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RESEARCH ARTICLE

Formulation, Evaluation and Optimization of Time and Enzyme Dependent Polymers Matrix Based Tablet for Colon Targeted Drug Delivery

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ABSTRACT

The present research examines the physicochemical attributes of formulation needed to retard drug release of polymer matrix prior to its arrival at colon and evaluate the therapeutic value of polymer matrix in association with colon polyps. The colon specific drug delivery is a current need for the treatment of colon polyps or familial adenomatous polyposis (FAP), because the FAP is further converted into colon cancer. The colon targeted matrix tablets of Indomethacin were formulated by using pectin and HPMC K 100 M polymers. All the formulations were evaluated for hardness, drug content uniformity and other physical properties. The drug release studies were carried out in simulated gastric fluid of pH 4.5 followed by phosphate buffer pH 7.4 and pH 6.8 solutions. A 3^2 full factorial design was used for optimization by taking the amounts of HPMC K100M (X1) and Pectin (X2) as independent variables and percentage drug released at the end of 2^{nd}, 16^{th} and 24^{th} hours as dependent variables. X-ray Roentography study of the optimized batch tablet was carried out, from which it was concluded that colon targeting was successfully achieved.

KEYWORDS

Indomethacin, Pectin, HPMC K100M, Roentography, Matrix Tablet

INTRODUCTION

Colonic drug delivery has gained increased importance not just for the delivery of drugs for the treatment of local diseases of colon but also for its potential for the delivery of proteins and peptides.[1] Over the last few years, different approaches have been reported in order to achieve specific colonic drug delivery. Most of the previous literature reports on colonic targeting which had focused on the development of a colonic delivery system, based on time- and pH-dependent delivery systems as well as systems that utilize bacteria, which colonizes the colon or enzymes produced by these bacteria to affect drug release. The poor site specificity problem occurs with time release dosage form due to large variation in gastric emptying time and passage across the ileocecal junction. In addition, poor site specificity of pH-dependent system was very well established due to large variation in pH of the gastrointestinal tract (GIT).[2,3]

Biodegradable systems formulated using natural polysaccharides which are increasingly being developed. Use of naturally occurring polysaccharides is attracting attention for drug targeting to the colon, since these polymers of monosaccharides were found in abundance,

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inexpensive, and available in variety of structures with varied properties. They can be easily modified chemically and biochemically and are non-toxic, hydrophilic, gel-forming, as well as biodegradable in nature. Conventionally, various polysaccharides were used in the tablet formulations to retard drug release. These have been used either as matrices or as a coating material. For matrices, generally a high concentration of polymer is required. Alternatively, these can be used as binders in tablets. Thus, varying the polysaccharides and their concentration affects drug release from the prepared tablet. [4]

The colon specific drug delivery is a current need for the treatment of colon polyps or familial adenomatous polyposis (FAP), because the FAP is further converted into colon cancer. The present research examines the physicochemical attributes of formulation needed to retard drug release of polymer matrix prior to its arrival at colon and evaluate the therapeutic value of polymer matrix in association with colon cancer. The matrix tablet was formulated in combination with time and enzyme dependent polymers. NSAID (non-steroidal anti-inflammatory drug), was selected as a model drug because it has good indication for colonic delivery. Colorectal cancer is the second largest cause of cancer related deaths in industrialized countries. NSAID like sulindac, aspirin, Indomethacin and cox-2 inhibitors etc. has shown anticancer potential in the treatment of colorectal cancer.[5] Amongst the several mechanism proposed for their tumor inhibition potential includes induction of apoptosis, reduction in proliferation rates of HT-29 colon cancer cells, and down regulation of surviving [an apoptosis inhibitor].[6] Hence, it will raise the level of treatment in the prevention of colon polyps and thus preventing the colorectal cancer. The matrix tablet was prepared by using Indomethacin as a drug while HPMC K 100 M as a time dependent polymer and Pectin as an enzyme dependent polymer. For the evaluation of colon targeted tablet, *in-vitro* drug release studies were carried out in simulated colonic fluid with and without rat cecal content, also by using Bacteroides ovatus culture due to its known polysaccharide degradable activity.[7] In present research pectinase enzyme was used instead of rat cecal contents. The drug release studies were carried out in simulated gastric fluid of pH 4.5 followed by phosphate buffer pH 7.4 and pH 6.8 solutions. A 3^2 full factorial design was used for optimization.

MATERIALS AND METHOD

Materials

Indomethacin was a gift sample of drug obtained from Microlabs ltd. Bengluru. Pectin from Krishna pectin lab, Nagpur and HPMC K100 M from Marksan ltd. Goa. All other chemicals used were of analytical grade.

Methods

Preparation of Indomethacin Matrix Tablets

The drug was geometrically blended with excipients as stated in the formulae given in Table 2, using pestle and mortar. Before matrix tablet preparation the mixture were studied for the compatibility by Fourier Transform Infra-red (FTIR) Spectrophotometer and by Differential Scanning Calorimetry (DSC) study. Mixing was maintained for 10 minutes and the powder mixtures stored in well- specimen bottles. The powder mixtures were evaluated for micromeritic properties such as angle of repose, bulk density, tapped density, compressibility index and Hausner's ratio.[8,9,10,11,12] The drug and excipients were accurately weighed according to their quantity given in table 2. The drug and excipients were mixed and blended homogeneously. The final mixture of drug and excipients were compressed on Ten-station rotary tablet press (FLUIDPACK-GMP MODEL) using 12 mm round, plain die- punch. The prepared Indomethacin matrix tablets were obtained and tested for their hardness, friability, drug content, drug release study.

Formulation Development

Optimization of process variables by using 3^2 full factorial designs.

Independent variables:

X_1 –HPMC K100M Concentration

X_2 –PECTIN Concentration.

Dependent variables: *In-vitro* drug release (%) at the 2nd, 5th and 24th hours.

Table: 1 Three Levels of Factorial Design

Coded values	Actual Values (mg)	
	X_1	X_2
-1	50	75
0	75	100
+1	100	125

Table: 2 Composition of HPMC K100M and PECTIN for 9 batches

Bathes	Variables		Actual Values	
	X_1	X_2	HPMC K100M mg	Pectin Mg
F1	-1	-1	50	75
F2	-1	0	50	100
F3	-1	+1	50	125
F4	0	-1	75	75
F5	0	0	75	100
F6	0	+1	75	125
F7	+1	-1	100	75
F8	+1	0	100	100
F9	+1	+1	100	125

Evaluation of Tablets[8, 9,10,11,12]

The formulated tablets were evaluated for thickness and diameter (using a Vernier caliper), hardness test (using Monsanto hardness tester) and friability (using Roche friabilator). For weight variation test, 20 tablets of each formulation were selected at random and weighed individually. The individual weights were compared with average weight for determination of weight variation. For content uniformity test[8], twenty tablets from each batch were powdered individually, a quantity equivalent to 50 mg of Indomethacin weighed and added to 10 ml of water in a 100 ml volumetric flask and allowed to stand for 10 minutes with occasional swirling. Then methanol added to produce the 100ml solution. The resultant solution was filtered. To 5ml of filtrate mixture of equal volumes of methanol and phosphate buffer solution was added to produce 100 ml, absorbance of the resulting solution was measured at 320 nm by using Ultra violet- Visible (UV-VIS.) Spectrophotometer.

***In-vitro* Drug Release Studies[13,14,15]**

The drug release studies were carried out using USP type I dissolution test apparatus at 75 rpm and 37 ± 0.5 °C. The Simulated gastric fluid (S.G.F.) (900 ml) of pH 4.5 was used as dissolution medium in the first 2 hr. of study as the average gastric emptying time was found to be 2 hr. 5 ml of the dissolution medium was withdrawn after every hour to determine the drug release. The volume withdrawn was replaced with fresh media and this was accounted for during calculation of cumulative percentage drug release. The amount of drug release was measured using a double beam UV-VIS. spectrophotometer at λ max of 320 nm.

The dissolution media was replaced at the end of 2nd hr with phosphate buffer of pH 7.4 solutions and drug release study was continued for another 3 hr (i.e. total 5 hr) as the average small intestine transit time is about 3 hr.

The dissolution media was replaced at the end of 5th hr with phosphate buffer of pH 6.8 containing pectinase enzyme. The 3ml of 1% pectinase solution was added to phosphate buffer of pH 6.8 solution to maintain simulated colonic condition instead of rat ceacal content medium. Drug release study was continued for another 19 hr (i.e. total 24 hr). As before, samples were withdrawn at regular 2hr time intervals and correspondingly replaced with

fresh media. The amount of drug release was measured using a double beam UV-VIS. spectrophotometer.

Accelerated Stability Testing According to ICH Q1a (R2) Guidelines

For Accelerated stability study, tablets of F-5 batch were selected (optimized batch). Forty tablets were wrapped in aluminium foil and were placed in amber colored glass container, stored at 40^0C ± 2^0C temp. with the relative humidity of 75%RH ± 5%RH. The samples were withdrawn after one month and evaluation was done for its appearance, hardness, drug content and cumulative % drug release.

Roentography Study[16,17]

The *in-vitro* drug release studies were shown that formulation batch F5 was best for targeted drug delivery to colon. However, the evaluation of dosage form in human not support to *in-vivo* study. Hence roentography study was carried out in healthy volunteer to access the *in- vivo* performance of selected colon targeted tablet.

RESULTS

Compatibility Study[8,9]

IR Compatibility Study

All the principles peaks which are mentioned in FTIR spectrum of Indomethacin were found in physical mixture, maintained at 28^0C during the investigation of compatibility study as shown in fig. 1.

A - Drug Indomethacin

B - Drug + HPMC K100 M

C - Drug + Pectin

D - Formulation Mixture (Drug + HPMC K100 M +Pectin)

Hence IR spectroscopy results showed that the drug is compatible with the given polymers.

Differential Scanning Calorimetry (DSC)

In the DSC Thermogram of pure drug Indomethacin, it was shown an endothermic peak at 158.3^0C which corresponds to their melting points 158-160^0C.

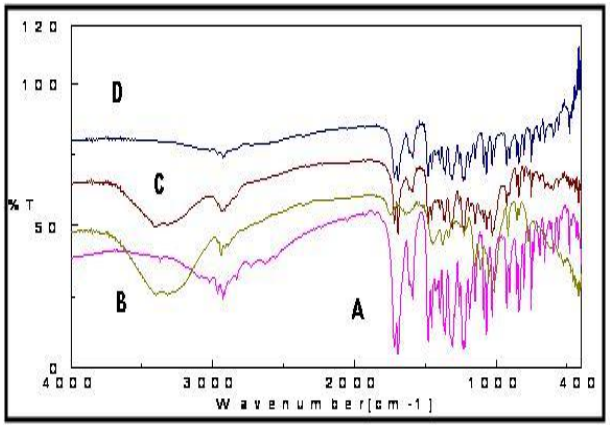


Figure 1: Compatibility study of drug and its mixture with polymers

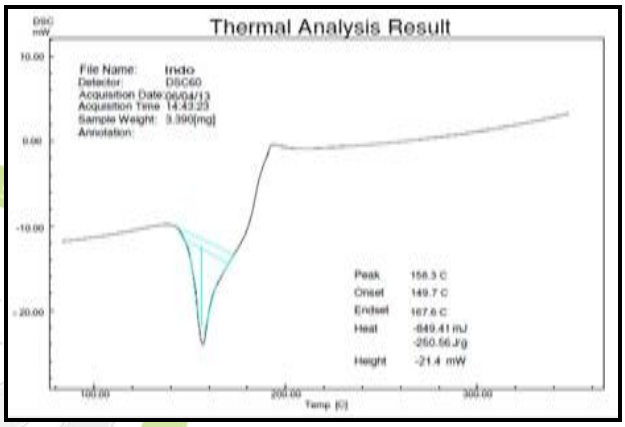


Figure 2: DSC Thermogram of Indomethacin

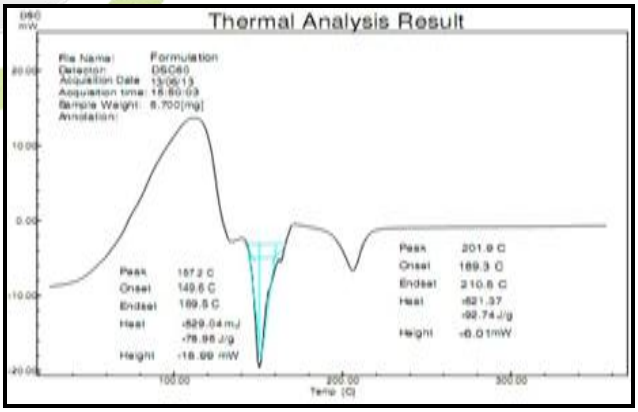


Figure 3: DSC Thermogram of the optimized formulation

In the DSC Thermogram of the optimized formulation batch, the drug Indomethacin also shown the same endothermic peaks at 157.2^0C, hence, it was concluded that the melting point of drug cannot be affected in the formulation and there is no any other derivative or polymorph was formed.

Table: 3 Micromeritics properties of Powder mixture

Formulation	BD*	TD*	C.I. (%)*	Hausner's ratio*	Angle of repose*
F1	0.593 ±0.17	0.716 ± 0.17	17.17 ± 0.15	1.20 ± 0.19	28.6º ± 0.21
F2	0.501 ± 0.11	0.622 ± 0.18	19.45 ± 0.19	1.24 ± 0.19	24.3º ± 0.17
F3	0.582 ± 0.16	0.745 ± 0.19	16.24 ± 0.16	1.27 ± 0.20	28.0º ± 0.16
F4	0.519 ± 0.12	0.609 ± 0.12	14.97 ± 0.13	1.17 ± 0.13	26.6º ± 0.12
F5	0.514 ± 0.10	0.604 ± 0.11	14.90 ± 0.13	1.14 ± 0.09	22.5º ± 0.09
F6	0.541 ± 0.14	0.652 ± 0.15	17.02 ± 0.16	1.21 ± 0.16	26.8º ± 0.16
F7	0.504 ± 0.10	0.624 ± 0.14	19.23 ± 0.20	1.23 ± 0.17	25.4º ± 0.17
F8	0.506 ± 0.11	0.590 ± 0.09	17.74 ± 0.18	1.17 ± 0.14	22.4º ± 0.15
F9	0.496 ± 0.09	0.603 ± 0.11	15.25 ± 0.14	1.21 ± 0.18	23.8º ± 0.16

*****mean ± S.D, n=3

Micromeritic Properties of Powder Mixtures

The powder mixtures of all the formulations were evaluated for angle of repose, bulk density, tapped density, compressibility index and hausner's ratio. The angle of repose was found to be 22.4^0 – 28.62°.

The values of angle of repose were found between good and passable ranges. The bulk density (BD) and tapped density (TD) was found to be in the range of 0.496- 0.593 g/mL and 0.603-0.716 g/mL respectively. The compressibility index (C. I.) and Hausner's ratio was found to be 14.97 to 19.45 and 1.14 to 1.27 indicating good flow character of the powder mixtures as shown in table 3. All the results were found to be within the prescribed limits.[8,9]

Evaluation of Formulated Tablets

Thickness values vary between 3.9-4.1 mm. The hardness of the tablets for all the formulations was in the range of 6.9-7.3 kg/cm^2. The uniformity weight of 20 tablets of all the formulations was within 5% deviation. The friability of all the formulation was less than 1%. Drug content of all the formulations were found to be in the range of 98.06 to 100.32 % (Table 4). All the results were found to be within the prescribed limits.[8,9]

Dissolution Profiles of Tablets

Batches F1 and F2 were shown 91.12% and 91.38% drug release at the end of 16th hour, while batch F3 showed 91.50% drug release at the end of 20th hour and batch F4 showed 91.12% drug release at the end of 16th hour. These all 4 batches showing maximum drug release up to 5 hours about 14.02% to 19.08% i.e. maximum drug released in stomach and small intestine. Hence from the dissolution study, it was showed that release from the matrix tablet was largely dependent on the polymer drug diffusion and matrix erosion.

In-vitro drug release studies of formulations F5 to F9 showed satisfactory drug release in the targeted organ colon. Batch F5 showed lowest drug released in the stomach and small intestine about 7.03% upto 5 hours and maximum about 94% in 19 hours drug released to colon. The maximum drug release was observed in the phosphate buffer pH 6.8 because of degradation of pectin polymer by the pectinase enzyme. Remaining batches F6 to F9 had shown maximum drug released up to 5 hours as compared to batch F5. So from formulations F1 to F9, it was found that F5 batch had shown good drug release characteristics which meets the requirement of colon targeted drug delivery system.

Table: 4 Evaluation study of tablet

Formulation	Thickness*	Hardness* (kg/cm^2)	Friability* (%)	Weight variation** (w/w)	Drug content %
F1	4.0 ± 0.05	6.9 ± 0.38	0.55 ± 0.02	598.15 ± 0.19	98.06 ± 0.26
F2	3.9 ± 0.05	7.0 ± 0.28	0.52 ± 0.05	599.8 ± 0.15	98.74 ± 0.56
F3	4.1 ± 0.1	7.0 ± 0.40	0.60 ± 0.05	601.15 ± 0.31	100.18 ± 0.89
F4	4.0 ± 0.05	7.1 ± 0.60	0.66 ± 0.06	601.05 ± 0.54	98.90 ± 0.76
F5	4.1 ± 0.11	7.0 ± 0.33	0.47 ± 0.04	600.90 ± 0.62	100.32 ± 0.81
F6	4.0 ± 0.1	7.3 ± 0.42	0.77 ± 0.06	599.26 ± 0.49	98.32 ± 0.63
F7	4.1 ± 0.1	7.0 ± 0.51	0.83 ± 0.07	598.70 ± 0.26	98.90 ± 0.54
F8	4.0 ± 0.11	7.2 ± 0.42	0.86 ± 0.03	598.30 ± 0.38	99.06 ± 0.75
F9	4.1 ± 0.05	7.0 ± 0.30	0.74 ± 0.04	600.75 ± 0.91	99.60 ± 0.84

** mean study on for 20 tablets,*****mean ± S.D. n=3

Table: 5 Drug dissolution study (*mean ± S.D. n=3)

Time (hr)	*F1	*F2	*F3	*F4	*F5	*F6	*F7	*F8	*F9
	SGF(Simulated gastric fluid) pH 4.5								
0	0	0	0	0	0	0	0	0	0
1	2.86 ± 0.02	2.74 ± 0.02	1.62 ± 0.42	2.11 ± 0.21	0.98 ± 0.01	1.65 ± 0.42	2.11 ± 0.21	1.26 ± 0.54	0.89 ± 0.02
2	4.96 ± 0.05	4.27 ± 0.42	3.61 ± 0.34	4.32 ± 0.07	1.94 ± 0.07	3.03 ± 0.02	3.39 ± 0.07	2.81 ± 0.21	2.13 ± 0.09
	Phosphate buffer pH 7.4								
3	9.91 ± 0.01	8.14 ± 0.04	8.04 ± 0.22	9.66 ± 0.09	3.98 ± 0.76	6.26 ± 0.32	6.91 ± 0.09	6.01 ± 0.65	3.96 ± 0.71
4	13.99 ± 0.03	13.04 ± 0.09	11.08 ± 0. 12	12.01 ± 0.21	5.31 ± 0.04	8.53 ± 0.09	9.84 ± 0. 21	8.21 ± 0.43	6.89 ± 0.08
5	19.08 ± 0.12	16.94 ± 0.24	14.02 ± 0.21	16.08 ± 0.01	7.03 ± 0.24	11.15 ± 0.06	12.52 ± 0.01	11.0 ± 0.54	9.42 ± 0.20
	Phosphate buffer pH 6.8								
6	28.55 ± 0.32	25.79 ± 0.51	22.01 ± 0.05	26.85 ± 0.23	15.25 ± 0.16	20.88 ± 0.31	21.27 ± 0.23	17.10 ± 0.32	17.98 ± 0.04
8	39.15 ± 0.04	36.84 ± 0.31	31.16 ± 0.08	37.15 ± 0.04	24.67 ± 0.32	28.60 ± 0.63	31.79 ± 0.04	26.04 ± 0.03	25.06 ± 0.11
10	47.33 ± 0.09	47.47 ± 0.06	43.04 ± 0.23	45.33 ± 0.22	36.49 ± 0.46	42.30 ± 0.98	47.93 ± 0.23	32.94 ± 0.34	32.11 ± 0.09
12	61.52 ± 0.01	60.22 ± 0.02	53.09 ± 0.33	60.52 ± 0.32	45.66 ± 0.23	54.38 ± 0.42	59.97 ± 0.32	39.12 ± 0.76	39.80 ± 0.71

14	77.63 ± 0.07	76.90 ± 0.06	62.14 ± 0.04	77.03 ± 0.28	56.21 ± 0.78	63.38 ± 0.01	71.11 ± 0.28	47.64 ± 0.65	48.00 ± 0.11
16	91.12 ± 0.09	91.38 ± 0.28	73.03 ± 0.54	91.12 ± 0.43	68.20 ± 0.73	73.51 ± 0.04	82.90 ± 0.43	54.71 ± 0.47	56.34 ± 0.08
18	99.01 ± 0.02	98.06 ± 0.09	84.71 ± 0.25	99.90 ± 0.52	78.96 ± 0.69	85.40 ± 0.04	90.12 ± 0.52	62.40 ± 0.54	64.78 ± 0.12
20	99.46 ± 0.54	98.77 ± 0.01	91.50 ± 0.04	99.60 ± 0.62	86.12 ± 0.13	93.16 ± 0.54	96.40 ± 0.62	73.01 ± 0.43	72.90 ± 0.08
22	99.51 ± 0.60	99.30 ± 0.12	97.22 ± 0.54	99.31 ± 0.34	93.24 ± 0.63	97.69 ± 0.51	99.54 ± 0.60	84.62 ± 0.16	81.02 ± 0.06
24	99.30 ± 0.47	99.11 ± 0.32	99.02 ± 0.21	99.38 ± 0.56	101.12 ± 0.08	98.90 ± 0.60	99.20 ± 0.58	90.10 ± 0.48	88.60 ± 0.09

Drug Release Kinetics

Table 6: Release kinetics of all formulations with models

Batch Code	Zero order	First order	Higuchi	Hixson Crowel	Korsemeyar peppas parameters			Best fitting model
					N	R	K	
F1	0.982	0.926	0.986	0.912	0.739	0.948	0.776	**Higuchi**
F2	0.984	0.943	0.989	0.973	0.898	0.978	0.291	**Higuchi**
F3	0.977	0931	0.978	0.961	0.988	0.997	0.018	**Peppas**
F4	0.959	0.894	0.965	0.946	0.894	0.971	0.504	**Peppas**
F5	0.970	0.932	0.975	0.968	0.934	0.980	0.234	**Peppas**
F6	0.958	0.912	0.961	0.946	0.801	0.979	0.023	**Peppas**
F7	0.955	0.947	0.937	0.968	0.912	0.977	0.528	**Peppas**
F8	0.935	0.914	0.858	0.946	0.930	0.973	0.043	**Peppas**
F9	0.887	0.896	0.804	0.967	0.898	0.975	0.012	**Peppas**

Table 7: 3^2 full factorial design layout

Batch No.	Variable levels in coded form		Drug release* (%)		
	X_1	X_2	2^{nd} hr	5^{th} hr	24^{th} hr
F1	-1	-1	4.96 ± 0.05	19.08 ± 0.12	99.30 ± 0.47
F2	-1	0	4.27 ± 0.42	16.94 ± 0.24	99.11 ± 0.32
F3	-1	+1	3.61 ± 0.34	14.02 ± 0.21	99.02 ± 0.21
F4	0	-1	4.32 ± 0.07	16.08 ± 0.01	99.38 ± 0.56
F5	0	0	1.94 ± 0.07	7.03 ± 0.24	101.12 ± 0.08
F6	0	+1	3.03 ± 0.02	11.16 ± 0.06	98.90 ± 0.60
F7	+1	-1	3.39 ± 0.07	12.52 ± 0.01	99.20 ± 0.58
F8	+1	0	2.81 ± 0.21	11.00 ± 0.54	90.10 ± 0.48
F9	+1	+1	2.13 ± 0.09	9.42 ± 0.20	88.60 ± 0.09

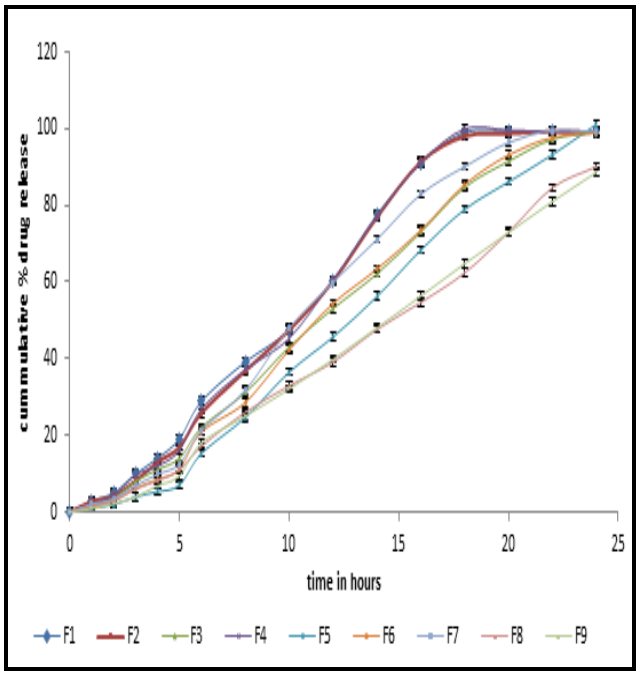


Figure 4: Dissolution profile of all batches

It was found that the *in-vitro* drug release of batch F1 and F2 were best explained by Higuchi model. Higuchi model describes the release of drug from an insoluble matrix as a square root of time dependent process based on fickian diffusion.

As it showed highest linearity (R=0.986 and R= 0.989 respectively). This explains why the drug diffuses at a comparatively slower rate as the distance for diffusion increases, which was referred to as square root kinetics (Higuchi kinetics).

Similarly for batches F3 to F9, the best fit model was found to be Korsmeyer-Peppas, as it indicated a good linearity. (R=0.997, 0.971, 0.980, 0.979, 0.977, 0.973, 0.975 respectively). Both HPMC K100 M and Pectin were swellable type of polymers.

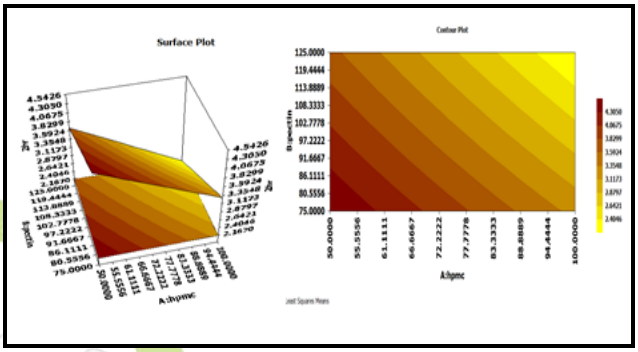
Korsmeyer-Peppas model is the best fit model for swellable type of polymers. The formulation batch F3 to F9 contains high concentrations of these two polymers, hence the possible model for these batches was Korsmeyer-Peppas model. The release exponent 'n' values was found to be in between 0.45 and 0.89, which indicates anomalous type of diffusion means a coupling of the diffusion and erosion mechanism.[18,19]

Table: 8 Coded & Actual values

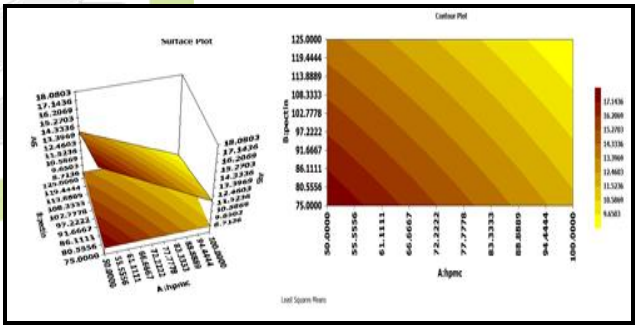
Coded values	Actual values	
	X_1(mg)	X_2(mg)
-1	50	75
0	75	100
+1	100	125

X_1 = Concentration of HPMC K100M,

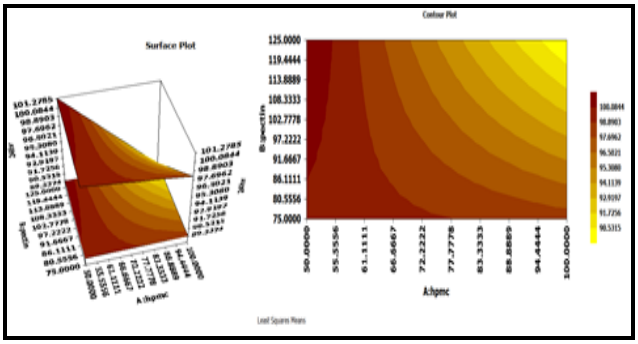
X_2 = Concentration of PECTIN



(At the end of 2nd hr)



(At the end of 5th hr)



(At the end of 24th hr)

Fig: 5 Surface response curve and contour graph for the effect of selected variables on the drug release

Factorial Design with Surface and Contour Plot & Optimization of Process Variables

The surface response curve showed that the both polymer concentration has a significant effect on % drug release of the formulation. As the concentration of HPMC K100 M increase the drug release decreases, while as the concentration of PECTIN decrease the drug release increases. Hence the Optimized Batch was found to be with medium level of concentration of HPMC K100M (X1, 0) and medium level of concentration of PECTIN (X2, 0) that is Batch F5. This batch was optimized by Optimization parameter of software Reliasoft which showed highest regression.

Stability Study of Optimized Batch

A optimized batch tablets was wrapped in aluminium foil and stored at 40 ± 2^0C temperature with relative humidity of 75 ± 5%. The sampling was done after one month and evaluation was done for appearance, drug content and cumulative % drug release. The all data shown in following table.

Table: 9. Evaluation of optimized batch F-5 tablets after stability study

Sr. No.	Parameter	Initial	After 1month
1	Appearance	White	No change
2.	Drug content	100.32	100.17 ± 1.35
3.	%Cumulative drug release	101.52 ± 0.08	101.56 ± 0.09

Table: 10 Cumulative % Drug release study of optimized batch F5

Time(hr)	F5 (before Stability study)	F5 (after Stability study)
SGF(Simulated gastric fluid) pH 4.5		
0	0	0
1	0.98 ± 0.01	1.04 ± 0.06
2	1.94 ± 0.07	1.96 ± 0.08
Phosphate buffer pH 7.4		
3	3.98 ± 0.76	4.01 ± 0.74
4	5.31 ± 0.04	5.36 ± 0.08
5	7.03 ± 0.24	7.11 ± 0.21
Phosphate buffer pH 6.8		
6	15.25 ± 0.16	15.34 ± 0.05
8	24.67 ± 0.32	24.79 ± 0.11
10	36.49 ± 0.46	36.58 ± 0.08
12	45.66 ± 0.23	45.77 ± 0.74
14	56.21 ± 0.78	56.40 ± 0.14
16	68.20 ± 0.73	68.29 ± 0.09
18	78.96 ± 0.69	79.08 ± 0.12
20	86.12 ± 0.13	86.23 ± 0.09
22	93.24 ± 0.63	93.41 ± 0.07
24	101.12 ±0.08	101.56 ±0.09

Roentography Study

The tablet was to be taken after breakfast and at the interval of 2nd, 4th, 5th and 12th hours the X-ray images of tablet was to be taken.

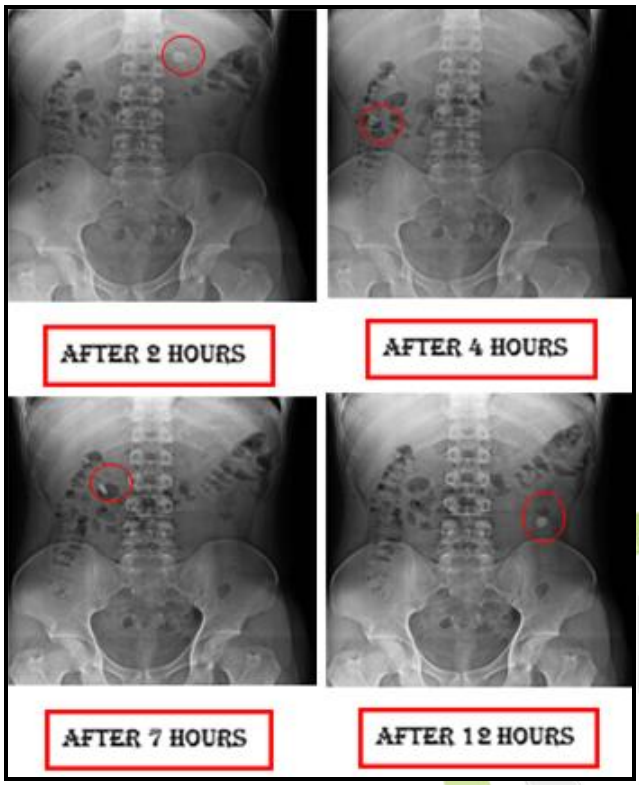


Figure 6: Roentography study for colon targeted tablet

From these Roentographs, it was seen that after 2nd hour tablet was entered in the stomach and after 4th hour the tablet was in small intestinal region. It was observed that tablet was swollen but remains intact till 4 hours.

It was seen that after 7th hour tablet was just entered in the ascending colon and found to be broken. The tablet began to disintegrate because of bacterial enzymatic action. After 12th hour the tablet was in descending colonic region. Hence, it was concluded from the Roentography study that tablet was successfully targeted to the colon.

CONCLUSION

The result was shown that Pectin as an enzyme dependent and HPMC K 100 M as a time dependent polymers in combination were showed the significant configuration effects in the different ratios rather than their individual contribution. It was observed that formulation batch F-5 was found to be optimized batch, which was showed lowest drug release in stomach and small intestine and maximum drug target to colon. The best fit model was found to be Korsmeyer-Peppas. Hence the combination of both these polymers matrix tablet were suitable for colon targeting than that of individual polymer.

REFERENCES

1. Gupta, V. K., Beckert, T. E., & Price, J. C. (2001). A novel pH-and time-based multi-unit potential colonic drug delivery system. I. Development. *International journal of pharmaceutics*, *213*(1), 83-91.
2. Rodríguez, M., Vila-Jato, J. L., & Torres, D. (1998). Design of a new multiparticulate system for potential site-specific and controlled drug delivery to the colonic region. *Journal of controlled release*, *55*(1), 67-77.
3. Khan, M. Z. I., Prebeg, Z., & Kurjakovic, N. (1999). A pH-dependent colon targeted oral drug delivery system using methacrylic acid copolymers: I. Manipulation of drug release using Eudragit® L100-55 and Eudragit® S100 combinations. *Journal of Controlled Release*, *58*(2), 215-222.
4. Sinha, V. R., & Kumria, R. (2001). Polysaccharides in colon-specific drug delivery. *International journal of pharmaceutics*, *224*(1), 19-38.
5. Chan, A. T., & Giovannucci, E. L. (2010). Primary prevention of colorectal cancer. *Gastroenterology*, *138*(6), 2029-2043.
6. Hull, M. A., Gardner, S. H., & Hawcroft, G. (2003). Activity of the non-steroidal anti-inflammatory drug indomethacin against colorectal cancer. *Cancer treatment reviews*, *29*(4), 309-320.
7. Chourasia, M. K., & Jain, S. K. (2003). Pharmaceutical approaches to colon targeted drug delivery systems. *J Pharm Pharm Sci*, *6*(1), 33-66.

8. "Indian Pharmacopoeia", Ministry of Health and Family welfare, Pharmacopoeia of India, 4th edition, Govt. of India, Controller of Publication, New Delhi, 2007, 609-611.

9. "The United State Pharmacopoeia", 19 (USP NF), The Official Compendia of Standards, Asian Edition, 2000, 2349-2352.

10. Lachman, L., Lieberman, H. A., & Kanig, J. L. (2005). The theory and practice of industrial pharmacy, 3rd edition, Varghese publication House, 171-194.

11. Aulton, M. E., & Wells, T. I. (2002). Pharmaceutics: The science of dosage form design." 2nd edition, edited by: Churchill Livingstone, Elsevier science ltd, Philadelphia, 113.

12. More, H. N., & Hajare, A. (2004). Practical Pharmaceutics (Physical Pharmacy)", Manas prakashan, 1st edition, Kolhapur, 95-97.

13. Amrutkar, J. R., & Gattani, S. G. (2009). Chitosan–chondroitin sulfate based matrix tablets for colon specific delivery of indomethacin. *AAPS PharmSciTech*, *10*(2), 670-677.

14. Kaur, G., Rana, V., Jain, S., & Tiwary, A. K. (2010). Colon delivery of budesonide: evaluation of chitosan–chondroitin sulfate interpolymer complex. *AAPS PharmSciTech*, *11*(1), 36-45.

15. Yehia, S. A., Elshafeey, A. H., Sayed, I., & Shehata, A. H. (2009). Optimization of budesonide compression-coated tablets for colonic delivery. *AAPS PharmSciTech*, *10*(1), 147-157.

16. Bower, W. H., & Hurst, L. C. (1994). Evaluation of Orthography and stress Roentography. *Journal of bone joint surgery*, *59(1)*, 519-524.

17. Cohen, J. G., Austin J. H., & Wilkins, E. J. (1992). Roentography and management of Brest cancer. *Journal of Clinical cancer*, *12(1)*, 72.