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Development of Colon Targeted Prednisolone Compression Coated Tablet

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Abstract: This study's aim was to make compression-coated Prednisolone pills that would be an effective and safe way to treat inflammatory bowel disease and ulcerative colitis. The carriers used were pectin, xanthan gum, and HPMC. For prednisolone core pills, xanthan gum: HPMC in a 1:1 and 1:2 ratio and pectin: HPMC in a 1:1 and 1:2 ratio were used to cover them. When compared to pectin by itself, HPMC-coated pellets protect against early drug release in the upper GI tract better. In situations like those that would happen in the gut, the pectin can still be broken down by enzymes, letting out more medicine. The compression-coated tablet may have different drug release patterns depending on how it is designed. For example, pectinolytic enzymes may cause more medicine to be released. By changing things like the molecular weight of the polymers or the ratio of pectin to HPMC, it is possible to make a system with a release profile that is tailored to the needs of each individual medicine. The results show that pectin:HPMC coated pills can be used to treat inflammatory diseases of the gut. Most of the time, gut bacteria break down natural carbohydrates like xanthan gum in the colon instead of in the small intestine or stomach. In the small intestine, the medicine came out of HPMC when enzymes from bacteria in the colon broke it down.

Keywords: Prednisolone, Colon-targeted drug delivery, HPMC, Compression coated tablet

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Introduction

In the past few years, a lot of study has been done on colon-targeted drug delivery, which could help treat disorders that only affect the colon better while lowering the risk of side effects that affect the whole body (Raju *et al.*, 2011). This part of the body is affected by ulcerative colitis (UC), irritable bowel syndrome (IBS), and Crohn's disease (CD). These medicines only reach the colon and not the upper gastrointestinal tract (GIT). This results in less overall absorption and a larger dosage of the medication entering the colon. Since the colon can hold food for up to five days and the lining of the colon has been shown to help drugs absorb, it is a great place to give medicine. Medicine can be given into the gut in two ways: by mouth orally or rectally (Rathnam and Bhadane, 2017). For colon-specific delivery, oral dose types are the best way to go because they are easy to use. Oral dosage forms do not have to be made in a sterile way, so they can be made and created in a more flexible way. This makes it easier for patients to follow their treatment plans, and they can be given pretty easily (Surana and Mahajan, 2024). It was hard to get medicine to specific parts of the gut when it was given directly through the rectal canal. Also, the amount of medicine spread varies between rectal dose types based on how long they stay in the body and how well they spread (Dasankoppa *et al.*, 2012). A colon-specific drug delivery system's (CDDS) effectiveness is contingent upon the drug's chemical and physical composition, the kind of delivery mechanism employed, any other variables that may affect the drug's rate of GI tract passage, and the degree to which the medication interacts with the GI tract (Garala *et al.*, 2011). Oral CDDS was needed to keep the medicine from being released in the small intestine and stomach. The goal of the methods used to make a CDDS is to delay the release of the drug until the system enters the gut. Some methods work better than others (Kunithala *et al.*, 2012).

It was hard to get to the stomach because the drug was close to the end of the alimentary canal. The fluid level in the colon was higher and thicker than in the upper GI tract. This made it hard for medicines that did not dissolve well to get to the colon. For this reason, the drug must be in solution before it gets there (Keservani *et al.*, 2020). Drugs may not be able to get through the mucous and into the bloodstream as easily because the colon's links are relatively tight and its surface area is low (Ahire *et al.*, 2023).

Glucocorticoids and other painkillers are now used to treat ulcerative colitis and Crohn's disease, a type of chronic colitis. When glucocorticoids are given by mouth or through an IV, like methyl prednisolone and dexamethasone, they can have bad effects on body's immune system, adenosuppression, cushinoid signs, and bone loss (Keservani *et al.*, 2023). So, delivering medicines specifically to the gut might help lower the side effects that come from high doses as well as the right dose. CTDDS are drugs that do not dissolve well in the stomach or intestines. Peptides are an example of this. Most of the time, medicines for diarrhoea, ulcerative colitis, IBD, and colon cancer are given locally. Some medicines used to treat GIT problems are not well absorbed by the upper GI system but are used locally in the colon (Yehia *et al.*, 2009).

As of 30 years ago, corticosteroids were the main way that people with mild to severe active inflammatory bowel disease were treated. 40–60 mg of prednisone every day is the first line of treatment. Giving prednisolone through an IV every eight hours is a good first treatment for hospitalised patients who are very sick (Jain *et al.*, 2023). When an IV corticosteroid is injected, most people feel better right away. Six to eight days after the treatment, its full effects were seen. The daily dose of prednisone is lowered by 5 to 10 mg until it hits 15 to 20 mg. This is done once it has been shown to help (Alkazzaz and Ali, 2015). Then, every week until the medicine stops, this dose is dropped by 2.5 mg to 5 mg. The study's goal was to make compression-coated prednisone pills that would be an effective and safe way to treat inflammatory bowel disease and ulcerative colitis. The carriers used were pectin, xanthan

Table 1: Formulation of Prednisolone Compression Coated Tablets

S. No.	Ingredients	Formulation Quantity per tablet (mg)				
	Formulation	**F1**	**F2**	**F3**	**F4**	**F5**
1	Prednisolone	20	20	20	20	20
2	Microcrystalline cellulose	40	40	40	40	40
3	Magnesium stearate	1.0	1.0	1.0	1.0	1.0
4	Talc	1.0	1.0	1.0	1.0	1.0
5	Xanthan gum	130	140	150	-	-
6	Hydroxy propyl methyl cellulose	40	40	40	40	40
7	Pectin	-	-	130	150	140

gum, and HPMC. A mix of xanthan gum (HPMC) and pectin (HPMC) was used to cover the core of the prednisolone pills (Maity and Sa, 2016).

Materials and Methods

Preformualtion Studies:

The goal of the preformulation study was to find out the physicochemical features of the drug and how well it works with the different ingredients that will be used in the formulation. There must be preformulation tests in order to get a steady, safe, and effective dose form (Kumari *et al.*, 2018).

Calibration Curve:

The prednisolone calibration curve was prepared in phosphate buffer with a pH of 6.8. 5 ml of ethanol and 100 mg of prednisone was mixed. The mixture was then shaken well, and phosphate buffer (pH 6.8) was added (Pawar and Saleem, 2013). Then, phosphate buffer with a pH of 6.8 was used to dilute it so that amounts between 2 and 16 µg/ml could be reached. When a UV-visible spectrophotometer was used, 239 nanometers were used to measure the absorption of the liquids. A calibration curve was made on a graph by putting content on the x-axis and absorption on the y-axis (Maity *et al.*, 2016).

Formulation Development:

Prednisolone Compression-Coated Core Tablets Formulation:

The Prednisolone core pills were made using the straight compression method (Table 1). A Cadmach 8 station rotating tablet press was used to mix and press predinisolone, microcrystalline cellulose, and talc into tablets while they were still dry. Next, different granular coat mixtures were pressed onto the core tablet in different amounts (Raghuvanshi *et al.*, 2014). For F1 and F2, xanthan gum and HPMC were mixed in equal parts (1:1). For F3, F4 and F5, pectin and HPMC were mixed in equal parts (1:2). To make the coat formulation pellets, the ingredients were mixed together and soaked in alcohol. The wet, chunky mass was dried in a hot air oven at 50°C for 2 h after going through sieve No. 22. For compression coating, granular material that made up about 45% of the coat weight was first put into the die hole (Farheen *et al.*, 2011). The last 55% of the coat grainy material was then put on top of the core tablet that had been placed by hand in the middle. Next, punches that were round, flat, and plain were used to squeeze the covering around the core tablet (Jagdale and Chandekar, 2016).

Evaluation of Prednisolone Compression Coated Tablets:

General appearance: Each formulation batch's tablets were examined for their overall appearance. Shape and colour are the general appearance elements that were assessed visually (Vemula *et al.*, 2014).

Weight Uniformity: Twenty tablets were chosen at random and weighed one at a time. Additionally, a

weight average was determined. The tablets' percentage deviation was computed and contrasted with industry standards (Surana *et al.*, 2024).

Measurements of thickness and diameter: Thickness and diameter were measured in order to assess uniform size and shape. Using a Vernier calliper, the tablets' diameter and thickness were measured (Hashem *et al.*, 2011).

Hardness: Also known as tablet crushing strength, hardness is the force needed to shatter a tablet in a diametric compression test. Using a Monsanto Hardness Tester, the produced formulations' hardness was assessed. It was stated as kg/cm^2 (Ahire *et al.*, 2023).

Friability: The Roche friabilator was used to assess the produced formulations' friability. After a pre-weighed sample of tablets was put in the friabilator and spun for 100 revolutions, the tablets were cleaned and weighed again (Sonawane *et al.*, 2023).

Study of drug release in vitro for the core tablet of prednisolone: Core tablet drug release was investigated *in vitro* utilizing a USP Type-II (Paddle) dissolution device in a sink environment. 900 ml of phosphate buffer (pH 6.8) was employed as the dissolving media. The temperature was 37±0.5ºC and the stirring rate was kept at 75 rpm. At several times during the experiment, the samples were removed from the dissolving media, and each time a new volume of medium was added. After that, the samples were examined at 234 nm using a phosphate buffer (pH 6.8) as a blank in a UV-Visible Spectrophotometer (Jarouliya and Keservani, 2023).

Compression core tablet of prednisolone: Through *in vitro* drug release in the USP dissolution test apparatus, the prepared compression-coated tablet formulation's ability to prevent or remain intact over time in the physiological environment of the stomach and small intestine in pH conditions prevalent in the stomach and small intestine was evaluated. Using two successive media, the USP paddle technique was utilized to establish the tablet's dissolving profile at 37±0.5ºC and 75 rpm. 900 ml of phosphate buffer (pH 6.8) solution in the presence and absence of 4% rat cecal content, then 900 ml of 0.1 N hydrochloric acid for 2 h preparing the cecal medic for rats. Rats were put to sleep and then killed. After opening the abdomen, tracing the ceca, ligating both ends, dissecting it, and pooling the contents, the mixture was added to the phosphate buffer (pH 6.8). In order to achieve a final cecal dilution of 4% w/v, the solutions were eventually added to the dissolving media (Rane *et al.*, 2021).

Results and Discussion

Calibration Curve of Prednisolone:

Linearity and Calibration: Using a graph of absorbance (nm) (y) against concentration (µg/ml) (x) in the concentration range of 3–15 µg/ml, the linearity of the calibration curve was determined. The absorbance at 239 nm was measured in order to create a calibration curve. Table 2 displays the results, while Figure 1 provides a visual representation of the data. The equation for the line of best fit was determined using linear regression analysis values, and it was $y = 0.052x + 0.029$. In the concentration range of 3 to 15 µg/ml, linearity was seen. There is a 0.996 R2 value.

Table 2: Calibration Curve of Prednisolone

Concentration (µg/ml)	Absorbance
0	0
3	0.148
6	0.271
9	0.411
12	0.661
15	0.852

Evaluation of Prednisolone Compression Coated Tablets:

Weight Uniformity:

Table 3 illustrates the consistent weight of the prepared tablets.

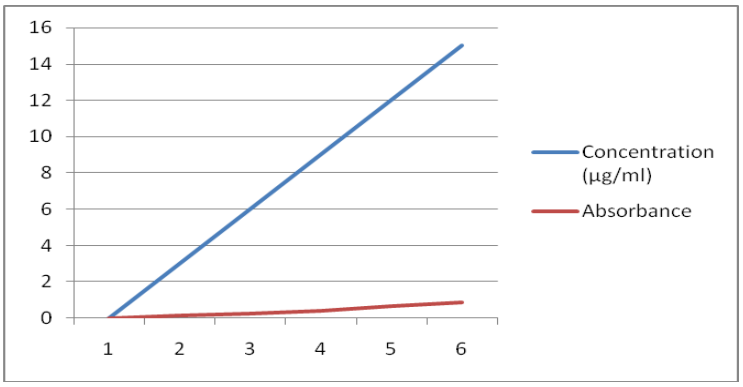

Fig. 1: Standard calibrations curve of prednisolone.

Table 3: Weight Uniformity for tablets

S. No.	Formulation code	Uniformity of weight* (mg)
1	F01	199.9±3.51
2	F02	222.1±4.10
3	F03	201.7±3.11
4	F04	224.5±2.25
5	F05	228.3±1.99

Thickness:

Table 4 depicts information on the prepared tablets' thickness.

Table 4: Thickness of tablets

S. No.	Formulation code	Thickness (mm)
1	F01	2.6±0.128
2	F02	2.8±0.261
3	F03	2.7±0.601
4	F04	2.8±0.301
5	F05	2.5±0.298

Hardness:

Table 5 depicts information on the prepared tablets' hardness. Each of the prepared tablets is the same thickness.

Friability:

Table 6 illustrates information on the prepared tablets' friability. The amount of friability for all of the formulations was within the limits set by the pharmaceutical industry.

Drug Content:

Table 7 shows the amount of drug in the tablets that were made. The amounts of drug in all of the versions ranged from 97.26% w/w to 90.21% w/w. It fits with the approved description for the drug. All of the pills met the IP requirements for weight change, breakability, and drug content. They didn't go over the limits set by the compendium.

In Vitro Drug Release Study Prednisolone Core Tablet:

Table 8 provides the *in vitro* drug release research of prednisolone core formulations using buffer pH 6.8.

Table 9 presents the results of the *in vitro* drug release analysis of predisolone formulations using 0.1N HCl and buffer pH 6.8 without rat cecal material (Fig. 2).

Table 5: Hardness of formulated prednisolone tablets

S. No.	Formulation code	Hardness (kg/cm²)
1	F01	5.3±0.050
2	F02	5.8±0.061
3	F03	5.6±0.061
4	F04	5.9±0.063
5	F05	5.7±0.059

Table 6: Percentage friability of formulated tablets

S. No.	Formulation code	Friability (%)
1	F01	0.171
2	F02	0.031
3	F03	0.132
4	F04	0.241
5	F05	0.252

Table 7: % Drug content of formulated prednisolone tablets

Formulation	Drug content (%)
F01	99.11±0.261
F02	98.11±0.112
F03	99.21±0.88
F04	98.32±0.91
F05	97.26±0.89

Table 8: Drug release study of formulated prednisolone core tablet

Time (min)	Core tablet
0	0
20	13.11
40	30.01
60	37.11
80	46.82
100	59.58
120	73.24

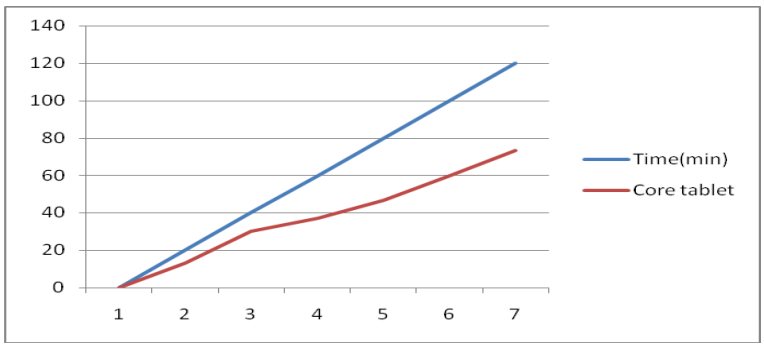

Fig. 2: *In vitro* study of prednisolone core tablet at pH 6.8.

Table 9: Drug release of formulated prednisolone tablet

Time (min)	Percentage drug release (%)				
	F01	F02	F03	F04	F05
60	6.23	5.83	6.23	4.61	4.89
120	11.51	10.55	11.23	11.86	10.58
180	17.90	16.73	20.82	18.98	19.25
240	20.63	24.85	30.25	27.63	26.33
300	33.53	31.11	37.91	36.63	35.25
360	41.36	41.12	45.89	46.09	45.85

At pH 6.8 buffer, 73.24% of the medicine was released from the core mixture in 2 h. There was a range of 9.56 to 10.89% drug release from pills F01, F02, F03, F04, and F05 after the first 2 h. The average amount of medicine that was released at the pH 6.8 buffer after 3 h was between 41.33 and 45.85%.The mean amount of drug released by F5 rose to 89.33% after 3 h in rat caecal media. Most of the drugs were released in the rat caecal media after 3 h, which was a lot more than in the control medium ($p<0.05$). One possible reason for this is that the pectinolytic enzyme lets prednisone into the colon's metabolic environment and showed how well the pectinolytic enzyme could break down the stuff.

Conclusion

This study's goal was to make compression-coated Prednisolone pills that would be an effective and safe way to treat inflammatory bowel disease and ulcerative colitis. The carriers used were pectin, xanthan gum, and HPMC. Core pills of prednisolone can be coated with xanthan gum:HPMC in a 1:1 to 1:2 ratio and pectin:HPMC in a 1:1 to 1:2 ratio. When compared to pectin by itself, HPMC-coated pellets protect against early drug release in the upper GI tract better. In situations like those that would happen in the gut, the pectin can still be broken down by enzymes, letting out more medicine. Most of the time, gut bacteria break down natural carbohydrates like xanthan gum in the colon instead of in the stomach or small intestine. In the small intestine, the medicine came out of HPMC when enzymes from bacteria in the colon broke it down. Xanthan gum is an extracellular polysaccharide with a high molecular weight. The molecule has a backbone like cellulose because its side chains are linked to glucose groups that change places. It is a hydrophilic polymer that, until recently, was only used to make water-based systems thicker, hold them, and mix them. It is getting more and more popular for making grids because it can delay drug release, have time-independent release rates, and be biocompatible and inert.

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