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FORMULATION AND *IN -VITRO* EVALUATION OF PREDNISOLONE COLON TARGETED DRUG DELIVERY SYSTEM

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ABSTRACT

The purpose of the present research study was to achieve successful delivery specifically to the colon, based on polysaccharides hydroxyl propyl methyl cellulose K4M (HPMC K4M), Xanthan gum, croscarmellose sodium (CCS) and microcrystalline cellulose as a compression coat over a core tablet of Prednisolone. The drug delivery system was based on the *In-vitro* evaluation system. In this study, each polysaccharide, along with microcrystalline cellulose, was used as a compression coating polymer and a combination of polysaccharides in the ratio of 1:1, 1:2, 1:3, 2:1, 2:2, and 2:3 was evaluated using *In-vitro* methods. The prepared tablets were evaluated for hardness, friability, weight variation, and drug content uniformity, and it was found that the results obtained complied with the official standards. The cumulative percentage release of Prednisolone after 12 hours in a pH 6.8 phosphate buffer was capable of maintaining the core tablet containing Prednisolone throughout this condition mimicking mouth to colon transit, according to *in-vitro* experiments. The kinetic analyses of the release confirmed that it followed the Korsmeyer-Peppas paradigm. The formulation having HPMC K4M, in particular, had an improved dissolving profile and bioavailability, indicating it a potential carrier for drug delivery to the colon.

KEYWORDS

Croscarmellose, Colon targeting, Compression coating, HPMC K4M, Polysaccharides and Xanthan gum.

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INTRODUCTON

Among all the routes of drug administration explored for the development of controlled release systems, the oral route has by far achieved the most attention and success. Its ease of administration and gastrointestinal physiology offer more flexibility in dosage form design than most other routes[1]. The scientific framework required to develop a successful oral controlled drug delivery dosage form consists of understanding three aspects

of the system. Namely[2].

The physicochemical characteristics of the drug.

Relevant G.I. anatomy and physiology.

Dosage form characteristics.

The factors to be considered in the design of colon-specific drug delivery systems[3]:

Anatomy and physiology of the colon

pH in the colon

Gastrointestinal transit

Colonic micro flora

Anatomy and physiology of colon:

Colon comprises the caecum, the ascending colon, the hepatic flexure, the transverse colon and the splenic flexure[4]. It is about 1.5m long and has an average diameter of about 6.5cm. The wall of the colon is composed of four layers: the serosa, muscularis externa, the sub mucosa, the mucosa and the lamina propria. The mucosa is divided into epithelium, lamina Propria, and muscular mucosae[5]. Mucus production in the Colon is a function of goblet cells, and the proportion of these increases in the elderly.

Functions of colon[2]

The colon serves four major functions; (I) creation of a suitable environment for the growth of colonic microorganisms; (II) storage reservoir of fecal contents; (III) expulsion of the contents of the colon at an appropriate time and; (IV) absorption of potassium and water from the lumen, concentration the fecal content, and secretion and excretion of potassium and bicarbonate[6].

pH in the colon[7]

Radio telemetry is used to measure the gastrointestinal pH in healthy human subjects. The average pH of the cecum and colon lumen is 6.8. The pH in the mid-colon was measured at 6.6±0.8 and in the left colon was 7.0± 0.74. In a group of 7 patients with untreated ulcerative colitis, the mean pH was 4.7. Table No.1 has the details about the pH of the various parts of the oral cavity.

Gastrointestinal transit[8]

Gastric emptying of dosage forms is highly variable. It depends primarily on whether the subject is fed or fasted and the dosage form properties, such as size and density. In healthy young and adult males, dosage forms such as capsules and tablets pass through the colon in approximately 20-30 hours. In patients with inflammatory bowel disease, the colonic residence of pharmaceutical dosage form tends to be the same as that in healthy subjects[9]. Both acute and chronic pathological conditions may affect the drug uptake from the colon. The transit times of dosage form in the G.I. tract are given in the following Table No.2.

Colonic micro flora[2]

A wide range of anaerobic and aerobic bacteria can be identified throughout the human gastrointestinal tract. The micro flora found in the G.I. tract of man is given in the following Table No.3.

Over 400 species of bacteria were found, predominantly anaerobes and a small number of fungi. Principal sources of nutrition for colonic microorganisms are carbohydrates arriving in the intestinal chyme. These processes may be responsible for the metabolism of many drugs and may also be applied to colon targeted delivery[10].

Approaches to colon-specific drug delivery[11]

Rectal administration is the most direct method for medication delivery into the colon. Colon-specific delivery systems that can be taken orally have been developed. There are three practical techniques by which a delivery system can be targeted into the colon following oral administration[2].

The targeting of orally administered drugs to the colon is accomplished by:

Coating with P.H. dependent polymers

Time-release dosage forms

Delivery systems based on the metabolic activity of colonic bacteria

Coating with pH-dependent polymers

Widely used polymers are methacrylic resins (Eudragits) which are available in water-soluble and water-insoluble forms[12]. The pH at which Eudragits dissolves is known as threshold pH and depends on the number of carboxyl groups in the molecules.

Ashford *et al*. have shown that Eudragit S, a model pH-dependent polymer, was used to coat rapidly disintegrating tablets[13]. The tablets were administered to healthy volunteers and studied for their *in vitro* behavior.

Time-release dosage forms

Pulsincap is a delivery system consisting of a capsule, half of which is non-disintegrating and the other half is enteric-coated. The main body is water-insoluble. The contents are contained within the body by a hydrogel plug which is covered by a

water-soluble cap[14]. An inner layer of HPMC and an outer layer of enteric polymer coat solid dosage forms. The inner layer of HPMC gels and slowly erodes after the outer layer has dissolved. The drug is released from the inner core of the dosage form when erosion reaches a threshold level. To achieve a suitable delay in drug release, a thicker layer of polymer was necessary[15].

Delivery systems based on the metabolic activity of colonic bacteria

Reduction and hydrolysis are two of the most fundamental metabolic activities carried out by colonic bacteria. Based on these actions, different ways were tried to target medications to the colon[16]. The site-specificity of these systems is their most distinguishing trait. These strategies are described below:

Coating with biodegradable azo polymers

Reducing azo bonds appears to be a common colonic bacterium reaction. Van den Mooter et al. looked into how colonic bacteria degraded several types of azo polymers[17].

Polysaccharides as matrices/coating agents

Several delivery systems based on polysaccharides that are selectively degraded in the colon have been reported. A mixed coating comprising amylose and ethyl cellulose has been reported to provide colon-specific delivery. Guar gum, LBG, tragacanth, and xylem have been mixed with methacrylate copolymers and used to coat tablets. Drug release was accelerated when galactomannan- degrading enzyme was added to the dissolution medium[18].

Colonic absorption (chemical, physical and metabolic barriers)

Several barriers can limit drug absorption from the colon. In the lumen itself, specific and non-specific drug binding can occur through the drug interaction with dietary components[19]. The mucus barrier at the epithelial surface can present a formidable physical barrier to uptake. The space between the mucus layer and epithelial cells, termed the unstirred water layer, presents another barrier to colonic absorption, particularly lipophilic drugs[20]. The low pH at the colonocyte surface may dramatically alter drug solubility and affect absorption. Drug transport in the colon occurs at the epithelium level. The lipid bilayer of the individual colonocytes and the occluding junctional complex (OJC) provide a physical barrier to the absorption of the drug. Small amphipathic drugs have a reasonable probability of transcellular transport by sequential partitioning from an aqueous to lipid and then back to an aqueous environment[21]. Facilitated drug uptake requires a Tran's membrane carrier at the apical plasma membrane typically composed of a protein or glycoprotein molecule. Transcytosis through receptor-mediated endocytosis and transport potentially provides a minimally invasive way to deliver a drug to the sub mucosal space. Paracellular transport may be the most promising means of general drug delivery in the colon. The presence of 1, 25 dihydroxy vitamin D3 stimulates both transcellular and paracellular colonic Ca 2+ ion influx[22].

Evaluation of prednisolone colon-specific drug delivery systems

A successful colon-specific drug delivery system remains intact in the physiological environment of the stomach and small intestine but releases the drug in the colon[23]. *In- vitro* methods are used to evaluate the colonic drug delivery systems. *In-vitro* methods are used to evaluate different carrier systems to deliver drugs specifically to the colon.

***In-vitro* method**

The ability of the coats/carrier to remain intact in the physiological conditions of the stomach and small intestine is generally assessed by conducting drug release studies in 0.1N HCl for 2 hrs[24]. (Mean gastric emptying time) and in phosphate buffer (pH 7.4) for 3 hrs. (Mean small intestinal transit time) using USP Dissolution rate test apparatus or flow through Dissolution apparatus.

Direct compression

"Direct Compression" is now used to define the process by which tablets are compressed directly from the powder blends of the active ingredients. Suitable excipients will flow uniformly into the die cavity and form into a compact mass[25].

Literature review

Hyo-Kyung Han *et al*, (2020) Colon-targeted drug delivery systems for macromolecules can provide therapeutic benefits including better patient compliance (because they are pain-free and can be self-administered) and lower costs. Increasing demand for a more patient-friendly drug administration system highlights the importance of

colonic drug delivery. PH-dependent systems, enzyme-triggered systems, receptor-mediated systems, and magnetically-driven systems are explored.

Cristina Maderuelo *et al*, (2020)[26] Colon drug delivery has become a field of growing interest. It can target certain drugs and/or peptides to the colonic region for the treatment of several diseases. Chitosan, polyethylene-oxide, hydroxypropyl methylcellulose, pectin, natural gums and alginates have shown promise.

Betty Philip *et al*, (2010)[27] the colon is a site where both local and systemic delivery of drugs can take place. Local delivery allows topical treatment of inflammatory bowel disease. Treatment can be made effective if the drugs can be targeted directly into the colon, thereby reducing the systemic side effects.

Manoj Kumar Sarangi *et al*, (2020)[28] Colon targeted drug delivery has a number of important implications in the field of pharmacotherapy. Targeting of drugs to the colon via oral administration protects the drug from degradation or release in the stomach and small intestine. Various drug delivery systems have been designed that deliver the drug quantitatively to the colon and then trigger the release of the drug. This review will cover different types of polymers which can be used in the formulation of colon targeted drug delivery systems.

Rajiv Bajracharya *et al*, (2020)[29] Colon-targeted drug delivery systems for macromolecules can provide therapeutic benefits including better patient compliance (because they are pain-free and can be self-administered) and lower costs. Increasing demand for a more patient-friendly drug administration system highlights the importance of colonic drug delivery. PH-dependent systems, enzyme-triggered systems, receptor-mediated systems, and magnetically-driven systems are explored.

Objectives of the study

The main objective of this present work is to formulate a colon targeted drug release tablet of Prednisolone by compression coating method using polymers such as HPMC K4M and Xanthan gum.

Prednisolone is a selective beta-2 adrenergic agonist used as a bronchodilator and tocolytic. Several methods of colonic targeting have been proposed. HPMC K4M and Xanthan gum is degraded in the colon by the bacterial enzymes. The main consequences of bacterial fermentation of such polysaccharides are faecal bulking, decreased transit of the colonic contents and increased nitrogen utilization in the gut and the formation of short-chain fatty acids which form a useful energy supply.

The objective of the present study is expected to

Improves Patient compliance by decreasing dosing frequency.

Drug releases in controlled manner for prolonged period.

Site-specific drug delivery to colon can be achieved.

MATERIAL AND METHODS

Materials

Prednisolone, Xanthan gum, Sodium hydroxide pellets, and Potassium bromide (I.R. grade) were the gift samples from S.D. fine Chem. Ltd, HPMC K4M was obtained from Alembic Pharma, Baroda, India. CCS, Microcrystalline cellulose, Sodium starch glycolate, Potassium dihydrogen phosphate, Potassium chloride, Hydrochloride (HCl), and Magnesium stearate were received Spectrum Pharma labs Hyderabad; Talc was the gift sample from Leo chem. Bangalore, India.

Methods

Compatibility studies by FT-Infrared (FTIR) spectroscopy

FTIR was carried out to determine the compatibility between the drug Prednisolone and the Xanthan gum, HPMC K4M. 5mg of the sample and 400mg of KBr were taken in a mortar triturated. A small amount of the triturated sample was taken into a pellet maker and was compressed at $10kg/cm^2$ using a hydraulic press. The pellet was kept onto the sample holder and scanned from $4000cm^{-1}$ to $400cm^{-1}$ in Brucker FT-IR spectrophotometer. Samples were prepared for the drug Prednisolone, polymer Xanthan gum, HPMC K4M, and a physical mixture of drug and polymer. The spectra obtained were compared and interpreted for the functional group peaks.

Determination of Absorption Maxima (λmax)

5mg of Prednisolone was weighed accurately and dissolved in 5ml of methanol and make up the volume to 100ml with PH 6.8 phosphate buffer in

100ml volumetric flask (stock solution). Transfer 1ml from stock solution into 100ml volumetric flask and diluted up to 100ml with PH 6.8 phosphate buffer. The resulting solution was labeled as a standard Working Solution. The spectrum of this solution was run in the 200-400nm range in UV-Visible Spectrophotometer. The λ max of the Prednisolone was found to be 246nm.

Preparation of Standard graph

From the standard working solution, 1ml, 2ml, 3ml, 4ml, and 5ml were withdrawn and diluted up to 10ml with PH 6.8 phosphate buffer in 10ml volumetric flask to get the concentration of 2µg, 4µg, 6µg, 8µg, and 10µg respectively. The absorbance of each solution was measured by UV-Visible Spectrophotometer at 246nm using PH 6.8 phosphate buffer as blank.

Preparation of Prednisolone tablets

Preparation of Prednisolone core tablets

For *in-vitro* drug release studies, each core tablet (average weight 75mg) contained Prednisolone (5mg), microcrystalline cellulose (MCC qs), and dried starch (4mg). To complete the mixing, the materials were weighed, mixed, and passed through a mesh (250m). On a single station tablet machine, the tablets were made by compressing the thoroughly mixed materials with 7mm round, flat, and plain punches (cadmach, India). The core tablet's thickness was 0.2mm, and their crushing strength was tested. It was around 3 kilogrammes per square metre.

Compression coating of Prednisolone core tablets

The Prednisolone core tablets were compression coated with various amounts of coating material (HPMC K4M, Xanthan gum) at various concentrations. To give the coats enough hardness, microcrystalline cellulose was used in the formulations. Half of the coating material was placed in the die cavity, and the core was carefully placed in the die cavity's center and filled with the remaining coating material. Using 10mm round, flat, and plain punches, the coating material was compressed around the core at a force of 5,000kg. The compression coat tablet's strength was 5kg/cm2.

Prednisolone compression coated tablets characterization

Hardness test

A hardness test was performed on the prepared tablets. It was done with a hardness tester and the results were expressed in Kg/cm2.

Friability test

The percentage of friability was calculated using the Roche friabilater (percent). 10 tablets from each batch were weighed separately (Initial) and placed in the friabilater, which was then turned 100 times at 25rpm for 4 minutes. The weights of the tablets were recalculated (Final), and The percentage friability of each batch was calculated using the formula below,

$$F\ (\%) = \frac{Initial\ weight - final\ weight}{initial\ weight} \times 100$$

Weight variation test

Twenty tablets were chosen at random from the batch, weighed individually, and the average weight calculated. The weight of each tablet was compared to the average weight and the percent deviation was calculated.

Uniformity of drug content

The drug content of the prepared Prednisolone tablets was determined. Each formulation's five tablets were weighed and finely powdered. The solution was filtered after 0.1gm equivalent was accurately weighed and completely dissolved in pH 6.8 phosphate buffer. With PH 6.8 buffer, 1ml of the filtrate was diluted to 100ml. A UV visible spectrophotometer was used to measure the absorbance of the resulting solution at 246nm.

***In vitro* drug release studies**

Type of USP dissolution apparatus I was hired to investigate the *in vitro* drug release of various formulations. The dissolution medium was 900ml of pH 1.2 acidic buffer for 2 hours and pH 7.4 phosphate buffer for 3 hours. In the basket, the tablet was kept. The temperature was kept at 37°C 0.5°C, and the stirring speed was set to 100rpm. 2 samples each of 1mL samples were taken, diluted appropriately, and spectrometrically analysed.

The drug release study was carried out with minor modifications to the USP dissolution apparatus. In the water bath of the apparatus, a beaker containing 200mL of PH 6.8 phosphate buffer was placed. The tablets were inserted into the apparatus' baskets and

submerged in the dissolution medium. The drug release tests lasted 21 hours (the average colonic transit time is 20-30 hours), with 1ml samples taken at regular intervals. A new dissolution medium was added to the same volume. The samples were diluted and measured against a blank using a UV-visible spectrophotometer at 246nm.

Release kinetics

The data from *in vitro* release studies of Prednisolone formulation P4F5 compression coated tablets was fitted to various kinetic equations, including zero order, first order, Higuchi model, and Korsmeyer-Pappas model.

Zero-order equation: $Q = Q_0 - K_0t$

First order equation: $\ln Q = \ln Q_0 - K_1t$

Higuchi equation: $Q = K_2t^{1/2}$

Korsmeyer - Pappas equation: $sQ/Q_0 = Kt^n$

K0 to K2 were release rate constants, Q/Q0 was the fraction of drug released at time t, K was a constant, and n was the diffusion constant. $n \leq 0.5$ for Fickian (diffusion-controlled) release; n 0.5 to 1.0 for non-Fickian (anomalous/ zero-order) release; n=1.0 for zero-order release; n > 1.0 for super case transport II.

RESULTS AND DISCUSSION

FTIR spectrophotometer Study of Drug Polymer Interactions

Drug-Excipient compatibility studies

An F.T. infrared (FT-IR) spectroscopy study was carried out to check the compatibility between the drug Prednisolone and the polymers HPMC K4M, Xanthan gum used to prepare the compression coated tablet of Prednisolone. The FT-IR was performed for drug polymers. The spectra obtained from F.T. infrared spectroscopy studies at a wavelength from $4000cm^{-1}$ to $400cm^{-1}$ are shown in Figures No.5 to No.8. The I.R. spectrum of Prednisolone drug was compared with the I.R. spectrum of Prednisolone with HPMC K4M, CCS, and Xanthan gum. The presence of all characteristic peaks of Prednisolone in the I.R. Spectra was obtained with Prednisolone and other polysaccharides. The spectral obtained from FTIR Spectroscopy studies at a wavelength between $4000cm^{-1}$ to $400cm^{-1}$ are given in table and figure.

Preparation of standard graphs

The standard graph for the drug Prednisolone was done in pH 6.8 phosphate buffer. Table No.7 shows the details of the calibration curve.

Characterization of Prednisolone core tablets

Physicochemical evaluations of Prednisolone core tablet tablets

The direct compression method was used to make the Prednisolone core tablets. Table No.9 shows the results of the physicochemical evaluation of prepared tablets. The weight variation, drug content, hardness and friability, and disintegration of the tablets were all assessed. The drug content was discovered to be between 98.52 percent and 100 percent. The hardness ranged from 4.2 (kg/cm2) to 4.2 (kg/cm2) in all cases, less than 1% of the friability was observed.

Physicochemical evaluations of compression coated tablet of Prednisolone

Prednisolone was prepared as a compression coated tablet. Table No.10 shows the results of the physicochemical evaluation of a compression coated tablet of Prednisolone. The weight variation, hardness, and friability of the tablets were also assessed. The hardness ranged from 4.0 to 4.9 (kg/cm2), and the friability was less than 1% in all of the cases.

Results of dissolution studies

The cumulative percentage drug released at different time periods from Prednisolone tablets compression coated with coat formulation P4F1, P4F6 in 0.1 N HCI (2 hrs), pH 7.4 phosphate buffer (3 hrs) and pH 6.8 Phosphate buffer were found to be Formulation P4F1 containing 1:1 ration of HPMC K4M (20mg) and Xanthan gum (20MG) released 98.86% of drug by the end of 8hrs, Formulation P4F2 containing 1:2 ratio of HPMC K4M (20mg) and Xanthan gum (40mg) released 99.42% of drug by the end of 10hrs, Formulation P4F3 containing 1:3 ratio of HPMC K4M (20mg) and Xanthan gum (60mg) released 97.54% of drug by the end of 11hrs, Formulation P4F4 containing 2:1 ratio of HPMC K4M (40mg) and Xanthan gum (20mg) released 97.63% of drug by the end of 10hrs, Formulation P4F5 containing 2:2 ratio of HPMC K4M (40mg) and Xanthan gum (40mg) released 96.66% of drug by the end of 12hrs and Formulation P4F6 containing 2:3 ratio of HPMC K4M (40mg) and Xanthan gum (60mg) released 84.79% of drug by the end of 12hrs respectively.

According to the findings, the rate of drug release from Prednisolone tablets decreased as the coating polymer concentration increased. The coat formulation P4F5 was completely disintegrated after 12 hours of testing.

Data of Release kinetics of compression coated tablet of Prednisolone

Table No.13 and Figure No.9 to Figure No.12 show the kinetics and release mechanism of Formulation P4F5

The results of *in vitro* release studies of the compression coated tablet of Prednisolone formulation P4F5 were fitted to various kinetic equations such as zero order, first order, Higuchi model, and Korsmeyer-Peppas model, and Table No.13 and Figure No.9 to Figure No.12 show the results.

The *in-vitro* dissolution data for best formulation P4F5 were fitted in different kinetic models, i.e., zero-order, first-order, Higuchi, and Korsmeyer-Peppas equation. Optimized formulation P4F5 shows an R^2 value of 0.987. As its value is nearer to the '1', it is confirmed as follows the zero-order release. The mechanism of drug release is further confirmed by the Korsmeyer and Peppas plot; if n = 0.45, it is called Case I or Fickian diffusion, 0.45 < n < 0.89 is for anomalous behavior or non-Fickian transport, n = 0.89 for case II transport, and n > 0.89 for Super case II transport.

The 'n' value is 1.991 for the optimised formulation (P4F5) i.e., n value was 0.45 < n < 0.89 this indicates non-fickian transport. The release kinetics for the optimized formula is shown in the table.

Discussion

The drug should not be released into the physiological environment of the stomach or small intestine if it is delivered to the colon. The polymer was applied as a compression coat over Prednisolone core tablets in this study. As a result, after 12 hours of testing, *in-vitro* drug release studies were performed in pH 6.8 phosphate buffer, which included testing simulated gastric and intestinal fluid.

Pre-formulation Studies

Melting Point Determination

The melting point of Prednisolone was determined by the capillary method. The melting point of Prednisolone was found to be in the range 235° C., which complied with B.P. standards, thus indicating the purity of the drug sample.

Solubility

Soluble in methanol, ethanol, Chloroform (95%); soluble in water; Soluble in octanol, but soluble in 6.8 phosphate buffer; it is very soluble in dimethylformamide.

Calibration curve

In Pre-formulation studies, it was found that the estimation of Prednisolone by spectrophotometric method at 246nm in pH 6.8 buffers had good reproducibility at the concentration between 2-10µg/ml. Correlation between concentration co-efficient was found 0.999 for pH 6.8 and slope for pH 0.036, respectively.

Drug-Excipient compatibility study

From the I.R. Spectrum no. 5.1 to 5.4, it was observed that there were no changes in these main peaks in I.R. Spectra of drug and polymers, which show there were no physical interactions because of some bond formation between drug and polymers.

The peaks obtained in the spectra of drug and polymer mixtures correlate with the peaks of the drug spectrum. It indicates that the drug was compatible with the formulation components.

Carr's Index

Carr's index was carried out, and the results were shown in Table No.8. It was found to be between 9.29 and 15.55, indicating have the required flow property for compression.

Angle of repose

The angle of repose for the formulated blend was carried out, and the results were shown in Table No.8. It can be concluded that all the formulation blends angle of repose was found to be in the range 22.85 to 28.25. Hence the entire formulation blends were found to possess good flow property.

Evaluation of coated tablets

Hardness test

The measured hardness of coated tablets of each formulation ranged between 4.5 to 4.9 kg/cm^2. It ensures good handling characteristics of all formulations.

Friability Test

Table No.10 shows the results of the friability test on coated tablets. In all of the formulations, the percent

friability ranged from 0.06 to 0.98, ensuring that the tablets were mechanically stable. From 3 hours onwards, the percent drug release from tablets coated with coat formulation P4F6 increased, indicating the start of gum coat breaking. After 12 hours of testing, 84.79 percent of the drug was released, and the tablet coat was found to be broken at one point, allowing the drug to be released. From 8 hours onwards, a significant increase in percent drug released was observed in tablets coated with coat formulation P4F5. Prednisolone was released in amounts of 96.66 percent respectively, at the end of the experiment. The drug was released into the dissolution medium after the coat was completely degraded. Because of the polymer content and coat thickness formulation. Because P4F6 was less than P4F5, the coat may have been completely hydrated and degraded at a faster rate, resulting in the release of approximately 96.66 percent Prednisolone.

Table No.1: P.H. of the G.I. tract

S.No	Name of the organ	pH of the organ
1	Oral cavity	6.2-7.4
2	esophagus	5.0-6.0
3	stomach	1.5-3.5
4	Small intestine: It is divided into three parts: The duodenum,	6
5	jejunum	7.0-8.0
6	And ileum.	7.0-8.0
7	Large intestine	Right colon: 6.4 Mid colon and left colon: 6.0-7.6

Table No.2: The transit time of dosage forms in the G.I. tract

S.No	Organ	Transit time (hr)
1	Stomach	< 1 (Fasting) >3 (Fed)
2	Small intestine	3 – 4
3	Large intestine	20-30

Table No.3: The micro flora found in the GIT of man

S.No	Bacterial counts (CFU/ml)	Stomach	Jejunum	Ileum	Feces
1	Total bacterial count	$0 - 10^3$	$0 - 10^5$	$10^3 - 10^7$	$10^{10} - 10^{12}$
2	Aerobic or facultative anaerobic Bacteria	-	-	-	-
3	Enterobacteria	$0 - 10^2$	$0 - 10^3$	$10^2 - 10^6$	$10 - 10^{10}$
4	Streptococci	$0 - 10^3$	$0 - 10^4$	$10^2 - 10^6$	$10 - 10^{10}$
5	Staphylococci	$0 - 10^2$	$0 - 10^3$	$10^2 - 10^5$	$10^4 - 10^7$
6	Lactobascillus	$0 - 10^3$	$0 - 10^4$	$10^2 - 10^5$	$10^6 - 10^{10}$
7	Fungi	$0 - 10^2$	$0 - 10^2$	$10^2 - 10^3$	$10^2 - 10^6$
8	Anaerobic bacteria	-	-	-	-
9	Bacteroides	Rare	$0 - 10^2$	$10^3 - 10^7$	$10^{10} - 10^{12}$
10	Bifidobacteria	Rare	$0 - 10^3$	$10^3 - 10^5$	$10^8 - 10^{12}$
11	Gram-positive cocci	Rare	$0 - 10^3$	$10^2 - 10^5$	$10^8 - 10^{11}$
12	Clostridia	Rare	Rare	$10^2 - 10^4$	$10^6 - 10^{11}$
13	Eubacteria	Rare	Rare	Rare	$10^9 - 10^{12}$

Table No.4: P.H. Dependent polymers investigated with various drugs in colon targeting[16]

S.No	Drug	Polymer	Threshold P.H.
1	5 ASA	Eudragit S	7
2	Prednisolone	Eudragit S	7
3	5 ASA	Eudragit L	6
4	Insulin	Eudragit L/S	6.5
5	BDP	Cellulose acetate phthalate	6

Table No.5: Formula for the preparation of Prednisolone core tablets

S.No	Ingredients	P1	P2	P3	P4
1	Prednisolone	5	5	5	5
2	Microcrystalline Cellulose	65	62	65	62
3	Sodium Starch glycolate	3	6	-	-
4	Corsscarmellose sodium	-	-	3	6
5	Talc	1	1	1	1
6	Magnesium stearate	1	1	1	1
7	Total tablet weight(mg)	75	75	75	75

Table No.6: Composition of Prednisolone compressed tablets

S.No	Coat Formulation	Core Weight mg	Coat ratio	Composition (mg)					Total weight mg
				HPMC K4M: Xanthan gum	PVP K 30	MCC	Magnesium Stearate	Talc	
1	P4F1	75	1:1	40	20	159	3	3	300
2	P4F2	75	1:2	60	20	139	3	3	300
3	P4F3	75	1:3	80	20	119	3	3	300
4	P4F4	75	2:1	60	20	139	3	3	300
5	P4F5	75	2:2	80	20	119	3	3	300
6	P4F6	75	2:3	100	20	99	3	3	300

Table No.7: Data for the standard curve of Prednisolone in pH 6.8 phosphate buffer

S.No	Concentration (µg/ml)	Absorbance
1	2	0.152
2	4	0.304
3	6	0.457
4	8	0.609
5	10	0.751

Table No.8: Results for Derived and Flow properties

S.No	Formulation Code	Bulk density	Tapped density	Angle of repose	Carr's index	Hausner's ratio
1	P1	0.41	0.49	23.57	10.97	1.21
2	P2	0.43	0.46	22.85	15.55	1.12
3	P3	0.45	0.48	24.74	11.86	1.19
4	P4	0.42	0.50	28.25	9.29	1.15

Table No.9: Physicochemical evaluations of Prednisolone core tablet tablets

S.No	Formulation Code	Weight variation (%)	Hardness (Kg/cm^2)	Friability (%)	The drug content in mg
1	P1	1.40	4.4	0.36	95.84
2	P2	1.39	4.2	0.25	97.26
3	P3	1.38	4.0	0.42	96.39
4	P4	1.40	3.9	0.67	95.48
Disintegration time 60 sec					

Table No.10: Prednisolone Compression Coated Tablet Physicochemical Evaluations

S.No	Batch Code	Parameter		
		Hardness (kg/cm^2)	Friability (%)	Weight variation (%)
1	P4F1	7.7	0.16	0.58
2	P4F2	7.5	0.08	0.63
3	P4F3	7.6	0.18	0.44
4	P4F4	7.9	0.26	0.78
5	P4F5	7.5	0.17	0.37
6	P4F6	7.0	0.06	0.51

Table No.11: Data of *in vitro* drug release studies Prednisolone core tablets

S.No	Time in Mins.	Cumulative percentage Release of Prednisolone			
		P1	P2	P3	P4
1	0	0	0	0	0
2	5	29.28	32.54	44.37	55.84
3	10	38.44	41.91	54.24	67.07
4	15	45.02	48.56	60.89	74.19
5	20	52.18	55.67	67.21	82.17
6	25	59.85	62.91	74.07	89.8
7	30	66.85	69.32	81.07	98.34
8	35	73.87	76.53	88.72	
9	40	80.19	83.26	95.87	
10	45	87.64	90.57		

Table No.12: Data of *in vitro* drug release studies Prednisolone compression coated tablets

Time in Hrs	Cumulative percentage Release of Prednisolone					
	P4F1	P4F2	P4F3	P4F4	P4F5	P4F6
0	0	0	0	0	0	0
1	0	0	0	0	0	0
2	0	0	0	0	0	0
3	16.24	10.88	8.56	10.82	14.64	11.82
4	32.98	23.26	18.73	22.28	23.47	19.76
5	50.75	36.14	29.87	35.19	32.54	27.64
6	67.58	49.24	40.08	48.15	40.97	35.76
7	83.81	62.31	51.25	61.34	50.16	43.17
8	98.86	74.33	63.16	73.54	58.07	51.27
9	-	87.15	74.64	85.51	67.17	59.54
10	-	99.42	86.34	97.63	76.34	67.92
11	-	-	97.54	-	87.54	76.64
12	-	-	-	-	96.66	84.79

Table No.13: Release kinetics of Prednisolone from Formulation P4F5

Time (h)	P4F5
0	0
1	0
2	0
3	14.64
4	23.47
5	32.54
6	40.97
7	50.16
8	58.07
9	67.17
10	76.34
11	87.54
12	96.66

Table No.14: Drug release kinetics

S.No	R^2 values					n values
	Formulation	Zero-order	First-order	Higuchi	Korsmeyer - Peppas	Korsmeyer-Peppas (n)
1	P4F6	0.987	0.784	0.859	0.930	1.991

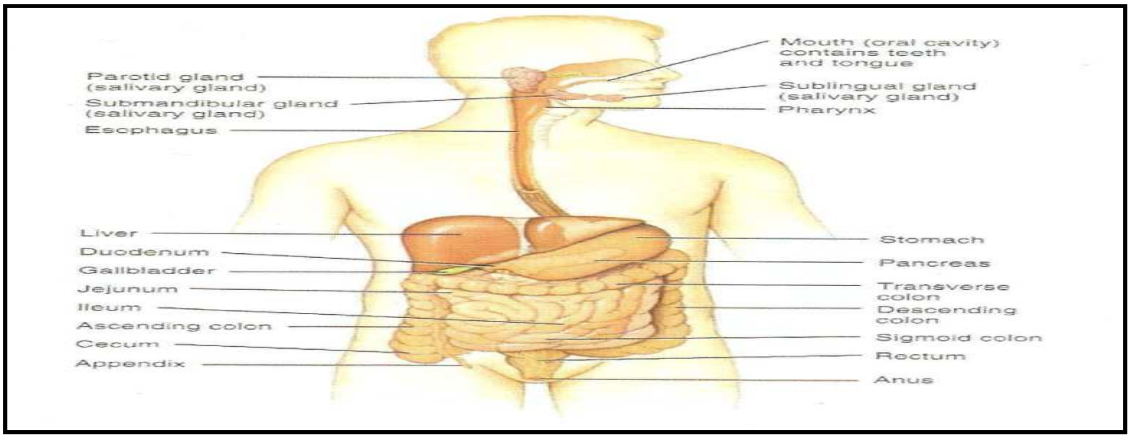

Figure No.1: Gastrointestinal tract

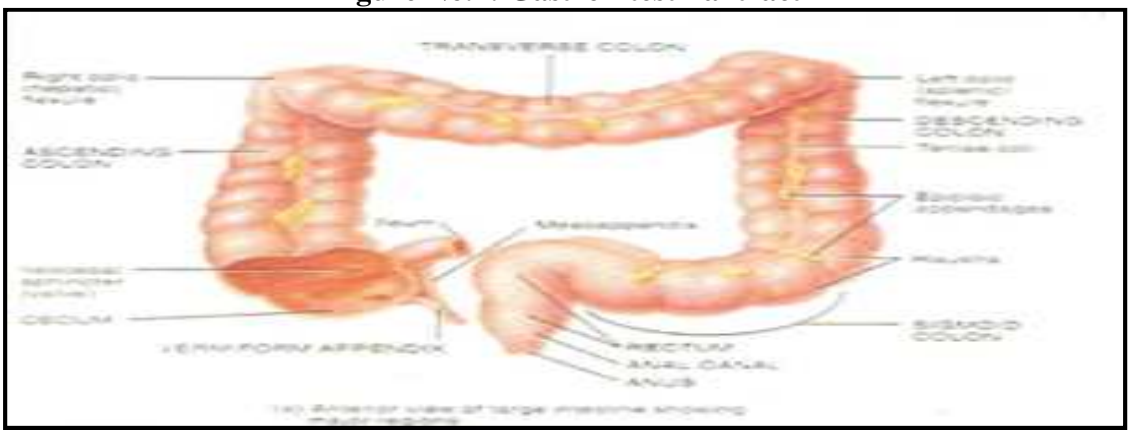

Figure No.2: Colon (Large intestine)

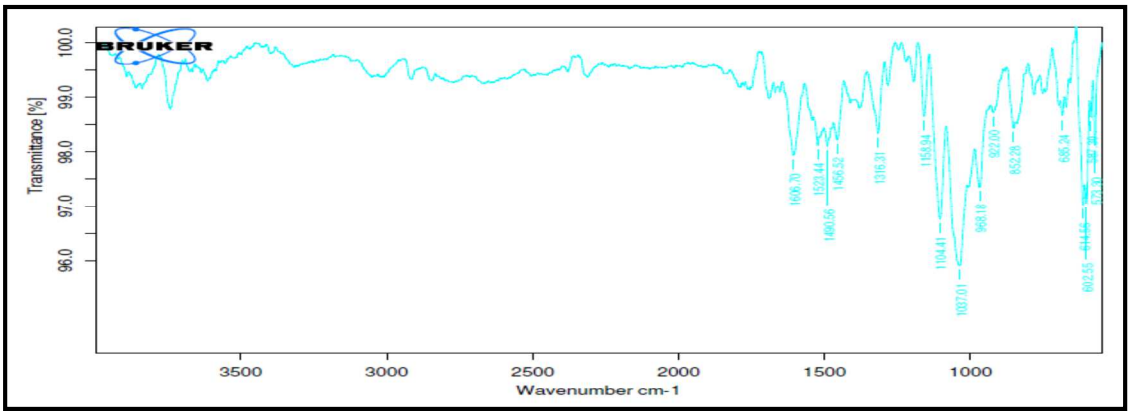

Figure No.3: I.R. Spectrum of Prednisolone

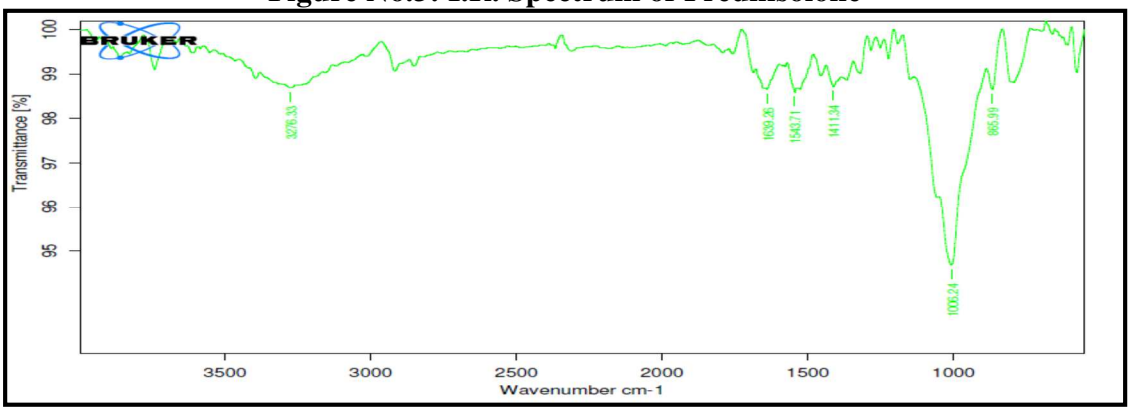

Figure No.4: I.R. Spectrum of Drug and Excipients

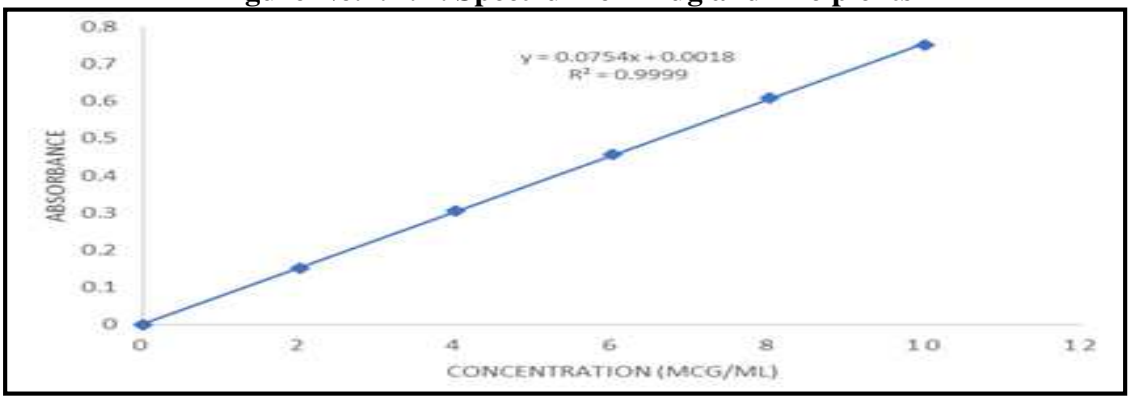

Figure No.5: Standard curve of Prednisolone in pH 6.8 phosphate buffer

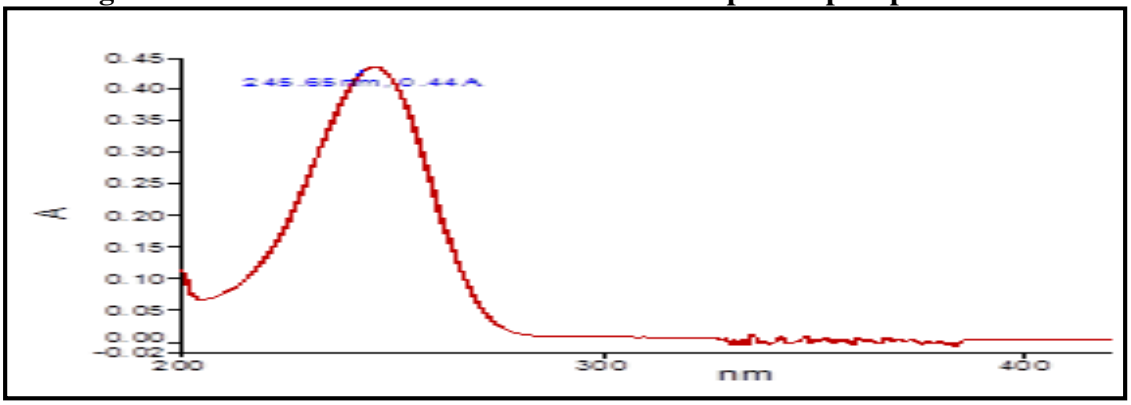

Figure No.6: U.V. spectrum of Prednisolone 246nm

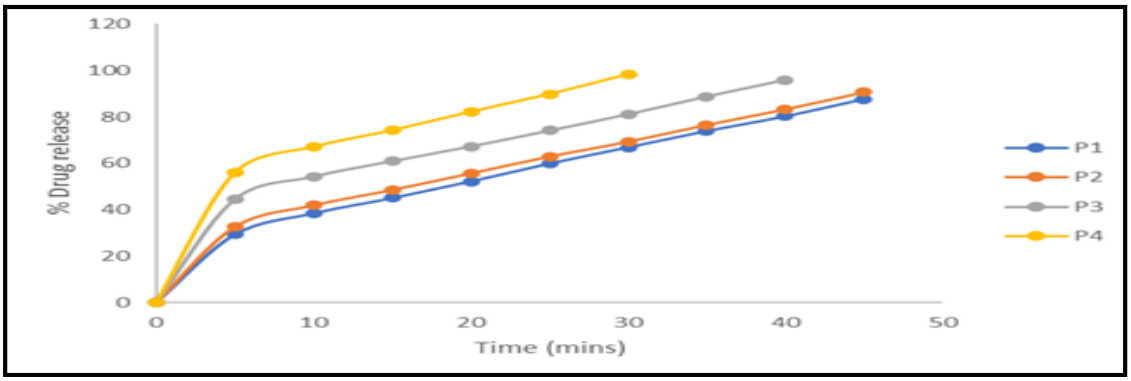

Figure No.7: Prednisolone Cumulative Percentage Release Profile in Formulations P1 to P4

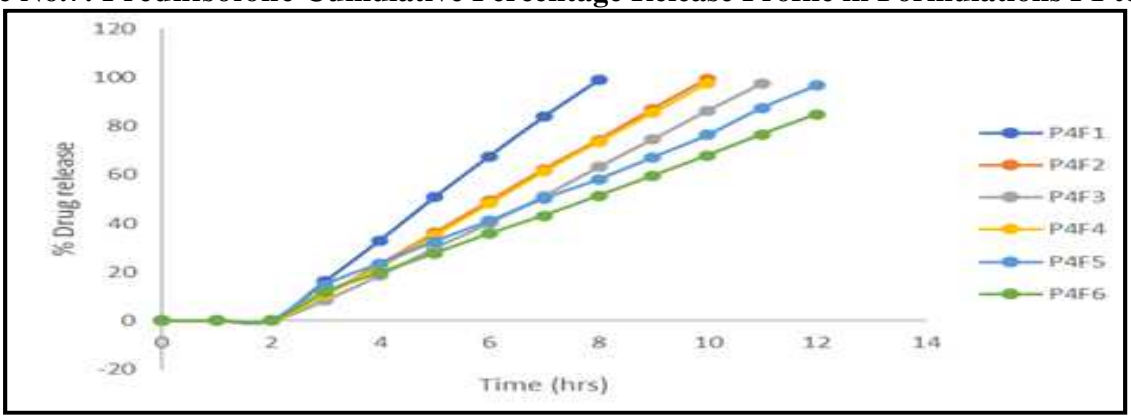

Figure No.8: Prednisolone's cumulative percent release profile in Formulations P4F1 to P4F6

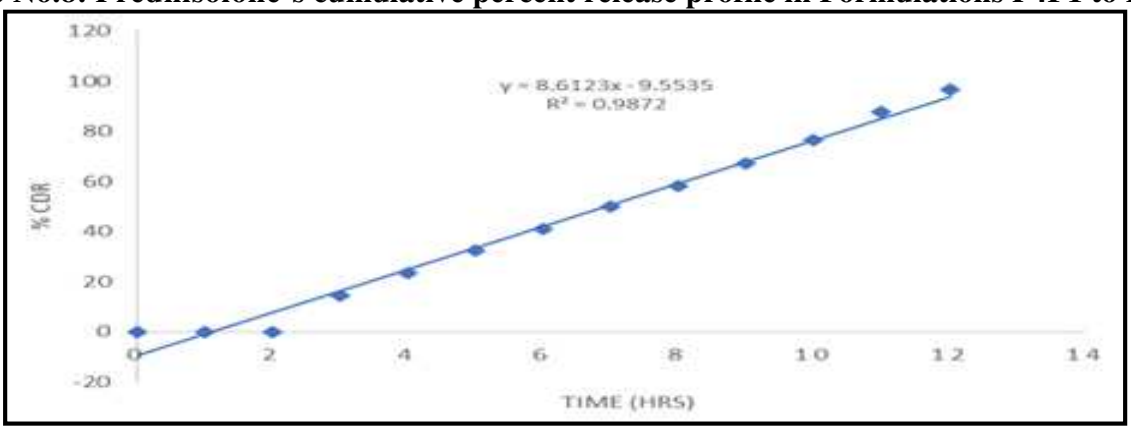

Figure No.9: Zero-order release kinetics of Formulation P4F5

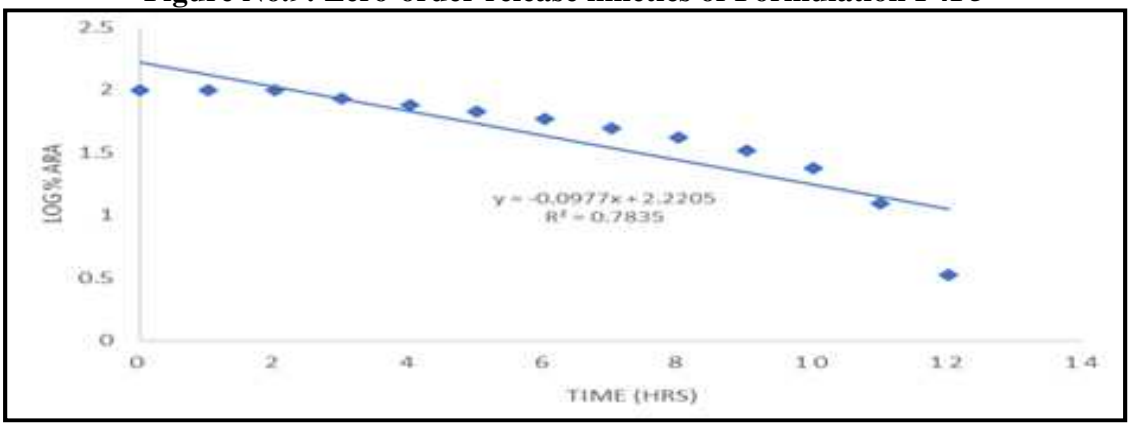

Figure No.10: First order release kinetics of Formulation P4F5

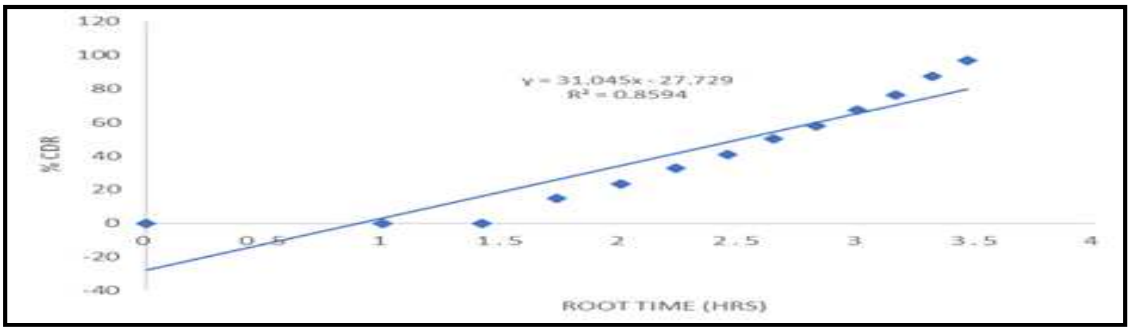

Figure No.11: Higuchi model release kinetics of Formulation P4F5

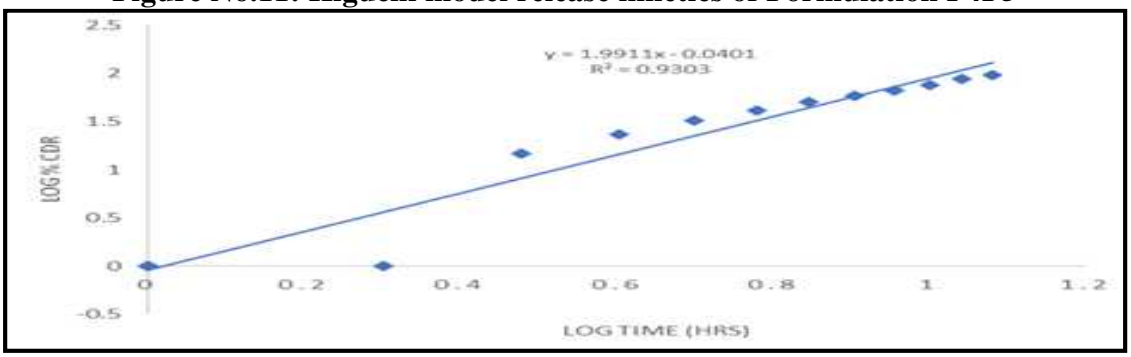

Figure No.12: Korsmeyer-Peppas model release kinetics of Formulation P4F5

CONCLUSION

Drugs delivered directly to the colon via the oral route have a number of therapeutic benefits. This study clearly shows that a compression coat containing 80 mg of HPMC K4M and Xanthan gum can be used to deliver drugs to the colon. These polysaccharides can delay the release of core materials until they reach the colon, which has a high concentration of enzymes that degrade HPMC K4M and Xanthan gum, allowing the drug to be released.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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