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Formulation and Evaluation of Ciprofloxacin Colon Targeted Tablets By Compression Coating Technique Using Guar Gum and Hydroxypropyl Methylcellulose

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ABSTRACT: The aim of the present study is to develop colon targeted drug delivery system for ciprofloxacin drug which is used to treat the Crohn's disease using various proportions of guar gum and HPMC K4M polymer using as coating materials for extending drug release. The compression coated tablets of ciprofloxacin were prepared and were evaluated for hardness, thickness, friability, diameter, drug content, weight variation and *in vitro* drug release studies. The IR spectrum of ciprofloxacin drug was compared with the IR spectrum of ciprofloxacin physical mixtures and crushed studies confirm that the drug and other excipients in the formulation were compatible with each other. At different pH, % drug release was calculated. The compression coated tablets with 175 mg of guar gum coat released 24.96±2.68 % for formulation F1, whereas combination of Guar gum and HPMC K 4M as coat in the ratio of 5% (F2), 10% (F3) and 20% (F4) release 51.79±1.65%, 36.53±0.79% and 31.61 ±1.87% respectively observed at different time periods in 0.1N HCl for 2hrs, 7.4 pH phosphate buffers for 3hrs and followed by 6.8 pH phosphate buffer for the remaining 19hrs indicating the susceptibility of the guar gum formulations in simulated colonic fluids. But the Formulation F5 (containing mixture of Guar gum in combination with 30% of HPMC K 4M as coat for compressed tablet) gave very soft coats and so more drug release occurs before it reaches to colon pH. The mechanism of drug release with the formulations F1 and F3 was dominantly case-II transport diffusion and followed zero order kinetics, whereas the formulation F4 followed Korsemeyer peppas equation. The ciprofloxacin compression coated tablets showed no change either in physical appearance, drug content or in dissolution pattern during stability study. Based on the R^2 value obtained, F3 is considered as the best formulation.

KEYWORDS: Ciprofloxacin; Guar gum; HPMC K 4M; Crospovidone; Colon targeted drug delivery; Compression coating technique.

1.INTRODUCTION

Oral route is considered to be the most convenient for administration of drugs to patients. Oral administration of conventional dosage forms normally dissolves in the stomach or intestinal fluid and absorb from the regions of the GIT depends upon the physicochemical properties of the drug [1].It has a serious drawback in conditions where localized drug delivery of the drugs in the colon is required or in conditions where a drug needs to be protected from the hostile environment of the upper GIT [2]. Controlled-release systems also offer a sustained-release profile but, in contrast to sustained-release forms, controlled-release systems are designed to lead to predictably constant plasma concentrations, independently of the biological environment of the application site. This means that they are actually controlling the drug concentration in the body, not just the release of the drug from the dosage form, as is the case of sustained-release system. The release kinetics is usually zero-order [3].

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The challenge in the development of colon-specific drug delivery system is to establish an appropriate dissolution method in designing in-vitro system. In past few decades colon drug delivery has been extensively studied and investigated. A number of diseases, e.g., Crohn's disease, ulcerative colitis and the irritable bowel syndrome, can be treated most efficiently by local delivery of drugs to colon. Site-specific systems might also reduce systemic absorption and side effects. The most critical challenge in such drug delivery approach is to preserve the formulation during its passage through the stomach and about first six meters of the small intestine. Another challenge in developing therapeutically effective products for the treatment of colonic pathologies is the impact of disease on the delivery system [4].

Guar gum is a potential carrier for colon targeting drug delivery. Guargumcontainsabout80%galactomannan,12%water, 5% protein, 2% acid insoluble ash, 0.7% ash and0.7% fat. In cold water Guar gum hydrates and swells forming viscous colloidal dispersion or sols which retard the drug release from the tablets. Guar gum is being used to deliver drug to colon due to its drug release retarding property and susceptibility to microbial degradation in the large intestine. HPMC was used to modify the drug release and improve the mechanical properties of the compressed coated tablets [5, 6, 7, 8].

Preparation of tablets with compression coating technique now a days widely used for extending drug release. Compression coated tablets have two layers, an inner core and an outer shell as shown in **Figure 1**.

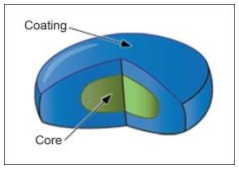

Figure 1: Illustration of Compression coated tablet

The drug ciprofloxacin which is used in the treatment of Crohn's disease is selected among other anti-infective drug as the appropriate one because it has fewer side effects and does not cause peripheral neuropathy up on continuous usage when compared to other drugs. Also, the compression coating method used is selected as the drug ciprofloxacin is heat labile. Ciprofloxacin retained some of its bactericidal activity after inhibition of RNA and protein synthesis by rifampin and chloramphenicol, respectively. These observations suggest ciprofloxacin may possess two bactericidal mechanisms, one of them is resulting from the inhibition of DNA gyrase and the other mechanism may be independent of RNA and protein synthesis [9].

The present topic mainly focuses on the use of guar gum and HPMC K 4M which were used as coating material for compressed tablet release drug in the colon region for the effective long period treatment of colon diseases like Crohn's disease.

2. RESULTS AND DISCUSSION

2.1. Characterization of the Dosage Form

Fourier transform infrared spectroscopy (FTIR) study was carried out to check the compatibility between the drug, crushed tablet and the physical mixtures used for the formulation. The spectra obtained from FT infrared spectroscopy studies at wavelength from 4000cm^{-1} to 400 cm^{-1}. The FTIR spectrum is shown in **Figure 5, 6, 7, and 8**. IR interpretation of drug, crushed tablet and physical mixtures of drug-polymer is mentioned in **Table 4**. The IR spectrum of ciprofloxacin drug was compared with the IR spectrum of ciprofloxacin physical mixtures and crushed tablets. The presence of all characteristic peaks of ciprofloxacin in the IR spectra was obtained with drug and other mixtures. The above studies confirm that the drug and other excipients in the formulation were compatible with each other.

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Table 4: IR interpretation of drug, crushed tablet and physical mixtures of drug-polymer

Functional group	IR band of pure drug in cm-1	IR band of drug-Guar gum in cm-1	IR band of drug-HPMC K4M in cm-1	IR band of crushed tablet in cm-1
C=O	1712.96	1734.06	1734.06	1747.57
N-H	1606.76	1610.31	1608.69	1608.69
C-O	1417.70	1467.73	1417.73	1419.66
O-H	1277.06	1214.06	1273.06	1273.06
C-F	1045.45	1185.63	1026.16	1163.11

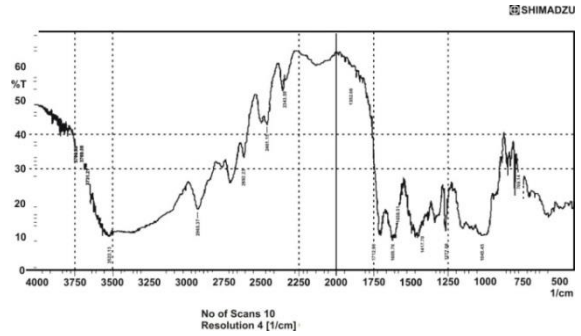

Figure 5: IR Spectrum of Ciprofloxacin

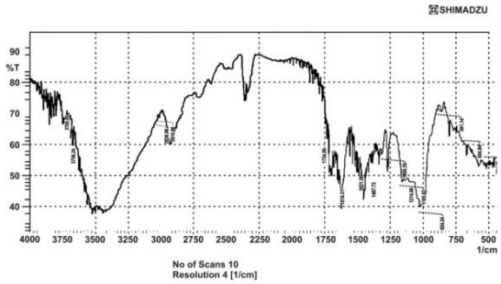

Figure 6: IR Spectrum of physical mixture of Ciprofloxacin and Guar gum

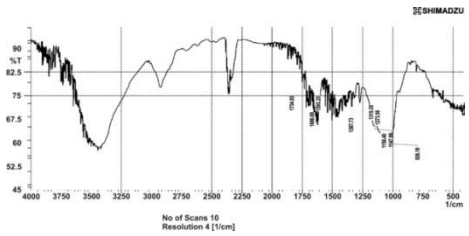

Figure 7: IR Spectrum of physical mixture of Ciprofloxacin and HPMC K4M

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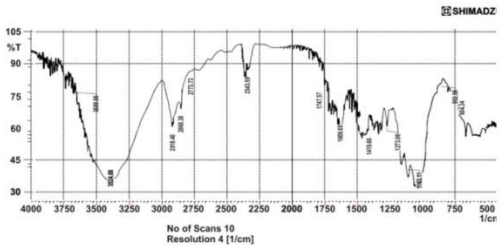

Figure 8: IR Spectrum of Crushed Tablet

2.2. Physicochemical Characters of Core tablets

The results of physicochemical evaluation of prepared core tablets are shown in **Table 5**. The tablets were evaluated for weight variation test, drug content, hardness and friability.

Table 5: Physicochemical Characters of Core tablets

S. No	Test	Evaluated value
1	Weight variation test(a)	149.01± 0.012
2	Hardness (b)	4.24±0.05
3	Friability (%) (c)	0.2±0.021
4	Drug content (d)	98.5±0.4

a, d (n=3±S.D); b(n=5±S.D) and c (n=20±S.D)

2.3. Physico-chemical parameters of prepared tablets

The core tablets were then coated with different polymers using compression coating technique which is a dry process. The formulations were divided in to 5 batches F1-F5 with 150 mg coat of guar gum alone to F1 batch tablet, and combination of Guar gum to HPMC K 4M in ratio of 5%, 10%, 20% and 30% for F2, F3, F4 and F5 batch respectively. The compressed tablets were subjected to physicochemical characterization. The tests performed were thickness, diameter, hardness, weight variation, friability and drug content. The compression coated tablets of ciprofloxacin were prepared in 5 batches. The results of physicochemical evaluations of the tablets are shown in the **Table 6**.

Table 6: Physico-chemical parameters of prepared tablets

Formulation	Thickness (mm) a	Hardness (Kg/m²) c	Weight of Tablet (mg) d	Friability (%) e	Drug content (%) f
F1	3.8±0.07	4.9±0.04	324±0.016	0.42±0.042	100.4±0.04
F2	3.9±0.46	4.9±0.04	323±0.065	0.34±0.036	100.1±0.42
F3	3.8±0.42	5.0±0.03	325±0.024	0.25±0.021	100.1±0.04
F4	3.8±0.26	4.9±0.02	325±0.021	0.17±0.020	100.3±0.02
F5	3.8±0.81	4.7±0.06	323±0.042	0.49±0.052	99.6±0.08

a, d, f (n=3±SD); c (n=5±SD) and e (n=20±SD).

The 5 batches of compressed tablets were subjected to physicochemical tests. The hardness was found to be from 4.76 to 5.06 kg/cm². The drug content was within the limits of 98-102%. In all cases friability was less than 1%.

2.4. Cumulative percentage drug release of F1-F5 formulations

The percentage drug release of ciprofloxacin compression coated tablets of F1-F5 formulation batches were observed at different time periods in 0.1N HCl for 2hrs, 7.4 pH phosphate buffers for 3hrs and followed by 6.8 pH phosphate buffer for the remaining 19hrs and drug release pattern is

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shown in **Table 7** and **Figure 9**. At the end of the study, a slight swelling of the coat was observed in all formulations due to water sorption. The % drug release for formulation F1 (where alone 175 mg of Guar gum coat was applied) was found to be 24.96±2.68 % at the end of 24 hour. This is correlated as from previous studies where it was found that a coat of considerable thickness of guar gum is usually required to protect the drug loaded in the core tablets and decrease in drug release as shown in formulation batch F1. Another reason is due to presence of Guar gum which is a naturally occurring galactomannan polysaccharide obtained from the endosperm of the guar plant Cyamopsis tetragonoloba and having high molecular weight hydro colloidal hetero polysaccharide composed of galactan and mannan units [10,11,12]. This property makes guar gum as a vehicle for colon targeting and retards drug release.

In our other formulation batches, we have taken combination of Guar gum and HPMC K 4M as coat in the ratio of 5%, 10% and 20% for F2, F3 and F4 respectively used to develop colonic delivery to modify drug release. In F2 percentage drug release was found to be 51.79±1.65%, whereas in F3 36.53±0.79% and in F4 31.61 ±1.87%. In F2, F3 and in F4 combination of Guar Gum and HPMC cause a reduction in gum leaching, with a consequent decrease in drug release and these results are well correlated with previous reports [13,14,15,16,17,18] which suggested that guar gum along with HPMC reduce the free water volume and increase the viscosity of the coat causing a reduction in the polymer leaching and subsequent reduction in drug release. However, compared to F3 and F4, the higher drug release in F2 is due to the low HPMC K 4M coating solution, which creates a porous structure of the coating and consequently increases the leaching of guar gum and drug release.

Similarly, formulation F5 (mixture of guar gum in combination with 30% HPMC) resulted in high drug release. Although HPMC causes swelling of the tablets, the use of guar gum in lower concentration in the formulation of compressed coated tablets resulted in very soft coatings and thus higher drug release before reaching pH in the colon.

From the above results, we selected F1, F3 and F4 as the most suitable formulation batch for further investigation.

Table 7: Cumulative percentage drug release of F1-F5 formulations

Time (h)	F1	F2	F3	F4	F5
0	0	0	0	0	0
1	1.21 ±1.87	1.93 ±3.02	2.62±0.79	1.08 ±3.02	5.18±0.95
2	1.76±2.68	4.06±1.46	5.13 ±1.87	2.27±0.79	8.14±2.68
3	3.91±1.46	5.98 ±1.87	6.93±1.79	5.34±0.95	14.24±1.46
4	5.01±1.46	7.37±2.68	7.86±1.46	7.26 ±3.02	21.63 ±1.87
5	5.99±1.13	15.79±2.68	10.32±2.68	8.22 ±1.45	31.47±0.95
8	9.31±0.95	27.11±0.79	12.91±1.13	11.96 ±1.45	39.54±1.46
12	14.36±2.68	38.77±0.95	15.79±0.79	14.56±0.95	45.96±1.13
16	16.53±0.79	39.63 ±1.13	21.43±2.68	20.01±2.68	48.62±2.68
20	20.74 ±3.02	48.64±2.86	29.15 ±1.87	26.16 ±1.45	61.34 ±3.02
24	24.96±2.68	51.79±1.65	36.53±0.79	31.61 ±1.87	74.79±0.79

n= 3; SD-standard deviation

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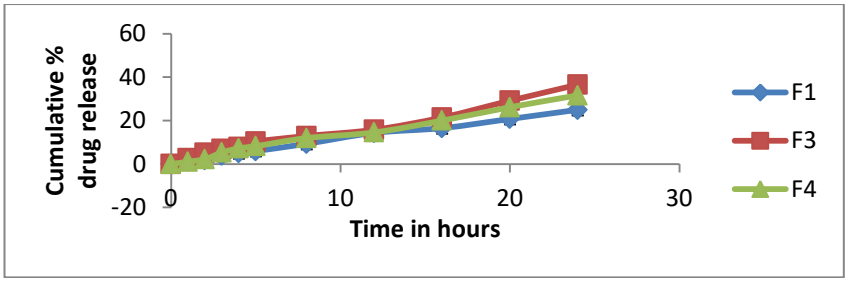

Figure 9: Cumulative percentage drug release of selected formulations (F1, F3, F4) Kinetics and release mechanism of Formulation F1, F3 and F4

2.5. Drug Release mechanism and Kinetic parameters of F1, F3, and F4

Data obtained from *in vitro* release studies of the compression coated of the ciprofloxacin formulation F1, F3 and F4 were fitted to various kinetic equations such as zero order, first order, higuchi model and korsemeyer peppas model. Different drug release mechanism is shown in **Figure 10, 11 & 12** and values are shown in **Table 8.**

The value of n is used to find out the type of diffusion
If n=0.45 it indicates Fickian diffusion.
If 0.45 < n < 0.89 it indicates anamolous or Non Fickian diffusion.
If n= 0.89 or above it indicates Case-2 relaxation or Super case transport-2.

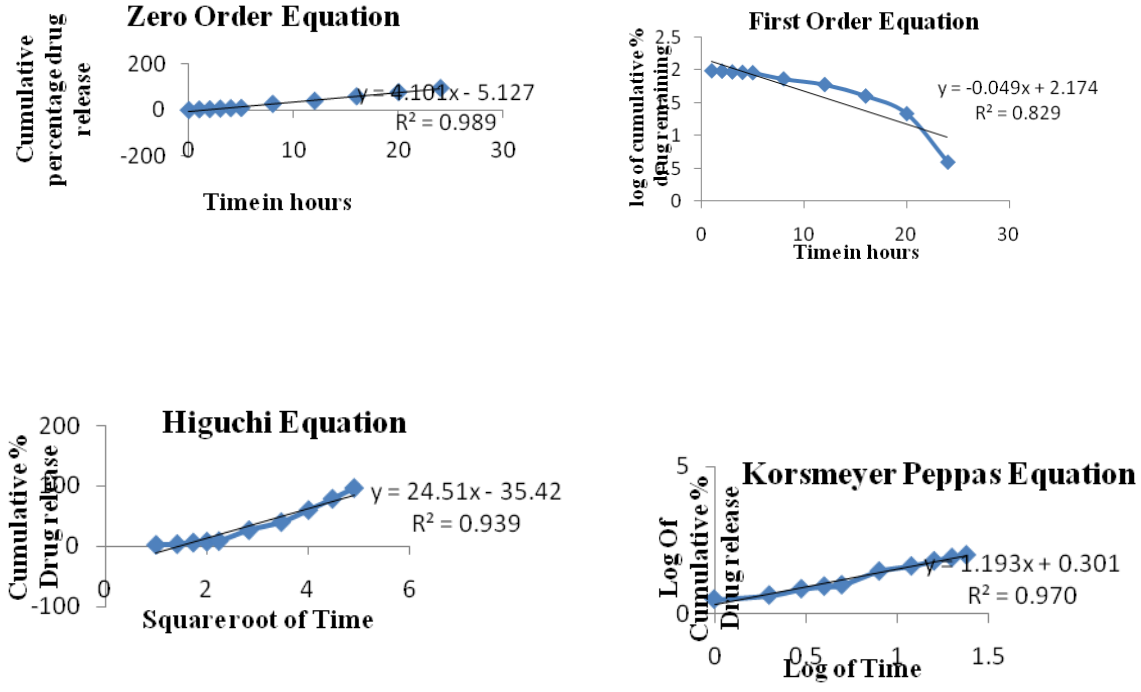

Figure 10. Release Kinetics of Formulation F1 (a) Zero order release kinetics (b) First order release kinetics (c) Higuchi model (d) Korsmeyer Peppas Equation

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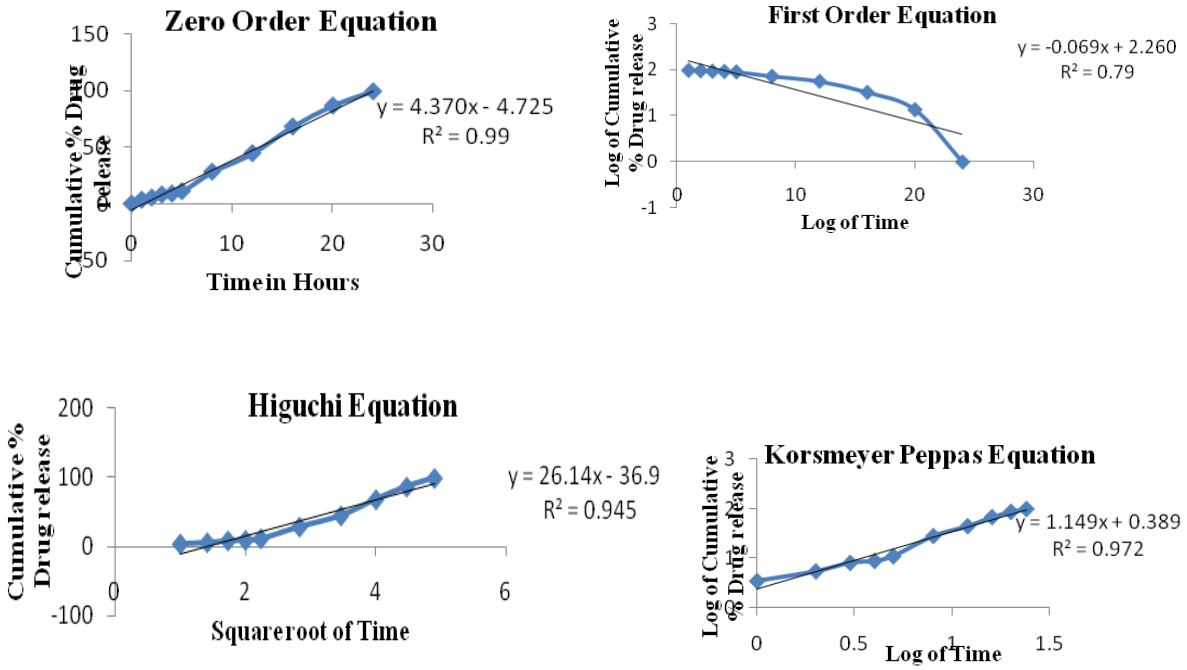

Figure 11. Release Kinetics of Formulation F3 (a) Zero order release kinetics (b) First order release kinetics (c) Higuchi model (d) Korsmeyer Peppas Equation

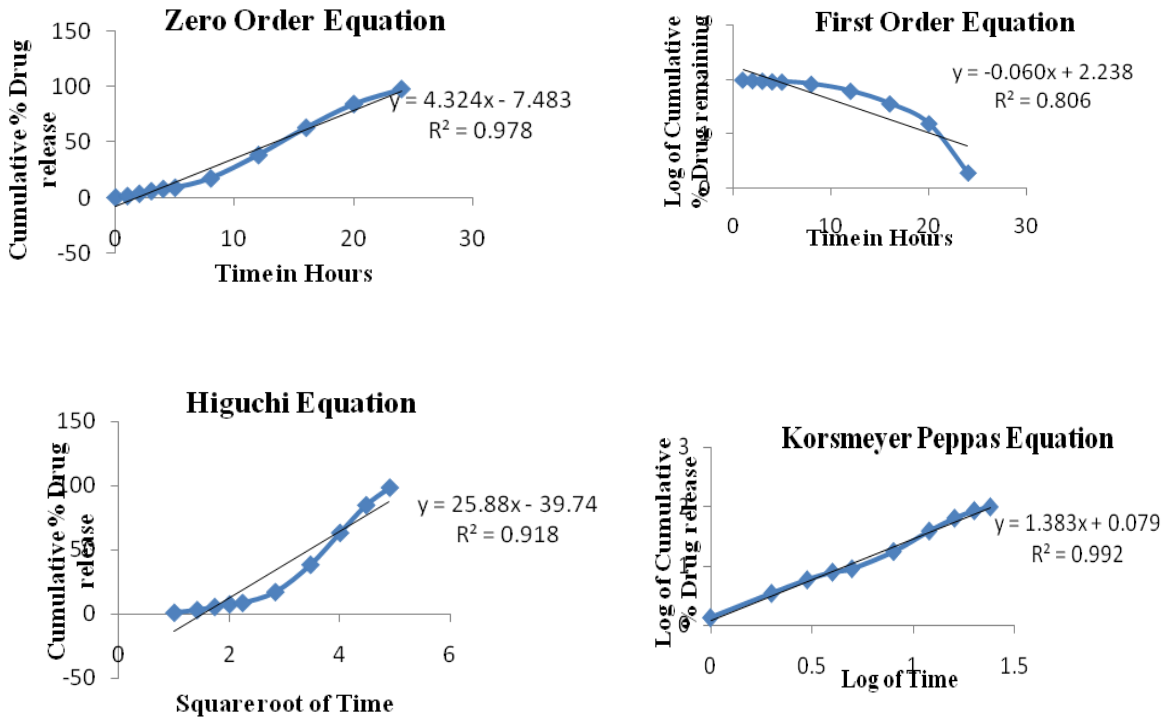

Figure 12. Release Kinetics of Formulation F4 (a) Zero order release kinetics (b) First order release kinetics (c) Higuchi model (d) Korsmeyer Peppas Equation

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Table 8: Kinetic parameters of F1, F3, and F4

Formulation	Zero order	First order	Higuchi	Korsmeyer Peppas	
				R^2	n
F1	0.989	0.829	0.939	0.970	1.193
F3	0.990	0.790	0.945	0.972	1.149
F4	0.978	0.806	0.918	0.992	1.383

According to the results mentioned above, the formulation F1 has followed Zero order kinetics with R^2 value of 0.989 and it is following the diffusion of Case-II relaxation or Super case transport-II which refers to the erosion of polymeric chain as the n value (1.193) obtained is greater than 0.89.

The formulation F3 has followed Zero order kinetics with R^2 value of 0.990 and it is following the diffusion of Case-II relaxation or Super case transport-2 which refers to the erosion of polymeric chain as the n value (1.149) obtained is greater than 0.89.

The formulation F4 has followed Korsmeyer Peppas equation with R^2 value of 0.992 and it is following the diffusion of Case-2 relaxation or Super case transport-2 which refers to the erosion of polymeric chain as the n value (1.383) obtained is greater than 0.89.

The higher values of n would be a consequence of a plasticization process in the gel layer arising from a reduction of the attractive forces among polymeric chains that increases the mobility of macromolecules.

2.6. Stability studies of compression coated tablet of ciprofloxacin

A study was carried out to assess the stability of the formulation F1, F3 and F4. Stability studies were carried out at room temperature and 40° C/ 75% RH over a period of 1month. Samples were evaluated every 10 days for different parameters such as physical appearance, hardness, weight variation, drug content and dissolution. The dissolution results are given in the **table 9** and shown in **figure 13**.

Table 9: Stability studies of compression coated tablet of ciprofloxacin

Time	F1	F3	F4
0	0	0	0
1	1.82 ±1.13	1.32±2.14	1.08 ±3.02
2	3.20±2.68	3.82±2.86	2.27±0.79
3	5.53±2.14	5.83 ±1.13	5.34±0.95
4	6.96 ±1.56	7.66±1.65	7.26 ±3.02
5	8.39±1.65	9.61±2.68	8.22 ±1.45
8	11.86 ±1.13	14.83±1.65	11.96 ±1.45
12	14.20±2.68	20.11±2.86	14.56±0.95
16	16.19 ±1.56	23.22 ±1.56	20.01±2.68
20	19.82±2.14	29.46±2.14	26.16 ±1.45
24	24.75 ±1.13	37.25±1.75	31.61 ±1.87

n=3±SD

Table 10: R^2 Values for the Stability Studies

F1	F3	F4
0.989	0.99	0.977

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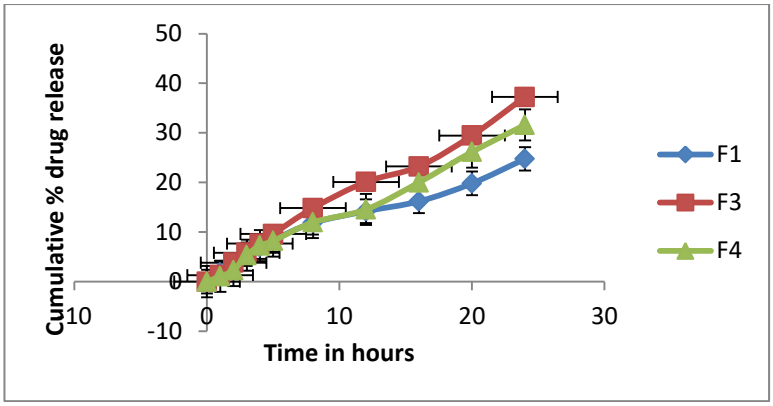

Figure 13: Cumulative percentage drug release of optimized formulation batches after stability testing.

The stability studies were performed for the three optimized formulations F1, F3, F4. All the parameters evaluated were within the range. As mentioned above all the dissolution results were obtained within the range. Hence it is stated that no degradation was observed for about one month after the formulation. By comparing the R^2 values of all three batches we have found batch F3 is considered as the best formulation as shown in **table 10**. An R^2 of 1 indicates that **the regression predictions perfectly fit the data.**

3. CONCLUSION

Administration of drugs directly into the colon by oral route has several advantages for the treatment of the disease at the target site. In the present topic, we took the drug ciprofloxacin, a fluoroquinoline derivative, and prepared tablets by the compressed coating technique using guar gum and HPMC K 4M polymer in different combinations to find out how the polymer increases the percentage drug release in the colon. The results showed that the drug release in the formulation containing 175 mg of guar gum in the form of compressed coated ciprofloxacin tablets was considered as a potential carrier for targeted drug release into the colon and can delay the release of core materials until they reach the colon. Similarly compressed coated ciprofloxacin tablets are released with a mixture of guar gum and HPMC K 4M in the formulation also produce a successful drug targeting to the colon with minimal amount drug in the gastrointestinal tract for the successful design of colon targeted delivery systems.

4. MATERIALS AND METHODS

4.1. Materials

Ciprofloxacin was procured from Pfizer India Healthcare Limited. HPMC K 4M, procured from Colorcon Asia Pvt. Ltd, India. Other ingredients like guar gum from Nutriroma, India and Crospovidone, talc, magnesium stearate was procured from S.D. Fine chemicals, Mumbai.

4.2. Preparation of ciprofloxacin core tablets

Each core tablet (average weight of 150mg) for *in vitro* drug release studies consists of Ciprofloxacin (100mg), Micro crystalline cellulose (38mg), Crospovidone (6mg), Talc (3mg), Magnesium stearate (3mg) as mentioned in **Table 1**. The materials were weighed ,mixed and passed through a mesh (200µm) to ensure complete mixing. The tablets were prepared by compressing the thoroughly mixed materials using 6mm round, flat and plain punches on a 16-station tablet punching machine (Cadmach, India).

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Table 1: Formula for the preparation of ciprofloxacin core tablets

SNo	Ingredients	Quantity for one tablet(in mg)
1	Ciprofloxacin	100
2	Cross povidone	38
3	Talc	6
4	Magnesium stearate	3
5	Microcrystalline cellulose	3

4.3. Compression coating of ciprofloxacin core tablets

The ciprofloxacin core tablets were compression coated with different quantities of coating material (guar gum, HPMC K4M) containing different concentration [19,20]. The coating materials of 175 mg guar gum alone and mixtures of guar gum in combination with 5%, 10%, 15% and 30%, HPMC K 4M were used to prepare F1, F2, F3, F4 and F5 respectively. Half the quantity of coating material was placed in the die cavity, the core was carefully positioned in the center of the die cavity and was filled with other half of the coating material. The coating material was compressed around the core using 9mm round, flat and plain punches.

4.4. Fourier transform infrared spectroscopy to find out the compatibility of drug with polymer.

This was carried out to find out the compatibility between the drug ciprofloxacin and guargum, HPMC K4M. 10mg of the sample and 400mg of KBr were taken in to mortar and triturated. A small amount of triturated sample was taken in to a pellet maker and was compressed at 10kg/cm^2 using a hydraulic press. The pellet was kept on to the sample holder and scanned from 4000 cm^{-1} to 400 cm^{-1} in Shimadzu FT-IR Spectrophotometer. Samples were prepared for drug ciprofloxacin, polymer guargum, HPMC K4M, crospovidone, magnesium stearate, microcrystalline cellulose and crushed tablet. The spectra obtained were compared and interpreted for the functional group peaks.

4.5. Calibration curve of ciprofloxacin

4.5.1. Calibration curve of ciprofloxacin in 0.1n HCL

100mg of Ciprofloxacin was accurately weighed and transferred in to 100ml volumetric flask, dissolved and adjusted the volume up to 100ml with 0.1N HCL to get stock solution A. From the stock solution A, primary standard solution was prepared and serial dilutions were performed to give concentrations of 0.5µg/ml, 1.0, 1.5, 2.0, 2.5…5.0 µg/ml. Solutions are analysed by UV-Visible double beam spectrophotometer (Genesis-2, USA) at a λ max of 269nm. Observations are tabulated in **Table 2** and standard graph is represented in **Figure 2**.

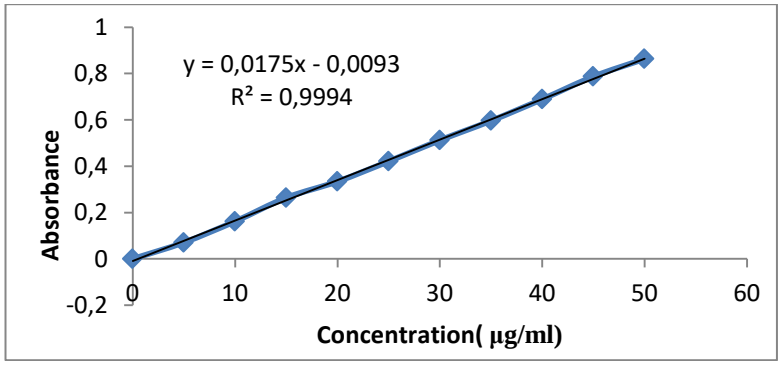

Figure 2: Calibration curve of Ciprofloxacin in 0.1N HCl

4.5.2. Calibration curve of ciprofloxacin in 6.8 pH phosphate buffer

100 mg of Ciprofloxacin was accurately weighed and transferred in to 100ml volumetric flask, dissolved and adjusted the volume up to 100ml with 6.8 pH phosphate buffer to get stock solution A.

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From the stock solution A, primary standard solution was prepared and serial dilutions were performed to give concentrations of 0.5µg/ml, 1.0, 1.5, 2.0, 2.5…5.0 µg/ml. Solutions are analysed by UV-Visible double beam spectrophotometer (Genesis-2, USA) at a λ_{max} of 271nm. Observations are tabulated in **Table 2** and standard graph is represented in **Figure 3**.

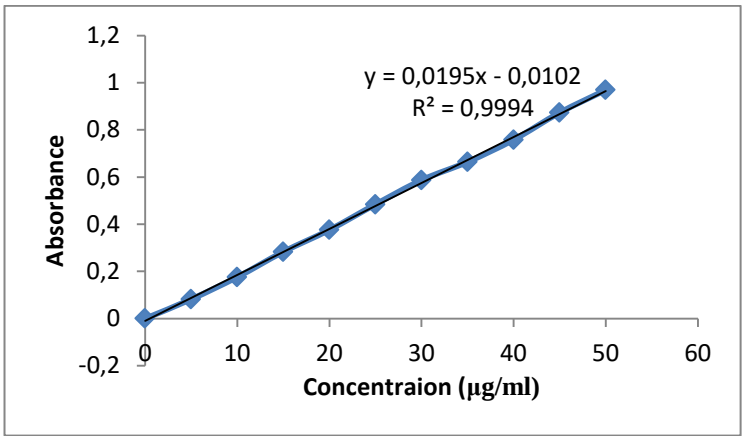

Figure 3: Calibration curve of Ciprofloxacin in 6.8 pH

4.5.3. Calibration curve of ciprofloxacin in 7.4 pH phosphate buffer

100mg of Ciprofloxacin was accurately weighed and transferred in to 100ml volumetric flask, dissolved and adjusted the volume up to 100ml with 7.4 pH phosphate buffer to get stock solution A. From the stock solution A, primary standard solution was prepared and serial dilutions were performed to give concentrations of 0.5µg/ml, 1.0, 1.5, 2.0, 2.5…5.0 µg/ml. Solutions are analysed by UV-Visible double beam spectrophotometer (Genesis-2, USA) at a λ max of 277nm. Each study was conducted in triplicate. The results are shown in the **table 2** and **Figure 4**.

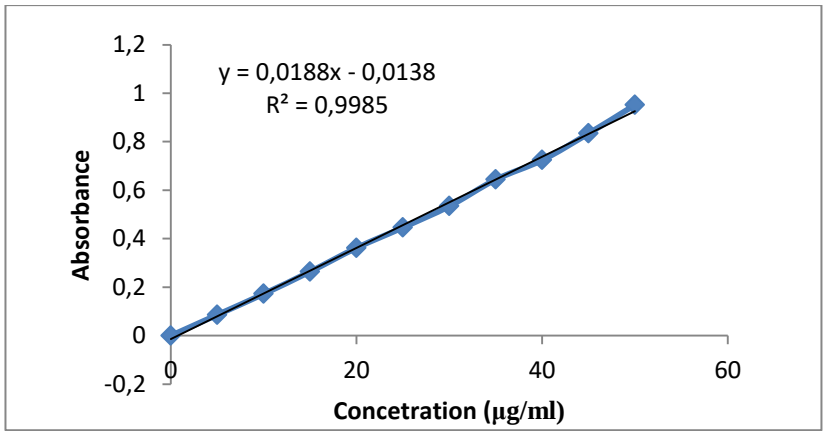

Figure 4: Calibration curve of Ciprofloxacin in 7.4 Ph

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Table 2: Concentration and Absorbance value of Ciprofloxacin in different media

S.No.	Concentration in mcg/ml	Absorbance in 0.1N HCl (nm)	Absorbance in Phosphate Buffer of 6.8pH (nm)	Absorbance in Phosphate Buffer of 7.4 pH (nm)
0	0	0.000	0.000	0.000
1	5	0.071±0.24	0.082 ±0.02	0.086±0.42
2	10	0.162 ±0.07	0.176 ±0.06	0.172±0.32
3	15	0.264 ±0.09	0.283±0.14	0.264 ±0.05
4	20	0.334 ±0.16	0.376±0.02	0.362±0.08
5	25	0.421±0.14	0.484±0.12	0.446±0.26
6	30	0.512±0.21	0.587 ±0.07	0.534±0.28
7	35	0.596 ±0.42	0.664 ±0.04	0.644 ±0.42
8	40	0.689 ±0.14	0.758 ±0.21	0.724±0.17
9	45	0.787±0.35	0.873±0.14	0.834±0.14
10	50	0.863±0.24	0.969±0.32	0.952±0.06

(n=3±SD)

4.6. Solubility determination:

Solubility of drug is determined by shake flask method. In this an excess amount of drug was added to 25ml of water and placed on a gyratory shaker for 24hr. Then solution is filtered and diluted with the water. Absorbance of this sample is found by UV-spectrophotometer and results are interpreted in terms of solubility.

4.7. Characterization of ciprofloxacin core tablets:

The characterization tests like Hardness, Friability, Uniformity of drug content and Thickness were performed for the formulated compressed coated tablets of 5 batches (F1-F5).

4.7.1. Hardness test

The prepared five tablets were subjected to hardness test. It was carried out by using pfizer hardness tester and expressed in Kg/cm^2.

4.7.2. Friability test

The friability of the tablets was determined in Roche Friabilator and expressed in %. 10 tablets from each batch were weighed accurately and placed in the tumbling chamber and rotated at 25 rpm for a period of 4 min. Tablets were taken and reweighed. The percentage weight loss was determined by using formula given below. The experiment was repeated for three times and average was noted.

% Friability = (Initial Weight of Tablets - Final Weight of Tablets/ Initial Weight of Tablets) X 100

4.7.3. Weight variation test

Twenty tablets were selected randomly and weighed individually. Average weight was calculated standard deviation and percent coefficient of variance was computed. The test requirements are met, if not more than two of the individual weights deviate from the average weight by more than 5% and none more than 10%. Ranges of Weight variation test as per IP is shown in **Table 3.**

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Table 3: Ranges of Weight variation test as per IP

Average Weight of a tablet	Percentage Deviation
130mg or less	± 10
>130mg and <324mg	± 7.5
324mg or more	± 5.0

n= 3; SD-standard deviation

The prepared ciprofloxacin tablets were tested for their drug content. Five tablets of each formulation were weighed and finely powdered. About 0.1gm equivalent of ciprofloxacin was accurately weighed and completely dissolved in pH 6.8 phosphate buffer and the solution was filtered. 1ml of the filtrate was further diluted to 100ml with pH 6.8 buffer. Absorbance of the resulting solution was measured by UV- Visible spectrophotometer at 271nm.

4.8. In vitro drug release study

The *in vitro* dissolution study must be conducted in the dissolution medium which simulates the *in vivo* condition. The *in vitro* drug release studies for the prepared formulations were conducted for a period of 24hrs using USP dissolution apparatus type II set at 100rpm [21] and the temperature of 37±0.5˚C. Formulation was placed in 900ml of respective dissolution media [22].

The drug release studies were conducted in 1.2 pH buffer for 2hrs followed by 7.4 pH buffer for 3hrs and finally to mimic the conditions of colon 6.8 pH phosphate buffer is used as a dissolution media for 19hrs and at specified intervals 5ml samples were withdrawn from dissolution media and replaced with fresh media to keep the volume constant. The concentration of drug was estimated using UV Visible spectrophotometer (1.2pH -269nm, 7.4pH-277nm and 6.8pH-271nm).

4.9. Release kinetics:

Data obtained from the *in vitro* release studies of compression coated tablet of ciprofloxacin formulations were fitted to various kinetic equations such as zero order, first order, Higuchi model and Korsmeyer - pappas model.

Different mathematical models may be applied for describing the kinetics of the drug release process from the formulation matrix; the most suited being the one which best fits the experimental results. The kinetics of drug release from tablets was determined by finding the best fit of the dissolution data (drug release *vs.* time) to distinct models:

Zero order [eq.1], first-order [eq.2] , Higuchi [eq. 3] and Korsmeyer - pappas equation[eq. 4]

$Qt = k0\ t$ [1]

$Qt = Q\infty\ (1-e^{-k1t})$ [2]

$Qt = k_H\ t^{1/2}$ [3]

$Q/Q_0 = k\ t^n$ [4]

Where $Q\infty$ being the total amount of drug in the matrix, k0 the zero order kinetic constant, k1 the first order kinetic constant and k_H representing the Higuchi rate constant.

In Korsmeyer - pappas equation Q/Q_0 was fraction of drug released at time t, K was constant and n was diffusion constant that indicates general operating release mechanism. For Fickian (diffusion controlled) n ≤0.45; for non Fickian (anomalous/zero order) release 'n' value is in between 0.45 to 0.89; for zero order release n=1.0; for super case transport II, n >0.89.

4.10. Stability studies:

Stability study was carried out to assess the stability of the compression coated tablet of ciprofloxacin. Generally, the observation of the rate at which the product degrades under normal room temperature requires a long time. To avoid this undesirable delay, the principles of the accelerated stability studies were adopted. The tablets were packed in glass container. Stability studies were carried out at 40˚C and 75%RH over a period of 1 month. Samples were evaluated at 10^{th}, 20^{th} and 30^{th} days for different parameters such as physical appearance, hardness, weight variation, drug content and dissolution.

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