethyl cellulose + Hydroxypropyl Cellulose	1:0.5:1:1

4. Characterization of aceclofenac CDDS

Bulk density = Weight of the powder/Bulk volume
Tapped density = Weight of thr powder/Tapped volume
Carr's index (%) = [(TD-BD)*100] / TD
Hausner's Ratio = TD / BD

4.1 Sieve analysis

Particle size distribution study was carried out by sieve analyser (Retsch AS 200) using standard screens of aperture size 16, 18, 20 and 100 gm pellets weighed and transferred to sieve shaker then allow for shaking 50 Amplitude per 10 min. The sieve analysis shows enteric coated pellets are well distributed between 20-24# screen. It indicates pellets were uniform, spherical and followed efficient process.

4.2 Morphology of pellets by scanning electron microscopy (SEM)

The external structure and snappy section of beads of optimum formulation was checked by means of scanning electron microscope. This was carried out to find the uniformity and thickness of coating, which is determining factor for evaluation of physical parameters.

5. *In-vitro* dissolution studies

Dissolution conditions for Aceclofenac formulation

Polymer coated pellets

Medium :
1. 0.1N HCl for 2 hrs.
2. pH 7.4 Phosphate buffer for 3 hrs.
3. pH 6.8 Phosphate buffer for 12 hrs.

5.1 Test Preparation procedure

Dissolution medium filled in bowls 900 ml and temp kept at 38±0.5 °C. Capsule doped to each glass beaker and test started. Withdrawn 10 ml of aliquot were at definite time interval with a magnitude of fresh media was replaced. Solution was filtered through 0.45 µ (Millipore) nylon filters. Reject the little quantity of filtrate and 5ml of solution was diluted to 10 ml with same solution.

6. *In vivo* studies

6.1 Animal organ distribution examination

Optimum formulations were selected to study the GI transit; protocol was approved previously by Institutional animal ethical committee (IAEC) and approved by CPSEA members as per the protocol and rules and regulations. Healthy Wister rats weighing 250- 300 gm are selected and set aside in well-spaced ventilated cages and preserve healthy with fixed diet (Bengal gram soaked in water).

The animals are divided in to two groups of standard and test for Aceclofenac delay release pellets as mentioned below
1. Standard group: 6 Rat for each time point (2, 4, 6 & 8 h).
2. Test group: 6 Rats for each time point (2, 4, 6 and 8 h).

The animals are kept on overnight fast (16-20 h). The pellet formulation equivalent to 100 mg pellets equivalent to 20 mg Aceclofenac polymer coated pellets and uncoated drug core pellets as reference in study was administered orally via cannula to stomach by suspending the pellets in suitable medium (dissolving Xanthan gum 0.2% in water and kept for 2-3 h for complete swelling and uniform suspension), flush water 2-3 ml to facilitate the entry of drug suspension.

The animals from both groups are sacrificed after anaesthesia at end of time points 2, 4, 6 & 8 h and the viscera was dissected to take portion starting from stomach to rectum isolated. The position of pellets travelled are located after 2 h at duodenum, 4 h at ileum, 6 h cecum and 8 h colon for test animals and length is visually checked and the distance travelled by the formulations of test and reference measured for the each time points[6-7]. The GI tract transversely dissected and then contents transferred to 30 mm of phosphate buffer pH 6.8 also added 1 ml acetonitrile and kept for 1 hour. The suspension was centrifuged to separate the supernatant liquid. The samples were analysed by UV method to calculate drug content. The percentage drug released in GI tract at each instance was calculated by subtracting the percentage drug recovered from each pellets from 100% to find out the drug loss during transit throughout GI tract.

7. Results and Discussion

7.1 Estimation of Aceclofenac SR pellets in Dissolution media.

The absorbance measured for Aceclofenac CDDS for the test and standard preparation at a fixed wavelength 275 nm. The results represented in figures 1 and 2.

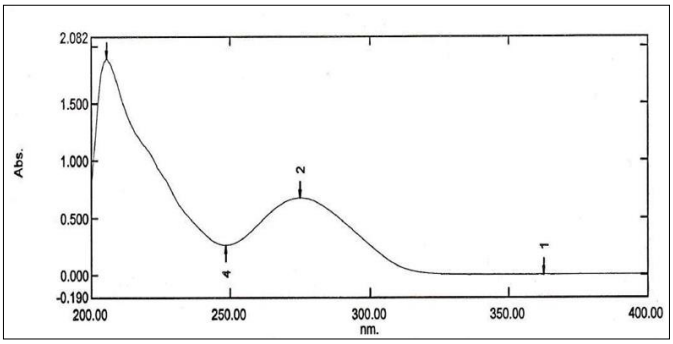


Fig 1: UV-spectrum of Aceclofenac drug (200-400 nm)

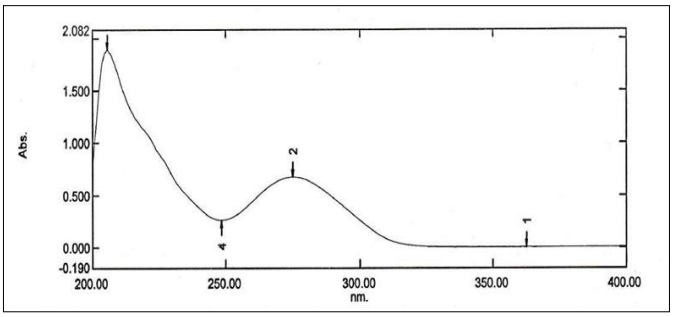


Fig 2: UV-spectrum of Aceclofenac formulation (200-400 nm)

7.2 Solubility Analysis of Aceclofenac

The solubility study of Aceclofenac API was carried out. The results represented in the below table 4 and graph 3. The solubility of Aceclofenac was 0.098 mg/ml at pH1.2 and observed to be increased gradually with increasing the pH reaching 9.2 mg/ml at pH 7.4 phosphate buffer. Therefore, the solubility study indicates that the solubility Aceclofenac is pH dependent.

Table 4: Solubility profile of Aceclofenac drug

S. No.	Media	Solubility (mg/ml)
1	Water	0.11
2	0.1 N HCl (pH 1-2)	0.098
3	pH 4.5 Acetate buffer	3.6
4	pH 6.8 Phosphate buffer	6.5
5	pH 7.2 Phosphate buffer	9.2

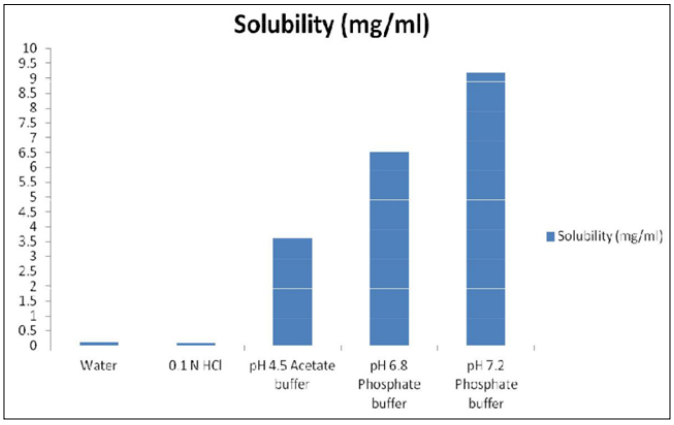
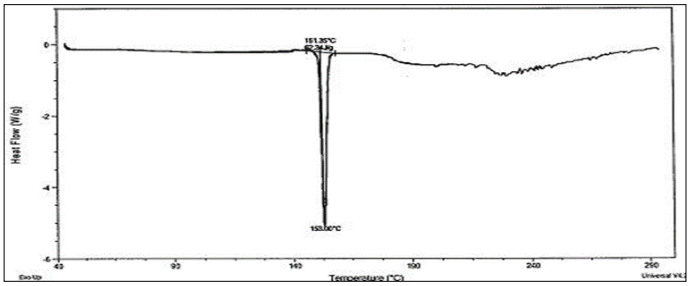


Fig 3: Graphical representation of Aceclofenac drug solubility



Compatibility Studies Aceclofenac along with Excipients

Fig 4: DSC of Aceclofenac pure API

Table 5: Physical description results of Aceclofenac and physical mixtures

S. No	Name of the Binary Mixture	Composition Ratio	Physical Observations
1	Aceclofenac	NA	No colour change
2	Aceclofenac + Sugar Sphere	1 : 5	No colour change
3	Aceclofenac + Hydroxypropyl Cellulose	1 : 1	No colour change
4	Aceclofenac + Ethyl cellulose 7cps	1 : 1	No colour change
5	Aceclofenac + Poly Ethylglycol 6000	1 : 0.5	No colour change
6	Aceclofenac + Hypromellose	1 : 0.5	No colour change
7	Aceclofenac + Hypromellose + Ethyl cellulose + Hydroxypropyl Cellulose	1:0.5:1:1	No colour change

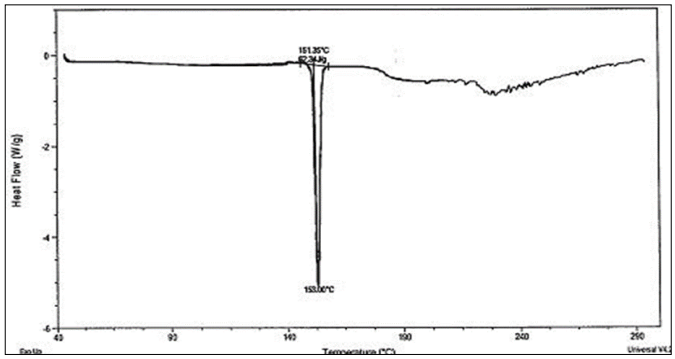


Fig 5: DSC of Aceclofenac + polymer physical mixer

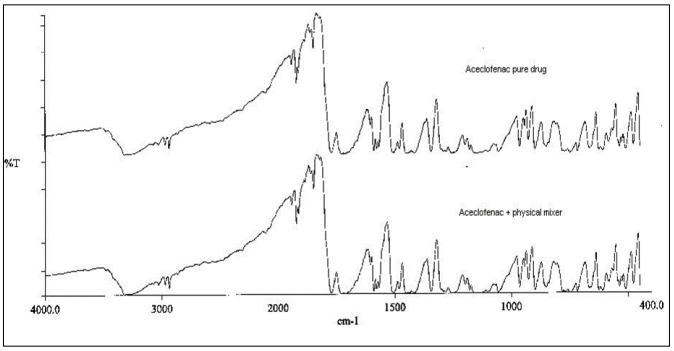


Fig 6: FT-IR spectrum of Pure Aceclofenac drug and Aceclofenac physical mixer

Table 6: Characteristic frequency of Aceclofenac API

Frequency (cm^{-1})	Functional Group
1771.47	C=O bending
1716.89	COOH bending
1589.53	NH bending
1055.90	OH bending

Table 7: Characteristic frequency of Aceclofenac Physical mix

Frequency (cm^{-1})	Functional Group
1771.62	C=O bending
1716.76	COOH bending
1589.84	NH bending
1055.88	OH bending

Aceclofenac exhibited an endothermic peak at 154.96^{0}C analogous to melting point of crystalline form[8]. For the physical mixture of drug and ingredients, the endothermic peak was observed at 153.0°C. Endothermic peak of drug and its physical mixture with ingredients at similar temperature confirms that there is no potential interaction between drug and ingredients.

The IR spectrum of pure drug, showed powerful bands at 1771.47 cm^{-1}, 1716.89 cm^{-1}, 1589.53 cm^{-1} and 1055.9 cm^{-1} consequent to functional groups C=O, COOH, NH2 and O-H bending, respectively. Brand of these functional groups were noted at 1771.62cm^{-1}, 1716.76 cm^{-1}, 1589.84 cm^{-1}, 1055.88cm^{-1} in the spectrum of API and excipient. This explains foremost shift in frequency of above said main groups of Aceclofenac not occurred. Therefore, the visual observation of the physical mixture, DSC thermo gram and IR spectrum implied that the drug was compatible with the ingredients selected for its formulation development.

7.3 Physical and chemical properties of finished product

Bulk density, Tapped density and sieve analysis was carried out as per procedures for Aceclofenac final coated pellets. The results were demonstrated in table 8 and 9

Table 8: Physical characteristics of Aceclofenac CDDS DR pellets

Characteristics	F1	F2	F3	F4	F5	F6
Bulk density (g/ml)	0.548	0.556	0.545	0.521	0.550	0.534
Tapped density (g/ml)	0.616	0.626	0.607	0.637	0.609	0.634
Angle of repose (°)	33	32	33	33.4	32.6	33.2
Hausner's ratio	1.12	1.12	1.11	1.11	1.10	1.18
Carr's index (%)	11.0	11.18	10.21	10.54	9.69	11.0

Table 9: Cumulative percentage retain of drug pellets after sieve analysis

Mesh aperture size	F1	F2	F3	F4	F5	F6
#16	1.55	1.45	1.50	1.46	1.18	1.25
#18	4.3	4.33	4.1	4.0	4.81	4.55
#20	28.93	28.83	28.23	28.12	27.893	28.56
#24	99.42	99.22	99.18	98.65	98.72	99.87
Pan	100	100	100	100	100	100

Bulk density of all the formulations were very close with a narrow range of 0.521 - 0.556 g/ml. Similarly the tapped density of the different formulation was within the range of 0.607 - 0.634 g/ml. The density data confirmed that the required amount of pellets containing single dose of the Aceclofenac (50 mg) could be delivered with a '0' size capsule having volume capacity of 0.68 ml[9]. HR and CI of the all formulations were ranging from 1.10 to 1.18 and 9.69 - 11.18 %, respectively. It indicated that the formulations had good flow property to fill in the capsules[10]. The good flow property of the formulation was further supported by low angle of repose data which was ranging from 33.0° to 33.4°. The sieve analysis shows enteric coated pellets are well distributed between 20-24#. It indicates pellets were uniform in size, spherical in shape and almost no agglomeration. This reflects the efficiency of selected process range and its reproducibility.

7.4 Pellets outer layer texture

Images of the surface and cross sectional SEM for optimized formulation batch no F5 were shown in figure 7 and 8

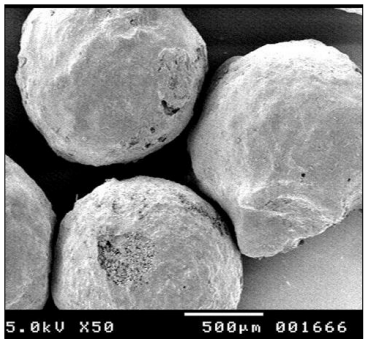


Fig 7: Surface morphology of Aceclofenac coated pellets

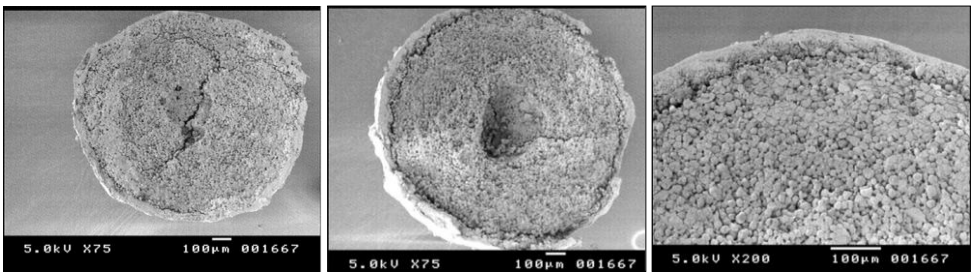


Fig 8: Cross sectional images of polymer coated Aceclofenac pellets

7.5 *In-vitro* profiles

The rate of drug dissolved at 0.1 N HCl, phosphate buffer pH 7.4 and pH 6.8 were performed individually and continues manner by changing the media one after other. The cumulative % drug release was illustrated in table 10, 11 and 12. The Graphical layout of dissolution profile of individual media portrayed at figure 9, 10 and 11. The cumulative percentage drug release of Aceclofenac colon targeted optimum formulation carried out at continues medium, results were depicted in table 5.33 and graphically at figure 5.36.

Table 10: Cumulative % Drug release in 0.1 N HCl media

Time (h)	F1	F2	F3	F4	F5	F6
0	**0**	**0**	**0**	**0**	**0**	**0**
1	17.52±0.43	16.4±0.46	15.6±0.61	4.9±0.76	3.9±0.36	1.6±0.07
2	24.52± 0.46	20.64±0.45	17.13±0.44	5.14±0.77	4.45±0.35	2.17±0.17

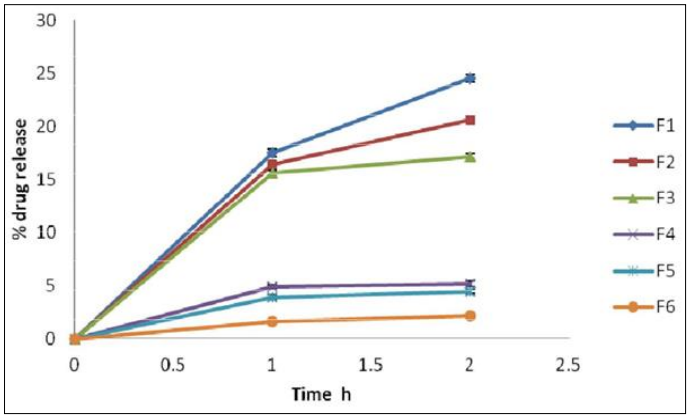


Fig 9: *In-vitro* drug release in 0.1 N HCl

Table 11: Cumulative % Drug release in pH 7.4 Phosphate buffer

Time h	F1	F2	F3	F4	F5	F6
0	**0**	**0**	**0**	**0**	**0**	**0**
1	26.84±1.68	22.15±2.89	19.52±2.94	16.88±1.69	14.5±2.56	13.14±0.93
2	32.23±0.73	28.65±0.79	24.5±0.89	23.04±0.78	22.2±0.95	20.07±0.66
3	39.89±0.78	36.68±0.88	34.15±1.02	32.43±0.79	28.6±0.98	26.01±0.42

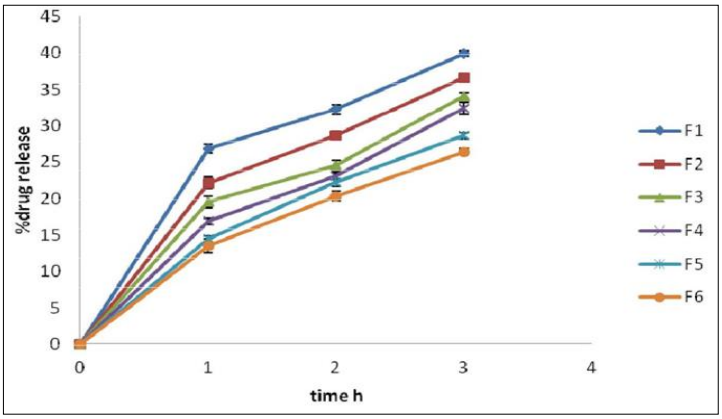


Fig 10: *In-vitro* drug release in pH 7.4 Phosphate buffer

Table 12: Cumulative Drug release in pH 6.8 Phosphate buffer

Time h	F1	F2	F3	F4	F5	F6
0	**0**	**0**	**0**	**0**	**0**	**0**
1	48.61±2.40	46.32±2.10	45.89±1.98	38.15±1.79	34.21±2.55	8.73±0.32
2	56.54±1.34	55.59±2.0	53.21±1.23	49.17±1.09	43.76±1.87	20.25±0.44
3	68.37±1.02	67.35±1.45	64.13±0.95	56.16±0.86	53.23±1.03	32.96±1.39
6	79.35±0.96	78.61±0.79	75.24±0.89	69.13±0.78	68.73±0.78	45.32±1.11
12	88.52±0.64	86.25±0.55	83.69±0.67	83.78±0.69	83.64±0.77	75.90±1.55

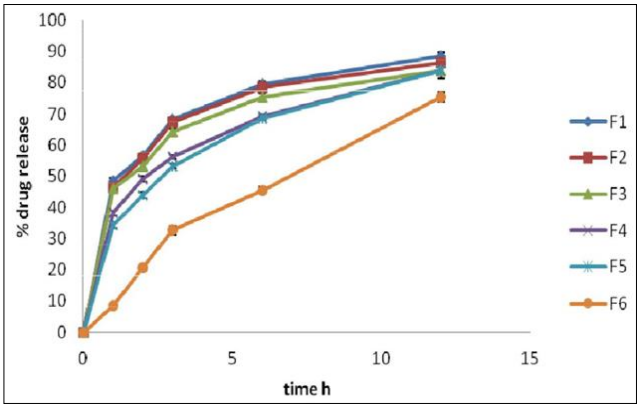


Fig 11: *In-vitro* drug release in pH 6.8 Phosphate buffer

Table 13: Cumulative % Drug release of F5 in continuous dissolution media's

Time (h)	% drug release
0	**0**
1	3.9±3.04
2	4.45±2.89
3	14.5±2.05
4	22.2±1.88
5	28.6±1.46
6	34.21±0.99
7	43.76±1.06
8	53.23±0.79
10	68.73±0.92
12	83.64±0.50

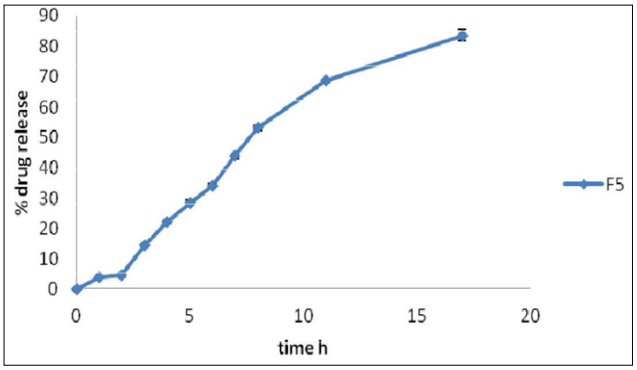


Fig 12: *In-vitro* drug release of batch F5 in Continuous

Media

It was observed that keeping 10 % EC coating constant, the drug release at the end of 2 h dissolution in 0.1N HCl media decrease significantly from 24.52 % to 17.13 % when HPC coating increased from 3 % to 7%. In addition, a dramatic reduction in the drug released from in 0.1 N HCl was noted with increase EC coating from 10 % to 20%. Therefore, this study indicated that EC coating level is more important to regulate drug release in 0.1 N HCl.

The percentage drug discharge in phosphate buffer pH 6.8 found at end of 12 hrs. to be 88.52 ± 0.16%, 86.25 ± 0.58%, 83.69 ± 0.24% for first three formulations (F1-F3). The polymer level increment decreased dissolution in formulation batch F4 and F5 was 83.78 ± 0.23% and 83.64 ± 0.67% individually. The drug release decreased with increased concentration of HPC and/or EC.

This delay depends on concentration and thickness of HPC coating, release rate pellets was controlled manner at colonic environment compared to other part of GIT. The experimental trials except F1 – F3 were not able to target the colon, but lot F5 made known prolonged release in all mediums than fourth lot.

Results divulge the percentage of drug dissolved for reproduced optimum formulation lot F 5 at pH 1.2 (for 2h almost nil release, less than 10 % at pH 6.5 (for 1 h), was not more than 25 % at pH 6.8 (for 2 h) and rest all drug released at pH 7.4 in a continue dissolution method. Therefore, this formulation was subjected for *in-vivo* GI transit time studies because the ethyl cellulose could protect the initial quick release and major amount of Aceclofenac DR pellets could pass on to the colon.

7.6 *In-vivo* studies

In-vivo study of Aceclofenac colon targeted pellets was carried out by dosing Wister rats. However, the pharmacokinetic analysis was out of scope in this study. Hence, *in-vivo* experiment was designed to ensure that the drug loaded formulation reaching to colon in a specified time without significantly releasing the drug in upper region of GI tract. The total length of GI tract and the site at which the unabsorbed test formulation found was measured for both groups were displayed at table 14 and 15, respectively. The percentage drug absorbed after deducting the values from the unabsorbed percentage was presented in table 16 and graphically represented at figure 13. The GI tract exploited at 6^{th} and 8^{th} hour interval to observe test formulation was pictured and image depicts at plate no 1 and 2.

Table 14: Total length of GI tract (stomach to rectum)

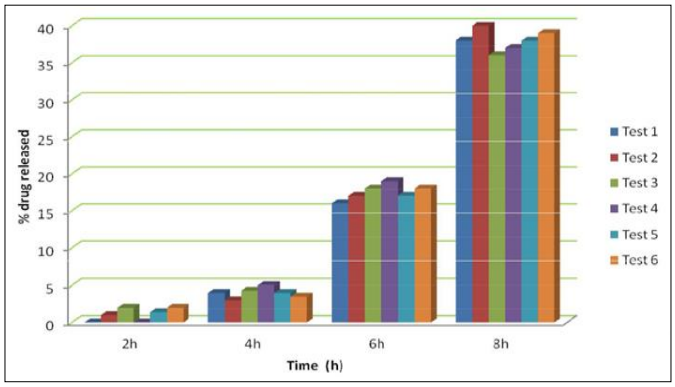
Group	STD (length)	Test (length)
I	95,90,100,93,95,98 cm	92,94,98,100,93,103 cm
II	90,94,99,100,93,101 cm	95,95,90,96,99,96 cm
III	93,90,97,105,92.3,94 cm	96,91,100,93,97,98 cm
IV	95,96,90,96,99,94 cm	93,92,97,104,92.3,94 cm

Table 15: Aceclofenac formulation measured at GI tract locations

Time (hrs)	Test (length)
2h (Duodenum-Jejunum)	14, 13, 15, 12.4, 13 and14.2 cm
4h (Jejunum –Ileum)	49, 52, 53, 54.2, 55 and 51cm
6h (Ileum – Cecum)	80, 84, 78, 79.4, 83 and 80.4cm
8h (Ascending to sigmoid colon)	94, 96, 96, 100, 98 and 97 cm

Table 16: Percentage drug released at GI tract of Wister rats

Time in hour	% drug released					
	Test 1	Test 2	Test 3	Test 4	Test 5	Test 6
2	1	1	2	0	1.4	2
4	4	3	4.3	5	4	3.5
6	16	17	18	19	17	18
8	38	40	36	37	38	39



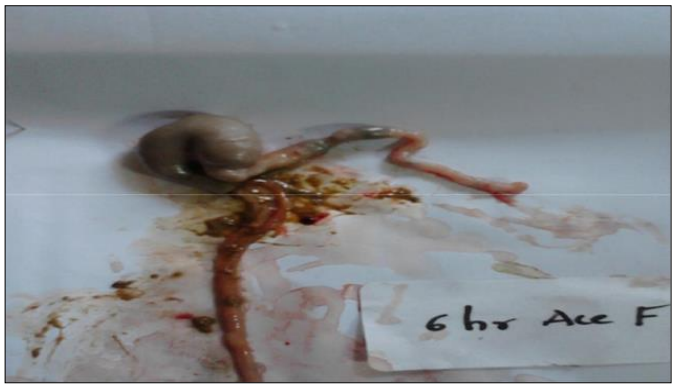


Fig 13: Percentage of Aceclofenac reached at various GI sites of Wister rats

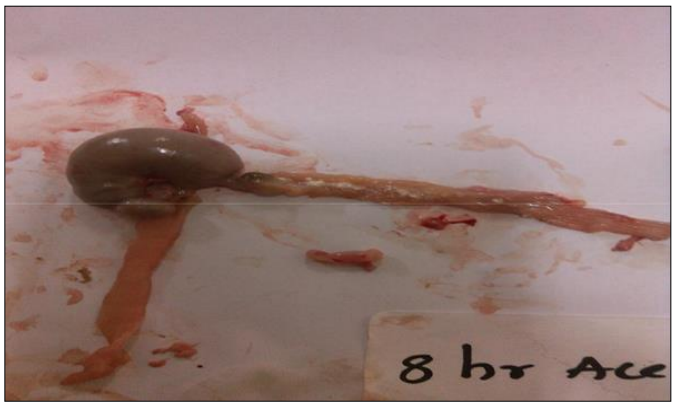


Plate 1: Photograph depicting location of Aceclofenac drug pellets in GI tract of Wister rats after 6th hour administration of test formulation

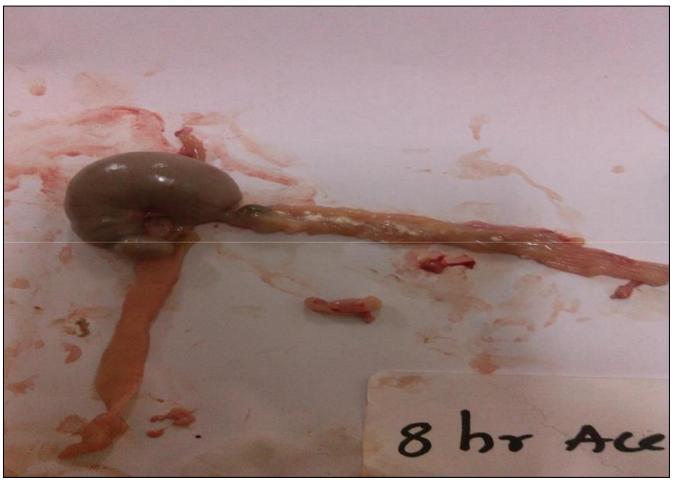


Plate 2: Photograph depicting location of Aceclofenac drug pellets in GI tract of Wister rats after 8th hour administration of test formulation

The total length of isolated rat GIT was found to be 97± 2.5 cm. The formulations was recovered at regular time intervals at a distance of 14.25± 2.53 cm (duodenum region) at 2 h, 54.50 ± 10.61 cm (small intestine) at 4h, 80± 3.54 cm (cecum) at 6h, and 97.50± 3.2 (colon) at 8 hr, the fraction of drug released in GI tract at each time point was calculated by subtracting the percentage drug recovered from formulation. The percentage pellets at each end of the fourth hour was nearly 80%, indicating that drug released release was minimal (20%) in upper GI tract however, release may have been rapid afterwards, as percentage drug recovered at 6h (from cecal region) was only 25% and that from the colon was less than 15%. The high amount of drug loss in cecal region is attributed to the relatively higher pH of the cecum (6.58 ± 0.4) that could have dissolved polymers and enhanced drug release. Thus, it was concluded that, as drug loss during passage to upper GIT was minimal, the formulation could act as a budding colon-specific delivery device.

7.7 Stability study

The compiled results stability studies reports for formulation F5 subjected to conditions were displayed in table 17.

Table 17: Compiled stability study results

Parameters	Time period			
	Initial	1 Month	2 Month	3 Month
Description	Complies	Complies	Complies	Complies
Drug content (%)	100.1	99.9	99.8	99.9
Dissolution				
Time (h)	Cumulative % drug release			
0	0	0	0	0
1	3.90±1.23	3.86±2.05	3.92±2.42	3.96±2.12
2	4.45±1.45	4.52±2.13	4.43±2.15	4.56±2.03
3	14.50±1.43	14.39±2.42	14.53±1.85	14.59±2.45
4	22.20±1.05	22.12±1.84	22.2±1.46	23.1±1.65
5	28.60±1.06	28.49±1.76	28.56±1.53	28.58±1.43
6	34.21±0.86	34.25±1.43	34.35±1.42	34.13±1.02
7	43.76±0.46	43.56±0.86	43.63±1.34	43.71±0.76
8	53.23±0.75	52.97±0.45	53.68±0.45	53.36±0.83
10	68.73±0.86	68.49±0.42	68.83±1.46	68.92±0.49
12	83.64±0.52	83.43±0.47	83.29±1.72	83.88±0.70

8. Summary and conclusions

The *in-vitro* data of formulation exhibits right disso profile and polymers can hold back the release of drug as indented. They were proven effect during *in-vivo* studies. Taking into account the complexity of CDDS and the ambiguity of present dissolution models in create promising *in-vitro*/*in-vivo* association, challenge stay on for developmental scientist to formulate and authenticate an *in-vitro* technique that integrate the physiological circumstances of large intestine and this can be utilized for quality control test for routine manufacturing.

The delivery systems manufactured for this study ought not to be gravely exaggerated by amplify or a decline in the habitation time because the outer coat is pH-dependent and/ independent. Nevertheless, further studies are required to assess the usefulness of these designs in patients for Rheumatic arthritis by Aceclofenac colon targeted formulations.

9. References

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