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Formulation and Evaluation of Colon Specific Ornidazole Matrix Tablets

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ABSTRACT

The main goal of this study is to formulate and analyze colon specific ornidazole tablets, which were effectively made using enteric coated polymers such as eudragit, guar gum, and hpmc k15m. There was no interaction between ornidazole and the excipients employed in the formulation, according to preformulation characteristics and FTIR analyses. In vitro release profiles of an enhanced version of F7 revealed a delayed release pattern in a highly tailored way, which was critical for colon-specific drug delivery. In vitro release profiles of an optimized formulation of ornidazole controlled release tablets (F-7) were found to be improved and followed zero-order kinetics, indicating that drug release from the dosage form was independent of concentration and followed the Higuchi model, indicating that drug release from the press coated tablet was due to diffusion. The drug delivery system was created to provide the drug at a time when it was most needed, which was during the night.

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Keywords: Colon specif delivery system,Eudragit,Ornidazole,Hpmc K15.

INTRODUCTION

Many pharmacological entities based on oral delivery have been commercialized, but many others are not easily available due to incompatibility with the physical and/or chemical conditions of the upper gastrointestinal tract (GIT) and/or inadequate absorption in the GIT. Due to a lack of digestive enzymes, the colon is thought to be a good place for medications to be absorbed. The key difficulty for scientists over the last two decades has been to target medications particularly to the colonic portion of the GIT. Previously, the colon was thought to be a harmless organ responsible only for the absorption of water, electrolytes, and the temporary storage of feces. However, it is increasingly recognized as a critical location for medication delivery [1-3].

Because the dosage form will be subjected to a physical and chemical attack meant to break down ingested components, retarding medication release in the diverse and hostile circumstances of the stomach and small intestine is difficult. The low fluid environment in the colon, along with the viscous nature of luminal contents, may make dissolving and releasing the medicine from the formulation difficult. Furthermore, the indigenous intestinal microbiota may have an impact on the drug's stability through metabolic breakdown. Despite these potential challenges, a range of methodologies and systems have been developed with the goal of attaining colonic targeting. The identification and exploitation of a trait particular to the target organ is required for targeted medication delivery. pH, transit length, pressure, bacteria, and prodrug approach are all exploitable gastrointestinal properties in the context of colonic targeting[4-6].

ANOTOMY AND PHYSIOLOGY OF COLON[7-8]:-

The stomach, small intestine, and large intestine make up the GI tract. The large intestine is divided into three sections from the ileocaecal junction to the anus. The colon, rectum, and anal canal are the three. The portions of the colon are either in the abdominal cavity or in the retroperitoneum behind it. The caecum, ascending colon, hepatic flexure, transverse colon, splenic flexure, descending colon, and sigmoid colon are the components of the colon. It measures around 1.5 meters in length, with the transverse colon being the longest and most movable part3, and a diameter of about 6.5 centimeters. The right colon is the section of the colon that runs from the cecum to the splenic flexure (the point where the transverse and descending colons meet). The left colon is what's left after that.

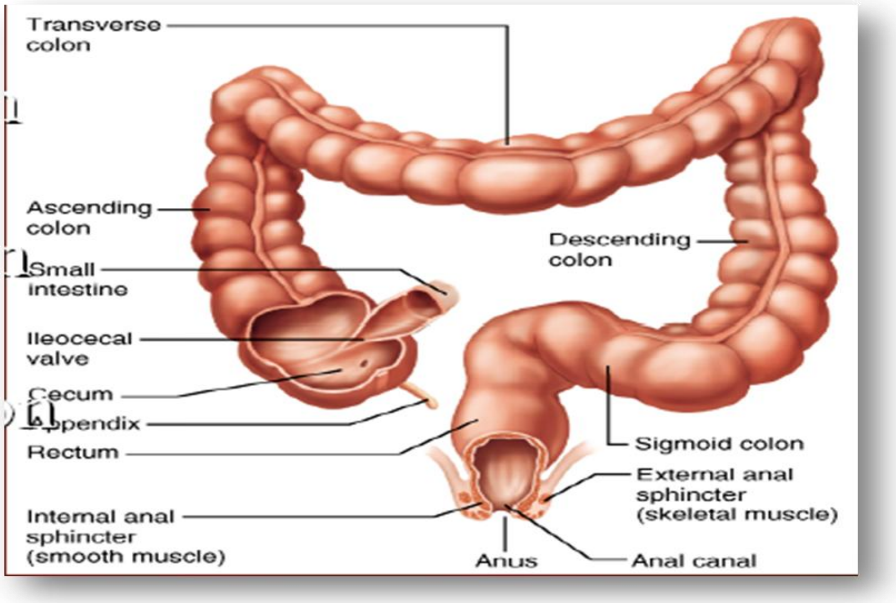

Fig.1.anatomy of colon.

METHODOLOGY

Preparation of standard graph of ornidazole[9,10]:-

A 100 mg of ornidazole was accurately weighed and placed to a 100 mL volumetric flask. The medication was dissolved in distilled water, and 100 mL of distilled water was used to make the principal stock solution. This yields an ornidazole stock solution with a concentration of 1 mg/mL. From this primary stock, 10 mL was transferred to another volumetric flask and made up to 100 mL with simulated gastric fluid (SGF, pH 1.2); from this secondary stock, 0.5, 1.0, 1.5, 2.0,2.5, and 3.0 mL were taken separately and made up to 10 mL with SGF (pH 1.2) solution, yielding 5, 10, 15, 20,25, and 30 g/ mL, respectively. A UV spectrophotometer was used to measure the absorbance at 320nm (Systronic, Ahmedabad, India)

Following the same approach and calibration curves, ornidazole standard graphs were plotted in simulated intestinal fluid (SIF, pH 6.8).

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Preparation of ornidazole matrix tablets [11]

Ornidazole, microcrystalline cellulose (MCC), guar gum, HPMC K4M, HPMC K15M, talc, and magnesium stearate were all included in each matrix tablet (average weight 800 mg) for in vitro drug release tests. To guarantee complete mixing, the ingredients were weighed, combined, and passed through a mesh no. 60. On a multiple station tablet machine, the thoroughly mixed ingredients were directly squeezed into tablets using 12 mm round, flat, and plain punches (Cadmach, Ahmedabad). The matrix tablets were subjected to quality control tests such as weight variation, hardness, friability, thickness, and dissolving in various mediums.

The compression coated tablets were subjected to quality control testing such as weight variation, hardness, friability, thickness, and drug release investigations in various mediums.

Determination of drug content [13-15]

The medication content of both ornidazole matrix tablets was determined. To ensure complete solubility of the medicine, ten tablets were finely pulverized; quantities of the powder equivalent to 50 mg of ornidazole were accurately weighed, transferred to a 100 mL volumetric flask containing 50 mL distilled water, and left to stand for 5 hours with occasional sonication. With distilled water, the mixture was brought up to volume. The solution was diluted appropriately, and the absorbance was measured at 320nm using a UV-Visible spectrophotometer. The calibration curve was used to calculate the medication concentration

Table 1.Different Formulations Of Ornidazole[12]:

Ingredients	Quantity (mg) present in each formulation							
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	**F7**	**F8**
Ornidazole	500	500	500	500	500	500	500	500
K4M	125	150	175	-	-	-	175	-
K15M	-	-	-	125	150	175	-	175
Guargum	150	125	100	-	-	-	75	75
Eudragit	-	-	-	150	125	100	75	75
Talk	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
Mg stearate	12.5	12.5	12.5	12.5	12.5	12.5	12.5	12.5
TOTAL WEIGHT	800	800	800	800	800	800	800	800

In *vitro* drug release studies[16] :-

Drug release studies of ornidazole matrix tablets

The dissolving rates of matrix tablets containing 500 mg of ornidazole were studied in SGF (pH 1.2) and SIF (pH 6.8) solutions. The USP dissolving test apparatus (Apparatus 1 50 rpm, 370.5 ℃) was used for the dissolution investigations. A 5 ml sample was taken at various time intervals and replaced with an equivalent volume of new medium. At 320 nm, the materials were spectrophotometrically examined. A USP basket-type dissolution device was used to release ornidazole from matrix tablets at a rotation speed of 100 rpm at a temperature of 370.5 ℃. Different dissolution mediums were used to simulate gastrointestinal transit conditions for tablets. Because the average gastric emptying time is roughly 2 hours, drug release tests were undertaken in simulated gastric fluid without pepsin (SGF, pH 1.2) during the first 2 hours. To imitate colonic circumstances, the dissolving medium was replaced with enzyme-free simulated intestinal fluid (SIF, pH 6.8) and drug release was examined. Ornidazole matrix tablets were dissolved in 900 mL of dissolving media and drug release was monitored. At 320 nm, samples taken at various time intervals were spectrophotometrically examined. All dissolution runs were done three times.

FT-IR spectroscopy[17]

To detect drug-excipient interactions, FTIR spectra of ornidazole, physical mixture of drug (ornidazole) and excipients, and placebo were recorded between 400 and 4000 cm-1. The IR spectra for the test substances were acquired using an FTIR spectrometer and the KBr disk method (PERKIN ELMER BX-I SYSTEM). The resulting spectra were examined to see if there were any differences in the peaks.

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RESULTS AND DISCUSSION

The goal of this study was to use natural gum (guar gum) and hydroxypropyl methyl cellulose to generate matrix ornidazole formulations for colon targeting (HPMC K4M). Guar gum/HPMC could be employed as a carrier for colon-specific drug delivery in the form of a matrix tablet or as a compression coat over a matrix tablet, as previously reported.

The current research reveals an active pharmacological agent that is manufactured as a tablet and is matrixed by non-interacting components. The phrases "compression-coated solid dosage form" and "compression-coated solid dosage form" as used herein refer to a solid matrix containing the active ingredient that is largely covered by a compression coating.

The benefits of compression coating include the ability to employ the specified dosage as an oral dosage form, as well as the following:

1. The harsh taste and odor of the active medicinal substance are eliminated.
2. Elimination of water or other solvents from the coating process, reducing the risk of active medicinal ingredient degradation; and

3. Manufacturing procedures that are simpler and more cost-effective.

By using guar gum/HPMC K4M as a compression coat over the ornidazole matrix tablets, it was possible to reduce drug release in the physiological environment of the stomach and small intestine while ensuring maximum drug release in the physiological environment of the colon. As a result, compression-coated tablets for targeting ornidazole for local action in the treatment of colonic inflammation were created.

Analytical method [18]

The standard graph of ornidazole in SGF (pH 1.2) showed good linearity with r^2 value of 0.9992, which suggest that it obeys the "Beer – lambert" law. The standard graphs in SIF (pH 6.8) had r^2 values of 0.9995.

Standard graph of ornidazole

SGF = simulated gastric fluid; SIF = simulated intestinal fluid

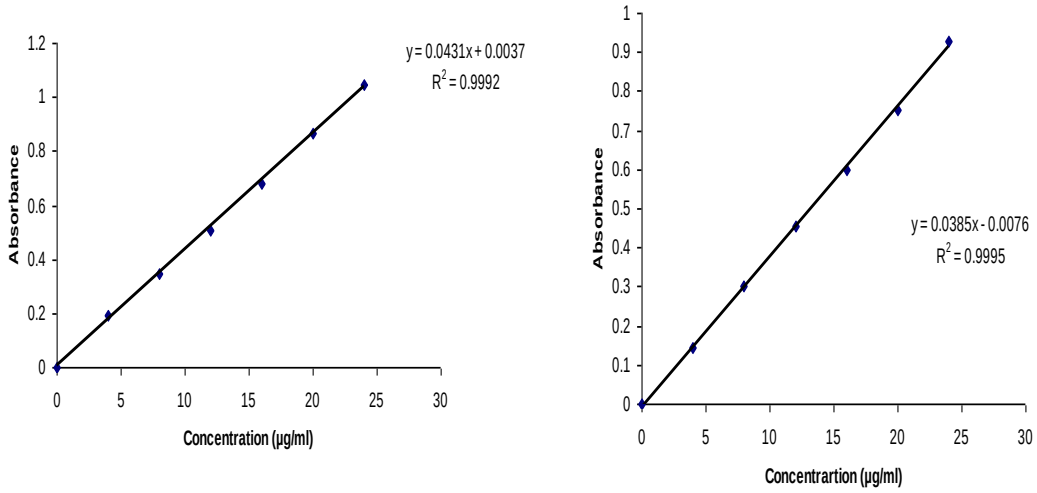

Fig 2. Standard graph of ornidazole in SGF pH 1.2 and SIF pH 6.8

Table 2. Characterization of powder mixture

Formulation code	Angle of Repose	Bulk density	Tapped Bulk density	% Carr's Index
Matrix	26.12±1.13	0.311	0.362	14.088
F1	29.12±1.24	0.321	0.402	20.149
F2	31.23±1.32	0.332	0.412	19.417
F3	30.35±1.35	0.312	0.386	19.170
F4	29.56±1.46	0.323	0.398	18.844
F5	27.12±1.13	0.325	0.405	19.753
F6	30.35±1.35	0.365	0.469	22.174
F7	32.12±1.84	0.344	0.436	21.100
F8	30.65±1.35	0.332	0.412	19.417

Evaluation of tablets

Table 3.Physical properties of ornidazole matrix tablets

Formulation Code	%Content of active ingredient	Hardness (Kg/cm^2)	Average Weight (gm)	Friability (%)	Drug Content (%)
F1	102.00(±1.11)	3.9±0.4	0.809±0.012	0.570	102.03
F2	98.06(±2.10)	3.9±0.5	0.808±0.16	0.206	103.04
F3	102.46(±1.30)	4.3±0.75	0.806±0.008	0.258	104.04
F4	101.46(±2.10)	4.2±0.6	0.807±0.034	0.256	102.51
F5	100.87(±1.24)	4.5±0.5	0.808±0.35	0.253	103.25
F6	102.65(±3.05)	4.5±0.76	0.805±0.02	0.256	101.09
F7	95.76(±4.99)	4.3±0.28	0.805±0.021	-	100.06
F8	96.56(±5.04)	10.66±0.27	0.905±0.019	-	99.90

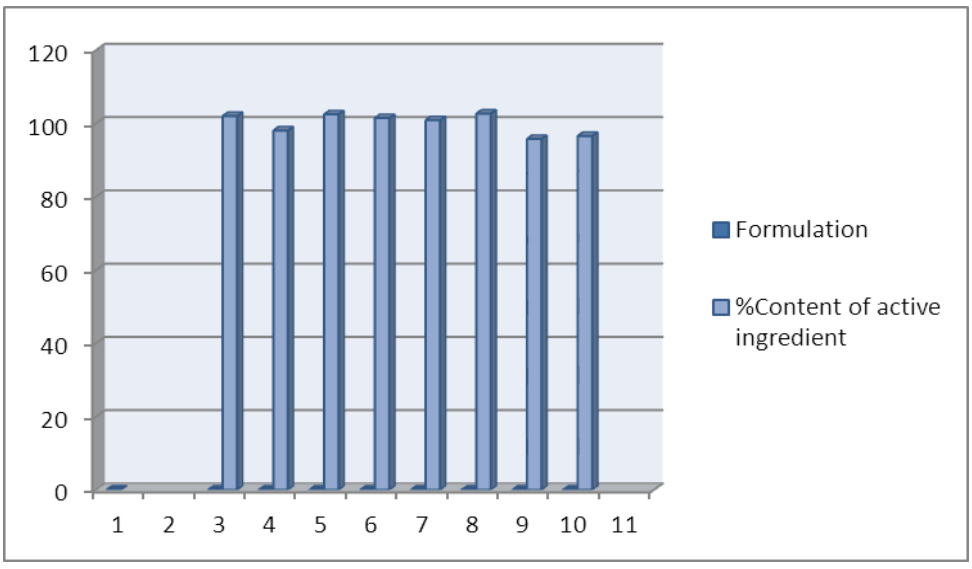

Fig3.percentage content of active ingredients

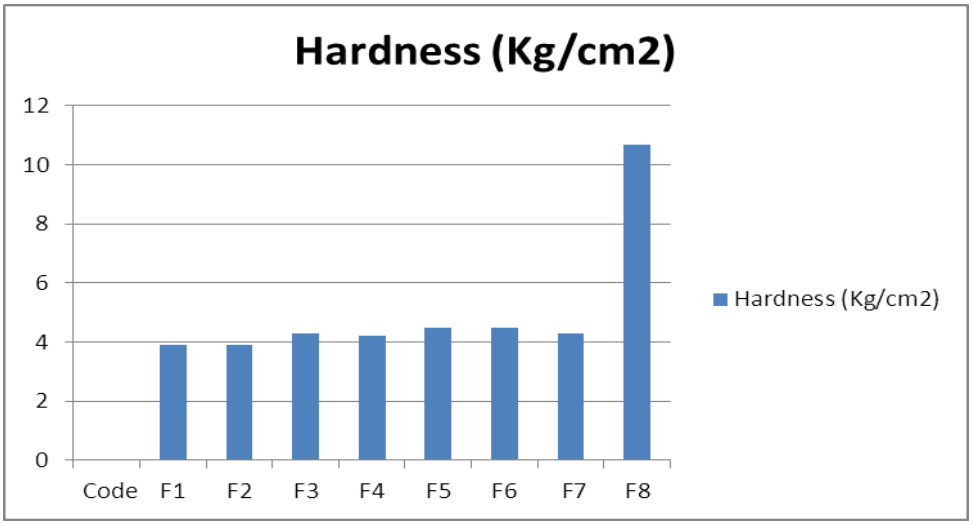

Fig 4.Hardness Of Different Formulations

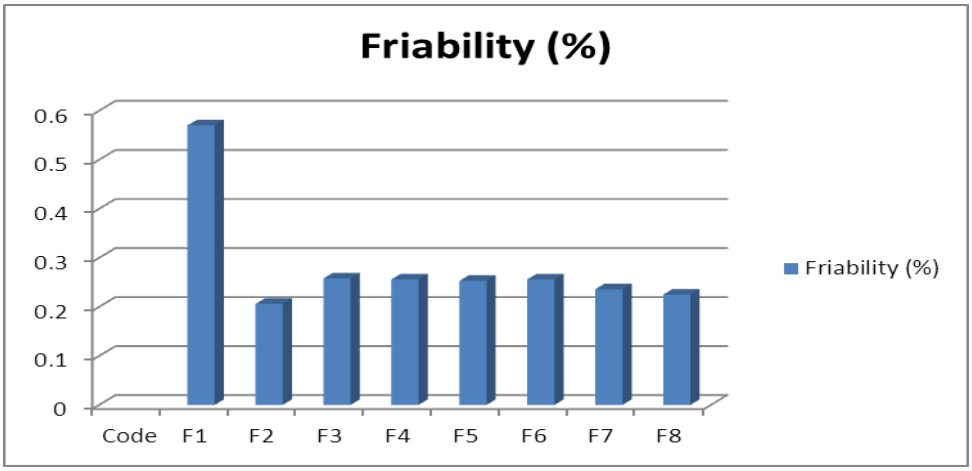

Fig 5. Friability percentage of different formulations

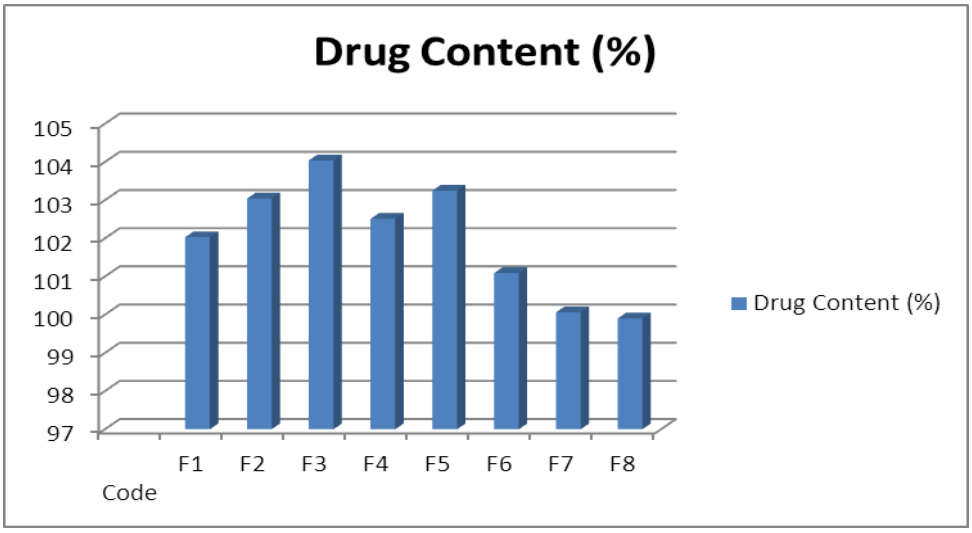

Fig 6. Drug content percentage of different formulations

Table 4.Cumulative percent drug release of F1-F8 formulations of ornidazole matrix tablets

TIME(hr)	F1	F2	F3	F4	F5	F6	F7	F8
1	17.62	16.3	19.99	15.2	17.19	17.56	12.25	14.06
2	27.55	28.82	25.05	28.86	26.45	27.49	27.85	25.31
3	40.86	41.88	42.8	49.84	44.34	35.56	38.3	39.51
4	47.45	45.05	54.57	55.56	46.99	42.98	44.84	44.65
5	52.83	50.45	58.37	59.3	50.53	50.61	55.14	49.83
6	62.64	54.5	54.7	59.31	55.53	55.35	61.86	57.25
7	58.86	58.58	64.73	61.31	58.67	60.76	68.96	61.08
8	66.33	68.97	69.79	63.33	60.14	68.76	70.98	66.15
9	69.47	71.56	72.49	65.89	65.48	71.89	72.45	70.78
10	73.84	74.48	73.8	72.8	69.45	75.15	75.98	74.19

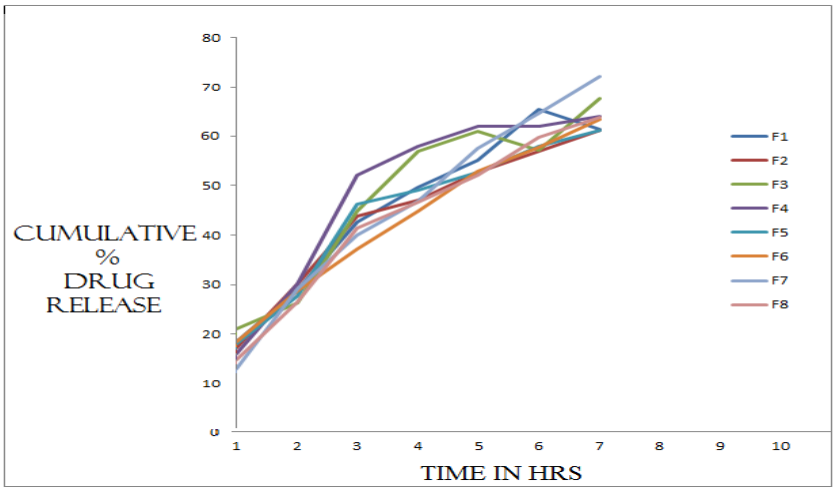

Fig 7. Cumulative percent drug release of F1-F8 formulations:-

CONCLUSION

Based on the results of the dissolution study, the prepared colon matrix tablets of Ornidazole (800 mg) could be used instead of 3-4 doses of 800 mg Ornidazole conventional tablet, allowing for better drug release control and targeted drug delivery, potentially improving patient compliance and reducing gastric side effects. In conclusion, the best formulations were F7, which contained a combination of Guar Gum and Eudragit (RF) as well as HPMC K4m matrix polymer, and demonstrated a slow controlled release of about 10 hours in the colon.

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