

Formulation And Characterization Of 5-Flourouracil Matrix Tablets Using Natural Polymers For Colon Specific Drug Delivery

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Abstract

Purpose: The objective of the present investigation is to develop colon targeted drug delivery system by using combination of natural polymers as a carriers for 5-Flourouracil (5-FU). Site-specific delivery of 5-FU to the colon overcomes the side effects associated with the parenteral delivery of the drug, which include gastrointestinal toxicity, hematological and neural disorders and cardiac manifestations. **Methods:** Matrix tablets containing various proportions of Pectin and Xanthan gum were prepared by direct compression technique. Multilayer tablets were formulated using pectin as release controlling layers, on either side of 5-Flourouracil matrix tablets. The matrix tablets were evaluated by different In Process Quality Control tests, content uniformity and in vitro drug release study. Comparison of pectin multilayer tablets collected at the end of test performed in the presence or absence of pectinolytic enzymes made it possible to visibly appreciate the effect of enzymatic activity on the the aspect of the residual matrix. **Results and Conclusion:** The FTIR spectra's study revealed that there were no interaction between polymers and drug. The tablets passed all the pharmacopoeial tests. The matrix tablets containing various proportions of Pectin and xanthan gum failed to control drug release in the physiological environment of the stomach and small intestine. On the other hand, multilayer formulations were able to protect the tablet cores from premature drug release. The multilayer tablets in the presence of pectinolytic enzymes, undergoes a faster erosion process which resulted in marked increase in the drug release rate.

Key words: 5-flourouracil, natural polymers, matrix tablets, multilayer tablets.

Introduction

Targeted drug delivery into the colon is highly desirable for local treatment of a variety of bowel diseases such as ulcerative colitis, Crohn's disease, amebiasis, colonic cancer, local treatment of colonic pathologies, and systemic delivery of protein and peptide drugs. Colorectal cancer^[1] is a malignant tumor arising from the inner wall of the large intestine. Colorectal cancer continues to be a major public health problem, although it is a preventable and potentially curable cancer. 5-Fluorouracil (5-FU) has been the first-choice chemotherapy drug for colorectal cancer for many years. Delivery of 5 – FU to colon as site specific delivery in the form of tablets may reduce the complications of toxicity, thereby, providing drug in therapeutically effective concentrations treating colorectal cancer.

The site specific drug delivery to colon is important for the treatment of diseases associated with the colon, reducing the side effects of the drug and reducing the administered dose. Microbially activated delivery systems for colon targeting are being developed to exploit the potential of the specific nature of diverse and luxuriant micro flora associated with the colon compared to other parts of the GIT. This vast micro flora in the colon survives by fermenting the various types of substrates that have been left undigested in the small intestine. The micro flora of the human gastrointestinal tract consists of a coexisting mixture of aerobic, facultative anaerobic and strict anaerobic bacteria in a complex ecosystem. The application of biodegradable natural polymers, which are resistant to degradation in the upper GIT (above the colon), has gained more importance^[2].

5-Fluorouracil is an antineoplastic anti-metabolite. It interferes with DNA synthesis^[3] by blocking the thymidylate synthetase conversion of deoxyuridylic acid to thymidylic acid. Fluorouracil inhibits thymidylate synthetase, leading to inhibition of DNA and RNA synthesis and cell death.

Pectins are a family of complex polysaccharides that contain 1, 4-linked α D-galactosyluronicresidues^[4]. They are refractory to host gastric and intestinal enzymes, but are almost completely degraded by the colonic bacterial enzymes to produce a series of soluble oligogalacturonates.

The primary structure of xanthan consists of a pentasaccharide repeating units. Xanthan gum exhibits pseudoplasticity^[5] (shear-reversible property) in aqueous solutions. This characteristic solution property of the xanthan gum can be explained on the basis of its helical structure. The viscosity of xanthan in solution instantaneously and reversibly decreases as the shear rate increases. This gelling property retards release of the drug from the dosage form as well as it is susceptible to degradation in the colonic environment.

Pectinex ultra SP-L (Pectinase) is a commercial enzyme preparation from *Aspergillus aculeatus*^[6] used in the food industry for fruit juice processing to reduce viscosity. It contains different pectinolytic and cellulolytic enzymes (endo-poly-galacturonase, endo-pectinylase and pectin esterase), and other activities such as β -galactosidase, chitinase and transgalactosidase^[7].

The present study was designed to formulate pectin-xanthan gum based matrix tablets of 5-fluorouracil for colon delivery based on controlled release mechanism.

Materials And Methods

Materials

5-Flourouracil was supplied by Natco Chemical Division, Hyderabad, India and Pectin, Xanthan gum were purchased from Lobachemie Pvt Ltd, Mumbai. Magnesium Stearate was purchased from Ferro Industries Limited, U.S.A and Micro crystalline cellulose (Avicel PH 102) was FMC Biopolymer, Japan and Talc was purchased from Luzenal Valchisone, Italy and Pectinex Ultra SP-L was purchased from Novozyme, U.S.A and others reagents were of analytical grade.

Methods

Method of Preparation of Matrix tablets^[8]

Matrix Tablets were prepared by direct compression technique. Accurately weighed quantities of 5-Flourouracil, pectin, MCC (Avicel PH102) and xanthan gum were passed through sieve no 30# and homogeneously blended. To the above blend sifted (40#) magnesium stearate and talc were added and homogeneously blended. Finally lubricated blend was evaluated for flow properties like Angle of repose, Bulk Density, Tapped density, Hausner's ratio and Carr's index value. The Lubricated blend was compressed in to tablets by using Mini Press II (Rimek) compression machine.

Punch Description: 17.50 X 7.90mm oval shaped punches with plain surface.

All the formulations were evaluated for their drug content uniformity, thickness, hardness, friability, swelling index and drug release.

Preparation of Multilayer Tablets^[9]

5-Flourouracil multilayer tablets composed of matrix formulation were prepared by using upper and lower layers of pectin, Half the quantity of Coating Material i.e pectin was placed in the die cavity, the core tablet was carefully positioned in the center of the die cavity, the other half of the coat was added and compressed in to Tablets by using single Rotary press. The thickness of both Matrix tablets and multilayer tablets was determined by using Vernier Callipers the difference between the thickness of multi layer tablets and Matrix tablets will give the thickness of coating layer all the formulations were evaluated for their drug content all the formulations were evaluated for their drug content uniformity, thickness, friability, swelling index and *in-vitro* drug release studies.

Process Variables

The following process variables were investigated (concentration of pectin and xanthan gum in both matrix tablets and multilayer tablets) and the different batches thus produced were analyzed for drug content uniformity, thickness, hardness, friability, swelling index and drug release.

Preformulation testing

Identification of drug

a. The Light Absorption ^[10]

The light absorption in the range 230 to 360 nm of a 0.001% w/v solution in Acetate Buffer (pH -4.7) exhibits a maximum only at 266nm.

b. Reaction of Chemicals ^[10]

To 5ml of 1% w/v solution of 5-flourouracil add 1ml of bromine water; the colour of bromine is discharged.

c. Melting Point Determination ^[10]

Melting point of the drug was determined by taking small amount of drug in a capillary tube closed at one end and placed in a melting point apparatus and the temperature at which drug melts was recorded. This was performed in triplicates and average value was noted. 5-Flourouracil melts between 280°-282°C.

d. Fourier Transform Infra Red studies ^[11]

The infrared (IR) spectra were recorded using an FTIR spectrophotometer (Perkin Elmer Spectrum GX) by the KBr pellet method in the wavelength region between 4000 cm⁻¹ and 400 cm⁻¹. The spectra obtained for 5-Flourouracil and physical mixtures of 5-Flourouracil with polymers were compared to check compatibility of drug with polymers.

Preformulation testing ^[8]

Preformulation testing need to be performed on lubricated blend of all batches like angle of repose, Bulk Density, Tapped density, Hausner's ratio and Compressibility Index Value.

$$\tan \theta = h / r$$

$$\theta = \tan^{-1} (h / r)$$

Where, h = height of pile, r = radius of the base of the pile, θ = angle of repose.

$$\text{Bulk Density} = (\text{Weight of the Blend} / \text{Bulk volume})$$

$$\text{Tapped Density} = (\text{Weight of the Blend} / \text{Tapped volume})$$

$$\text{Carr's Index (\%)} = [(\text{Tapped density} - \text{Bulk Density}) / \text{Tapped Density}] \times 100$$

$$\text{Hausner's Ratio} = \text{Tapped density} / \text{Bulk Density}$$

Evaluation of Tablets:

a. Weight variation test

Weight variation study for 10 tablets of each formulation were performed using digital balance as per the USP.

b. Hardness

Hardness of tablets was measured by using Hardness tester. (LabIndia TH 1050S Automatic Tablet Hardness Tester).

c. Thickness

Thickness of tablets was measured by using Digital Vernier Calipers. (Mitutoyo).

d. Disintegration Time

Disintegration time was measured by using Disintegration Tester (Electrolab ED-2AL).

e. Friability

Friability test was performed with Friability test Apparatus (Electrolab EF-2 Friabilator) and the Limit for % loss is Not More Than 1.0% w/w.

f. Drug Content ^[12]

The tablets of each formulation were weighed and powdered. The quantity of powder equivalent to 500mg of 5-fluorouracil was transferred into 100ml volumetric flask and extracted with (pH-7.4) phosphate buffer and kept aside for 2hr. Then the solution was filtered and absorbance was measured by using Double Beam UV-visible spectrophotometer (Shimadzu – 1700, Japan) at 267.5nm after suitable dilution.

g. Swelling studies ^[12]

The swelling index of tablets was performed to study the influence of swelling on drug release behavior of the formulation. In this study, tablets were accurately weighed (W_o) and placed in petridish containing 10ml of distilled water. At the end of 2h, the tablets were removed from petridish and the excess of water was removed carefully by wrapping with filter paper and swollen tablets weight was taken as (W_t). The swelling index value of tablets was calculated by using the following formula.

$$\text{Swelling Index} = [W_o - W_t] / W_o$$

W_o - Initial Weight of the tablets, W_t - Weight of the tablets after swelling.

h. In-Vitro Drug Release Studies ^[13]

5-Fluorouracil tablets were evaluated for the invitro drug release studies. Dissolution studies were performed by the paddle method (USP). The paddle was rotated at 100 rpm at a temperature of $37 \pm 0.5^\circ\text{C}$. Perfect sink conditions prevailed during the drug dissolution study period. The simulation of GI transit condition was achieved by changing the pH of dissolution medium at different time intervals. The pH of the dissolution medium was kept 1.2 for 2h using 0.1N HCL. Then KH_2PO_4 (1.7 g) and $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ (2.25 g) were added to the dissolution medium adjusting the pH to 4.5 with 1.0 M NaOH, and the release rate study was continued for an additional 2h. After 4h, the pH of the dissolution medium was adjusted to 6.8 with 0.1 N NaOH and maintained upto 2h. After 6h, the pH of the dissolution medium was adjusted to 7.4 with 0.1 N NaOH and the release study was continued. The samples were withdrawn from the dissolution medium at different intervals using pipette fitted with a micro- filter. The rate of 5-FU release was analysed using Double Beam UV-visible spectrophotometer at 267.5nm.

i. In-Vitro Drug Release Study in the Presence of Pectinase Enzyme ^[13]

5-Fluorouracil Multilayer tablets were evaluated for the in-vitro drug release in the presence and absence of pectinase enzyme for better In-vitro/In-vivo correlation. 5-Fluorouracil Multilayer tablet was accurately weighed and placed over the surface of 900 mL of dissolution medium (SGF). The content was rotated at 100 rpm at $37^\circ\text{C} \pm 0.5^\circ\text{C}$. The pH of the dissolution medium was kept 1.2 for 2 hours by using 0.1 N HCL. Then KH_2PO_4 (1.7 g) and $\text{Na}_2\text{HPO}_4 \cdot 2\text{H}_2\text{O}$ (2.25 g) were added to the dissolution medium by adjusting the pH to 4.5 with 1.0 M NaOH and the release rate study was continued for an additional 2 hours. After 4 hours, the pH of the dissolution medium was adjusted to 6.8 with 0.1 N NaOH and maintained up to 2 hours. After 6 hours, the pH of the dissolution medium was adjusted to 7.4 with 0.1 N NaOH, add 3 ml of pectinase enzyme (pectinex ultra spl) and maintained up to 2 hours. The samples were withdrawn from the dissolution medium at various

time intervals using a pipette fitted with a microfilter. The rate of 5-FU release was analyzed using UV -visible spectrophotometry at λ_{max} of 267.5 nm.

j. *In-Vitro* Drug Release Kinetics

Drug Release data were fitted to kinetic model including the (1) zero order (2) First order (3) Higuchi matrix (4) Korsmeyer-Peppas release equations to find the equation with the best fit.

$$R=Kt \text{ ----- (1)}$$

$$\text{Log UR} = kt/2.303 \text{ ----- (2)}$$

$$R=k\sqrt{t} \text{ ----- (3)}$$

$$R=K.t^{n*} \text{ ----- (4)}$$

Results And Discussion

In this project attempts have been made to prepare the Pectin–Xanthan gum based multilayer tablets bearing 5-fluorouracil by direct compression technique. On characterizing the tablets it was observed that the pectin concentration in both matrixes as well as in multilayers affect the tablet characteristics and the percentage release of drug. Better results were found by increasing the polymer concentration in matrix formulation along with the multilayers.

During preformulation studies of drug, all the tests for identification complies as per official compendium. The process variables were investigated and the different batches thus produced were analyzed drug content uniformity, thickness, hardness, friability, swelling Index and drug release. Optimized formula and process parameters are described by Table 8.

The FTIR spectra analysis of 5-Flourouracil and the physical mixtures shows that there was no significant interaction between drug and polymers as shown in Figure 1 to 4. The values of weight variation of both matrix tablets and multilayer tablets of 5-Flourouracil are within the pharmacopoeial limits (less than 5%).

The hardness of the matrix tablets were found to be in the range of 18.0 to 20.1kp and the hardness of the multilayer tablets were found to be in the range of 19.3 to 21.7kp. Friability of both matrix and multilayer tablets of 5-Flourouracil were found to be less than 1%. The thickness of the matrix tablets were found to be in the range of 5.31 to 5.46 mm and the thickness of the multilayer tablets were found to be in the range of 5.63 to 5.72.

The matrix tablets found to contain 98.9-101.0% of labeled amount of 5-Flourouracil and the multilayer tablets found to contain 98.5-100.1% of labeled amount of 5-Flourouracil. The angles of repose of all formulations were within the range of 30° (25.68° - 27.35°), indicating good flow properties for the blend. The tapped density values ranged between 0.452 to 0.525 g/ cm³ and the bulk density values ranged between 0.485 to 0.560 g/cm³. The result of Carr's index range from 6.07 to 8.14 % suggests excellent flow characteristics of the blend. Hausner's Ratio range from 1.06 to 1.08 % which indicates good flow property of blend.

The pectin–xanthan gum based matrix tablets and multilayer tablets were subjected to *in-vitro* drug release rate by dissolution profiles of 5-flourouracil is shown in Figure 5 to 8. Formulation batches FT1 to FT8 showed a cumulative percent release of 32.51%, 30.43%, 29.98%, 27.54%, 31.25%, 30.01%, 28.72% and 26.31% in initial 6 hrs and 88.27%, 83.57%, 82.41%, 81.30%, 87.78%, 85.32%, 85.01% and 83.24% at the end of 12 hrs respectively.

The hydrophilic nature of pectin may be the reason for the early release of drug from the matrix tablets of formulations FT1to FT8. The tablets may swell when they come in contact with aqueous fluids of GIT and cause the release of the entrapped drug through the diffusion and it may not be able to shield the drug load effectively during their passage through the stomach and small intestine. These results have been supported by the fact that as the concentration of pectin is increased in the multilayer formulation, pectin gels become more viscous and behave fatlike and this may be the probable reason for the decrease in the release of the drug as the formulation undergoes dissolution in the media.

Formulations FT5 to FT8 containing 6-20% w/w of pectin and 20-24% xanthan gum were selected for multilayer formulation trials with pectin to prevent initial release of drug in stomach and small intestine. Pectin

based multilayer tablets were subjected to *in-vitro* drug release rate in the presence of pectinase enzyme by dissolution profiles of 5-flourouracil is shown in Figure 9 to 12.

Comparison of pectin matrix tablets collected at the end of test performed in the presence or absence of pectinolytic enzymes made it possible to visibly appreciate the effect of enzymatic activity on the the aspect of the residual matrix. The multilayer tablets in the presence of pectinolytic enzymes, undergoes a faster erosion process which resulted in marked increase in the drug release rate.

Formulation batches FMT9 to FMT12 showed a cumulative percent release of 14.53%, 13.62%, 12.71% and 12.01% in initial 6 hrs and 97.25%, 96.12%, 94.57% and 90.06% at the end of 12 hrs respectively. It was found that drug release rate decreased as the concentration of pectin increased. The results of dissolution data from dissolution profile fitted to various drug release kinetic equations of zero order, first order, Higuchi and korsmeyer-peppas having r , n and k . r is value of correlation coefficient, k is a release rate constant and n is the diffusional release exponent. The drug release kinetic of different formulation in the presence and absence of pectinolytic enzyme can be described by Table 6 and Table 7.

Since FMT11 was the best formulation drug release mechanisms were determined by fitting *in vitro* drug release data to various the kinetic models. The curvilinear nature of the cumulative percentage drug released vs time plot suggests that formulation does not follow zero order drug release kinetics. By comparing correlation coefficient values for first order, Higuchi model and Peppas model formulation gave good fit to the Korsmeyer-Peppas model. Since the diffusion exponent (n) value was greater than 1, the drug release follows super case II transport. This model is used to analyze the release of pharmaceutical dosage forms when the release mechanism is not well known or when more than one type of release phenomena was involved.

Pectin – xanthan gum based multilayer tablets swells in water the result of swellability index can be described by Table 5. As a result of increasing the polymer concentration overall swelling of polymer increased significantly.

Conclusion

In the present study, an attempt was made to design colon targeted Multilayer tablets of 5-Flourouracil for treatment of colorectal cancer. The main interest in such dosage form was to target the drug to the colon by ensuring minimal amount of drug release in the physiological environment of the upper GI tract. The FTIR spectra's study revealed that there were no interaction between polymers and drug. The multilayer tablets of 5-Flourouracil containing different concentrations of pectin, xanthan gum, microcrystalline cellulose (Avicel PH 102), magnesium stearate and talc were prepared by direct compression method. The tablets passed all the pharmacopoeial tests. From the above results, it can be concluded that the matrix tablets containing various proportions of Pectin and xanthan gum failed to control drug release in the physiological environment of the stomach and small intestine. On the other hand, multilayer formulations were able to protect the tablet cores from premature drug release. It could be concluded that the pectin-xanthan gum based multilayer tablets can be used for effective and controlled delivery of 5-Flourouracil.

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Table 1

Formula and Composition of 5-FU Matrix Tablets

Sl.No	Ingredient	Qty. per tablet (mg)							
		Batch No.							
		FT 1	FT 2	FT 3	FT 4	FT 5	FT 6	FT 7	FT 8
1.	5-Flourouracil	500	500	500	500	500	500	500	500
2.	MCC (Avicel PH 102)	55	55	55	55	55	55	55	55
3.	Pectin	50	100	150	200	50	100	150	200
4.	Xanthan gum	150	150	150	150	200	200	200	200
5.	Magnesium stearate	10	10	10	10	10	10	10	10
6.	Talc	5	5	5	5	5	5	5	5
	Total weight of the tablet	770	820	870	920	820	870	920	970

Table 2

Formula and Composition of 5-FU Multilayer Tablets

Sl. No	Ingredient	Qty. per tablet (mg)							
		Batch No.							
		FMT 9		FMT 10		FMT 11		FMT 12	
		Upper	Lower	Upper	Lower	Upper	Lower	Upper	Lower
1.	5-Flourouracil Matrix Tablet		820		870		920		970
2.	Pectin	125	125	100	100	75	75	50	50
	Total weight of the tablet		1070		1070		1070		1070

Table 3

Flow properties of Lubricated Blend of all Formulations

Formulation Code	Angle of repose (θ)	Bulk Density (g/mL)	Tapped density (g/mL)	Carr's index (%)	Hausner's Ratio
FT 1	26.32	0.452	0.485	7.29	1.07
FT 2	25.83	0.459	0.497	8.14	1.08
FT 3	25.71	0.467	0.501	7.29	1.07
FT 4	25.68	0.484	0.515	6.53	1.06
FT 5	27.35	0.490	0.524	7.01	1.07
FT 6	27.24	0.502	0.537	7.05	1.07
FT 7	27.21	0.513	0.543	6.07	1.06
FT 8	27.09	0.525	0.560	6.81	1.07

Table 4

Physicochemical Parameters Of 5-Flourouracil Matrix and Multilayer Tablets

Formulation Code	Average weight of tablet (mg)	Weight variation (%)	Hardness (kp)	Thickness (mm)	Friability (%)	Drug content (%)
FT 1	771.5	0.19	18.7	5.31	0.13	98.9
FT 2	820.3	0.04	19.2	5.37	0.20	100.3
FT 3	870.8	0.09	19.0	5.41	0.17	99.0
FT 4	922.3	0.25	18.3	5.46	0.11	101.0
FT 5	821.7	0.21	18.0	5.34	0.15	100.2
FT 6	869.6	-0.05	20.1	5.39	0.21	99.7
FT 7	920.4	0.04	19.4	5.41	0.16	100.5
FT 8	972.5	0.26	19.1	5.45	0.15	99.4

Formulation Code	Average weight of tablet (mg)	Weight variation (%)	Hardness (kp)	Thickness (mm)	Friability (%)	Drug content (%)
FMT 9	1071.2	0.11	19.3	5.63	0.17	98.7
FMT 10	1068.3	-0.16	21.2	5.72	0.16	99.2
FMT 11	1073.5	0.33	20.6	5.64	0.13	100.1
FMT 12	1070.8	0.08	21.7	5.71	0.16	98.5

Table 5

Swellability Study Of 5-Flourouracil Matrix and Multilayer Tablets

Formulation Code	Weight of the tablet before swelling	Weight of the tablet after swelling	Swelling Index
FT 1	771.1	1349.43	0.75
FT 2	819.6	1573.63	0.92
FT 3	871.2	1803.38	1.07
FT 4	921.4	1981.01	1.15
FT 5	820.1	1828.82	1.23
FT 6	869.8	1974.45	1.27
FT 7	920.5	2153.97	1.34
FT 8	971.3	2360.26	1.43
FMT 9	1071.5	2667.3	1.49
FMT 10	1069.4	2713.5	1.54
FMT 11	1072.1	2791.1	1.60
FMT 12	1071.9	2805.5	1.62

Table 6

In-vitro Release Kinetics Parameters for 5-Flourouracil Matrix and Multilayer Tablets

(Absence of Pectinase Enzyme)

Formulation code	Zero Order Model		First-Order Model		H-M Model		Korsmeyer-Peppas Model	
	r ²	k ₀	r ²	k ₁	r ²	k _h	r ²	n
FT1	0.947	8.759	0.838	0.203	0.782	30.74	0.969	1.782
FT2	0.940	8.744	0.838	0.198	0.768	30.53	0.959	1.815
FT 3	0.937	8.571	0.849	0.184	0.764	29.89	0.958	1.845
FT 4	0.934	8.527	0.846	0.180	0.757	29.66	0.952	1.878
FT 5	0.941	8.638	0.841	0.191	0.769	30.16	0.962	1.821
FT 6	0.939	8.655	0.838	0.191	0.765	30.17	0.968	1.920
FT 7	0.933	8.697	0.843	0.189	0.757	30.25	0.960	1.940
FT 8	0.930	8.696	0.837	0.191	0.750	30.17	0.957	1.946
FMT 9	0.914	8.710	0.827	0.193	0.733	30.14	0.956	1.841
FMT 10	0.914	8.597	0.825	0.187	0.731	29.70	0.959	1.914
FMT11	0.910	8.565	0.823	0.182	0.725	29.54	0.956	1.950
FMT12	0.909	8.495	0.824	0.180	0.722	29.26	0.955	1.968

Table 7

In-vitro Release Kinetics Parameters for 5-Flourouracil Matrix and Multilayer Tablets

(Presence of Pectinase Enzyme)

Formulation code	Zero Order Model		First-Order Model		H-M Model		Korsmeyer-Peppas Model	
	r ²	k ₀	r ²	k ₁	r ²	k _h	r ²	n
FMT 9	0.906	9.240	0.761	0.244	0.728	32.00	0.947	1.890
FMT 10	0.909	9.062	0.777	0.228	0.730	31.37	0.954	1.914
FMT11	0.911	8.596	0.763	0.198	0.726	29.66	0.957	1.947
FMT12	0.908	8.364	0.816	0.175	0.723	28.83	0.950	1.949

Table 8

Optimized Formula and Process Parameters for 5-Flourouracil Multilayer Tablets

Sl. No	Ingredient	Qty. per tablet (mg)	
		FMT 11	
1.	5-Flourouracil	500	
2.	MCC (Avicel PH 102)	55	
3.	Pectin	50	
4.	Xanthan gum	150	
5.	Magnesium stearate	10	
6.	Talc	5	
	weight of the matrix tablet	770	
S.No	Ingredient	Upper	Lower
1.	Pectin	75	75
	weight of the matrix tablet	1070	
Sl. No.	Process parameter	Optimized Data	
1	Average weight of tablet (mg)	1070 mg ± 5 %	
2	Hardness (kp)	17-25 kp	
3	Thickness (mm)	5.30-5.80 mm	
4	Friability (%)	Not More Than 1 % W/W	

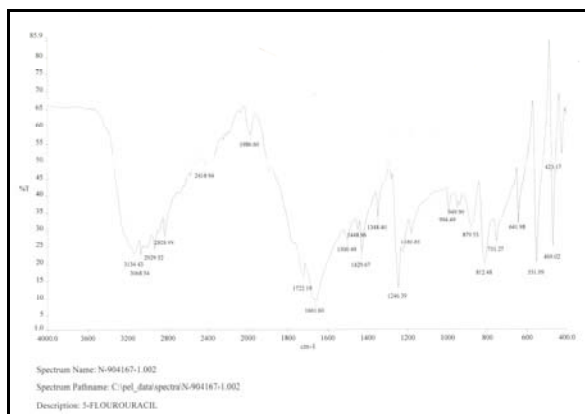


Figure 1: FTIR Spectra of 5-Flourouracil

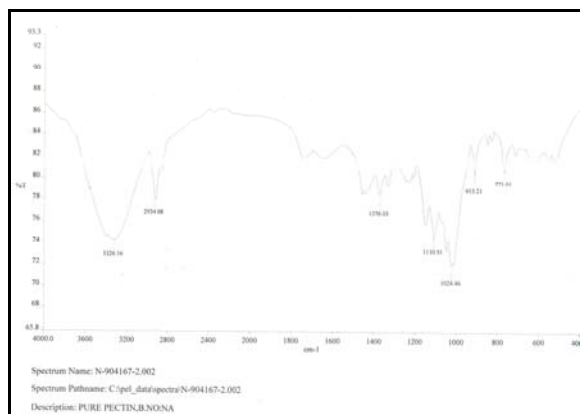


Figure 2: FTIR Spectra of Pectin

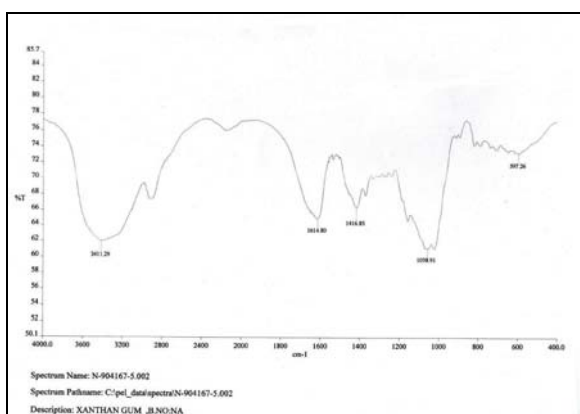


Figure 3: FTIR Spectra of Xanthan Gum.

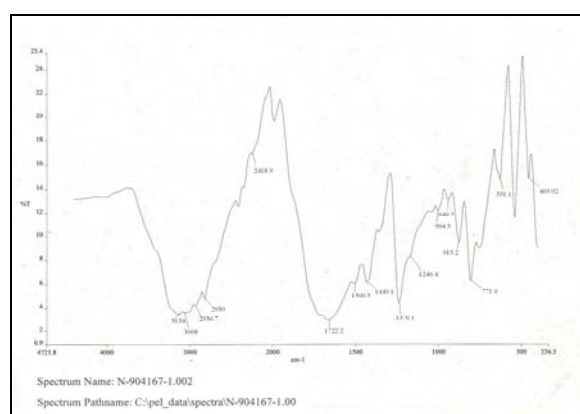


Figure 4: FTIR Spectra of 5-Flourouracil Tablets with Pectin and Xanthan Gum.

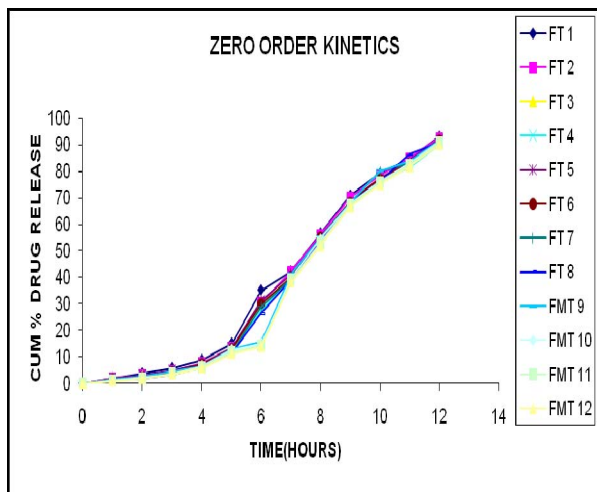


Figure 5: Release data of 5-FU fitted in Zero Order Kinetics for formulations From FT1to FMT12

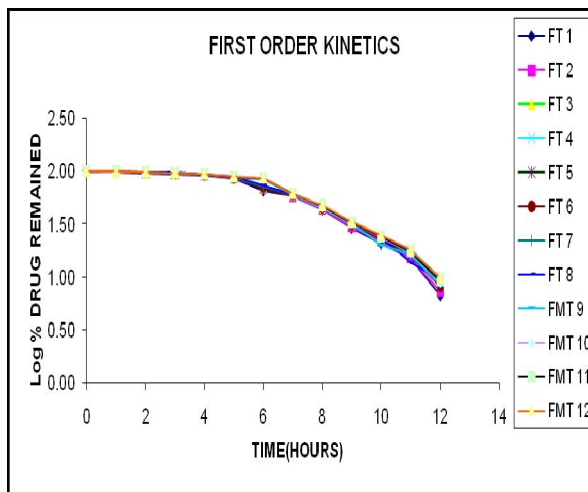


Figure 6: Release data of 5-FU fitted in First-Order Kinetics for formulation From FT1to FMT12

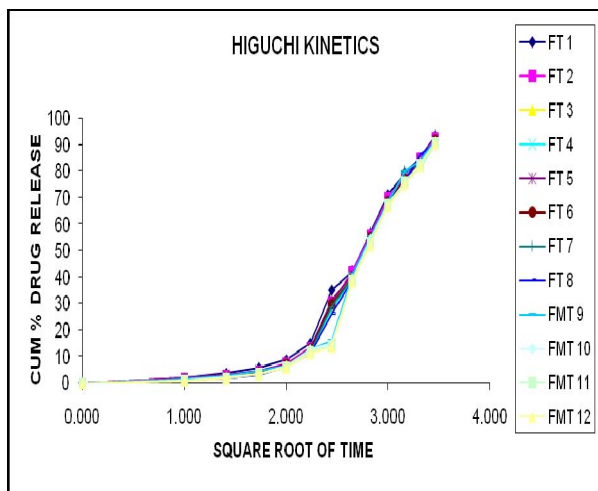


Figure 7: Release data of 5-FU fitted in Higuchi Kinetics for formulation From FT1 to FMT12

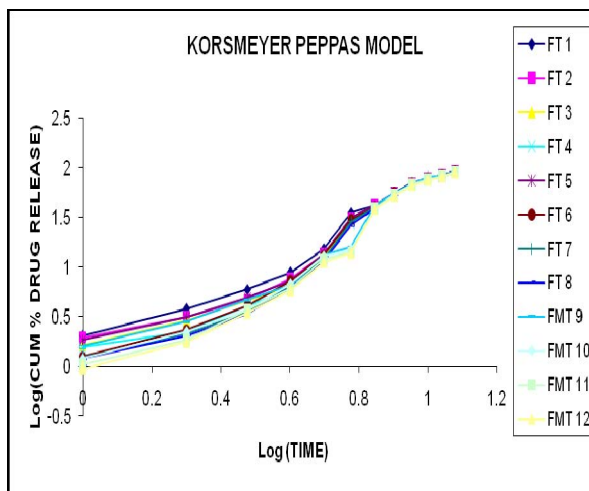


Figure 8: Release data of 5-FU fitted in Korsmeier-Peppas kinetics for Formulations From FT1 to FMT12

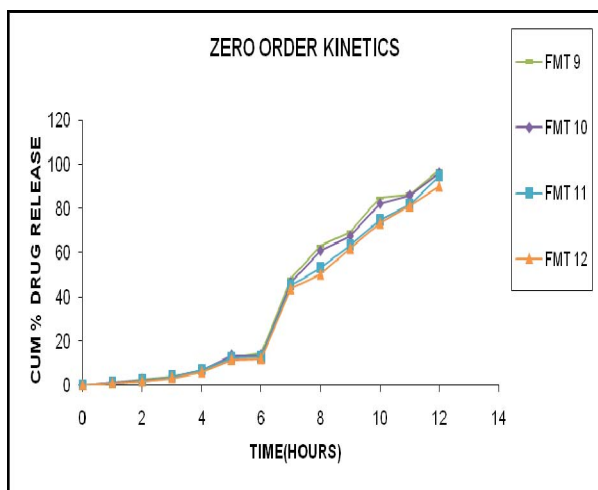


Figure 9: Release data of 5-FU fitted in Zero Order Kinetics for formulations From FT1 to FMT12 (Presence of Pectinase)

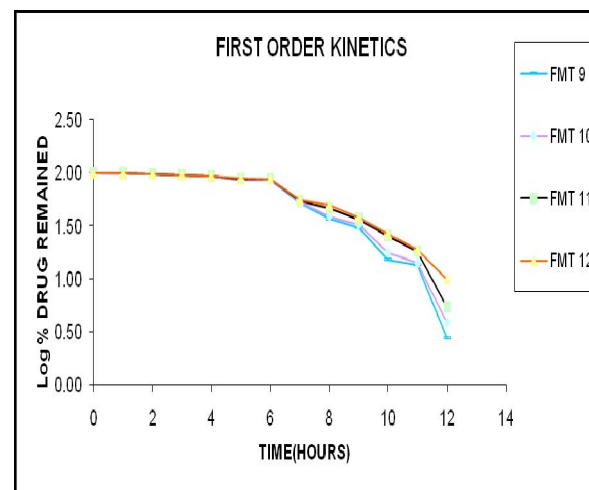


Figure 10: Release data of 5-FU fitted in First-Order kinetics for formulations From FT1 to FMT12 (Presence of Pectinase)

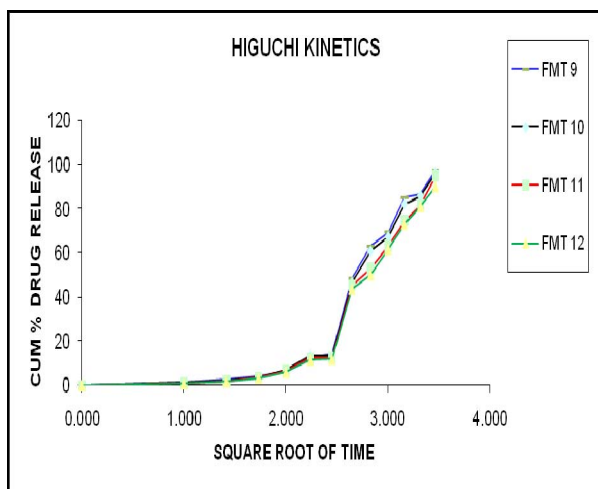


Figure 11: Release data of 5-FU fitted in Higuchi kinetics for formulations From FT1 to FMT12 (Presence of Pectinase)

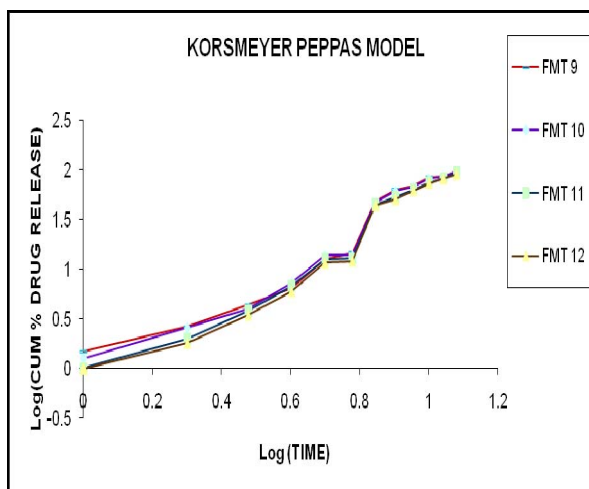


Figure 12: Release data of 5-FU fitted in Korsmeier- Peppas Kinetics for Formulations From FT1 to FMT12 (Presence of Pectinase)