International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

Formulation and Evaluation of Colon Targeted Matrix Tablet of Ornidazole

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ABSTRACT

Background: The current study aimed to develop matrix tablets of ornidazole targeted for delivery to the colon, specifically for the treatment of ulcerative colitis and Crohn's disease. The tablets were designed to release the drug locally in the colon, minimizing systemic absorption and improving therapeutic outcomes. The formulation strategy involved the use of the dry granulation technique to create matrix tablets with consistent weight and pharmacological composition.

Results: The matrix tablets were successfully manufactured and subjected to comprehensive evaluation for stability, friability, drug content uniformity, and various analytical examinations including Fourier Transform Infrared Spectroscopy, Differential Scanning Calorimetry. Additionally, physical parameters such as hardness, density, Carr's index, and Hausner's ratio were assessed. The in vitro drug release study was conducted using dissolution apparatus in gastric and intestinal fluids. Ornidazole release from the matrix tablets was measured at different time points using a Ultra Violet spectrophotometer. Formulation F5 demonstrated potential for colon targeting, ensuring localized drug action.

Conclusion: The developed colon-targeted matrix tablet of ornidazole exhibited stability in terms of physical properties, drug content uniformity, and dissolution pattern after storage at 40°C for two months. These findings suggest that the formulated tablets have the potential for effective treatment of ulcerative colitis and Crohn's disease by delivering ornidazole directly to the colon. Further studies are warranted to assess the in vivo performance and therapeutic efficacy of the colon-targeted ornidazole matrix tablets.

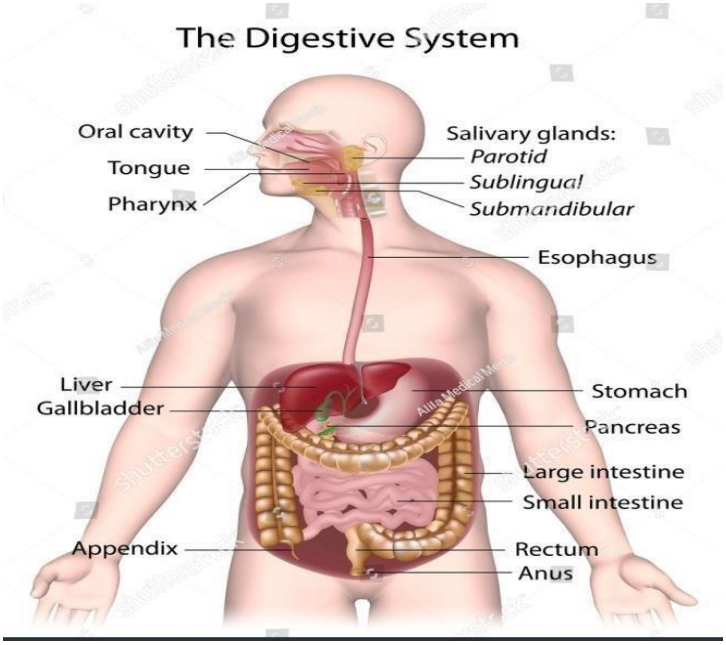
Keywords: Matrix Tablet; Ornidazole; Locust Bean Gum; Inulin; Pectin; Dry Granulation Method

1. Introduction

“Numerous studies have concentrated on colon targeted drug delivery in recent years due to its potential to improve the treatment of local disorders affecting the colon while reducing systemic side effects [18]. The GI tract has presented various severe challenges to the drug delivery, despite the fact that oral delivery has become a commonly accepted method of administering therapeutic medications. Irritable bowel disorders, including Crohn's disease and ulcerative colitis, can benefit from colon targeting as a treatment. Protein and peptide administration by oral route when a delay in systemic absorption is medically desired (nocturnal asthma, arthritis, angina). [4]

The gastrointestinal system is made up of a variety of parts, with secretion, digestion, and absorption ranking as their three main functions. The entire gastrointestinal tract has a length of 450 cm. The stomach

and small intestine, which differ from one another in terms of architecture, function, and pH, are the digestive tract's primary functional components. [9] STOMACH: The stomach, often known as the belly, is a bag-like structure with a smooth mucosa and a modest surface area. Because to the excretion of HCL, its pH is acidic. As a result, the helps the acidic pills absorb. 1.5 hours is the typical transit time [9] SMALL INTESTINE: Due to its enormous surface area, it is the primary location for the highest API to be absorbed. The surface area is increased by three folds as a result of the folds in the gut mucosa. These folds, which have projections resembling fingers and are located 30 times on the boom surface, are known as villi.) The intestinal surface increases significantly and is many times larger than the gastric region as a result of all the projections. The basic tablets maintain their union at gut pH. The intestine's peristaltic action is slow, its transit time is lengthy, and its permeability is high. Gut is the best location for the quantitative absorption of tablets as a result of the aforesaid factors working together [9] LARGE INTESTINE Its length and mucosal surface are smaller than those of the small intestine, and while the absorption of medications from this region of the digestive system is minimal, it aids in the absorption of some electrolytes and water. A medicine must be absorbed through the entire gastrointestinal tract and have a gastrointestinal transit time of between 10 and 12 hours in order to be a candidate for the sustained release dosage form. Food passes via the oesophagus and into the stomach after being chewed and ground. Meal that has been partially broken down and digested enters the small intestine. The term "tiny" again relates to diameter. Most of the nutrients are absorbed in the small intestine, which continues to break down the food. The right lower abdomen and the small bowel are joined. The colon constantly absorbs water and mineral nutrients from dietary items, and it also serves as a storage area for waste products left over from this process, such as faeces, which enter the rectum, the final six inches of the digestive tract. After that, it exits the body through the anus.[9]



Oral rectal administration is a viable method for achieving colonic delivery. Rectal dose forms, such as suppositories and enemas, are not consistently effective since a large degree of heterogeneity in their distribution is seen. Due to their limited dissemination, suppositories work best in the rectum, while enema solutions can only treat the sigmoid and descending colon topically. The formulation for colonic delivery is also suitable for the administration of medications that may be polar and/or vulnerable to chemical and enzymatic degradation in the upper GI tract, once those are significantly impacted by hepatic metabolism,

the specific therapeutic proteins and peptides (10) Therefore, oral delivery is preferred, but several physiological obstacles need to be removed for this. The main barrier to effective colonic distribution is the absorption or degradation of the active components in the upper part of the GI tract.

The colon is made up of five primary parts, each measuring roughly 150 cm in length.

- Cecum – 6cm
- Colon - 20-25 cm, pH – 6.4
- Ascending Colon – 10 – 15 cm, pH – 6.6
- Transverse Colon - 40-45 cm , pH – 7.0
- Descending Colon - 35 – 40 cm, pH-7.0

"The medications enter the body passively through either the paracellular or transcellular routes. The channelling of the medications via cells is a part of transcellular absorption. And this is the method by which the majority of lipophilic medications are absorbed, whereas the majority of water soluble drugs are absorbed by the paracellular route, which involves drug transports through the tight junction between the cells. The tight connection between the epithelial cells in the colon allows the paracellular to absorb various medicines. Due to the colon's slower rate of transit than the small intestine, drugs remain in contact with the mucosa for longer periods of time, making up for the latter's significantly smaller surface area. Colonic fluid becomes more viscous due to water absorption, which allows it to pass through the colon more easily. This results in a delayed diffusion of the dissolved drug across the mucosa and a decrease in the dissolving rate. The entire GIT may theoretically absorb medications, however the duodenum and proximal jejunum are where most of them are absorbed. The bulk of proteins and peptide medicines have a relatively low oral absorption.

2. MATERIALS

SR NO	MATERIALS	SOURCES
1	ORNIDAZOLE	Unidrug innovative pharma
2	Locust Bean gum	Chemsworth , Mumbai
3	Insulin	Chemsworth , Mumbai
4	Pectin	Central drug house Ltd, New Delhi.

3. EQUIPMENTS:

SR NO	EQUIPMENTS	SOURCE
1	Dissolution Test Apparatus	Electrolab , UP XXXIII EDT-06P
2	UV Visible Spectroscopy	Uv – 1700, Schimadzu
3	Tablet Compression Machine	Rimake, RSB- 4 Minipress
4	Friability Tester	Pfizer Hardness Tester
5	IR Spectroscopy	Schimadzu 800 – S, Japasn

In Vivo Roentgenographic study:(31)

For the purpose of investigative studies, a healthy Rabbit weighing 4 – 5 kg was acquired from the source BLDEA's SSM COLLEGE OF PHARMACY, VIJAYAPUR

4. THE FORMULAE FOR THE PREPARATION OF ORNIDAZOLE MATRIX TABLET

SR NO	FORMULATION BATCH	F1	F2	F3	F4	F5	F6
1	Orinidazole	100	100	100	100	100	100
2	Locust bean gum	100	100	100	90	70	50
3	Insulin	100	80	60	80	90	100
4	Pectin	40	40	40	40	40	40
5	MCC	50	70	90	80	90	100
6	Mg. Stearate	5	5	5	5	5	5
7	Talc	5	5	5	5	5	5
8	Total	400	400	400	400	400	400

*All ingredients are in mg

5. METHODS:

Preparation of calibration curve for Ornidazole: In 0.1N HCl In a 100ml volumetric flask, 100mg of ornidazole were properly weighed and briefly dissolved in 0.1N HCl. The volume was then increased to 100ml using 0.1N HCl. This primary stock solution has a 1000 g/ml concentration. 1 ml of this primary stock solution was pipetted into a 100 ml volumetric flask, and the remaining volume was filled with 0.1 N HCl, which had a concentration of 10 g/ml (second stock solution). From the second stock solution, aliquots corresponding to 1 to 5 g (1, 2, 3, 4, and 5 ml) were pipetted into a series of 10 ml volumetric flasks, and the volume was topped off with 0.1N HCl. Using a UV-Visible double beam spectrometer, the absorbance of these solutions was determined using 0.1N HCl as a blank at 320 nm.

Preparation of standard curve for Ornidazole in Phosphate buffer pH 6.8

In a volumetric flask, 100 mg of ornidazole were precisely weighed and dissolved in a little amount of phosphate buffer at a pH of 6.8. Phosphate buffer was then used to bring the volume to 100 ml. This principal stock solution had a 1000 g/ml concentration. From this stock solution, 1ml was pipetted into a 100-ml volumetric flask, where it was combined with 10ml of phosphate buffer to make up the remaining volume (second stock solution). A series of 10ml volumetric flasks were used to pipette out aliquots from the second stock solution that were 1ml, 2ml, 3ml, 4ml, and 5ml in size. The volume was then brought up to 10ml using phosphate buffer as a blank and measured at 320 nm using a UV-Visible spectrometer

Preparation of Matrix Tablet:

Ornidazole, locust bean gum, inulin, pectin, and microcrystalline cellulose were taken in the required quantities, mixed, and passed through #60 sieves. They were then lubricated with magnesium stearate and talc, and compressed into tablets on a tableting machine (Rimek Mini Press-II, Karnavati Engineering Ltd.) using a 9mm punch. The tablets were then further coated with a coating solution called Eudragit S100. In a mixture of isopropyl alcohol and acetone, a coating solution called Eudragit S100 was created (1:1). The coating of the matrix tablet was created by submerging it in the coating solution and then using the deep coating technique.

6.EVALUTION PARAMETERS :

Hardness test : [41]

A particular amount of strength, or hardness and resistance to friability, is required for the tablets to withstand the mechanical stress of handling during the fabrication, packing, and shipping processes. Pfizer Hardness Tester was used to gauge the tablet's hardness.

Friability:[42]

Ries Friability apparatus for assessing the tablets' friability. 20 preweighed tablets were added to the device. which underwent 100 revolutions for four minutes. The tablets were then weighed again. The formula was used to calculate the percentage of friability.

$$\%\text{Friability} = initial\ weight - final\ weight\ /initial\ weight$$

Weight variation:[43]

SR.NO	AVERAGE WEIGHT OF THE TABLETS	% DEVIATION
1	80mg or less	+10
2	More than 80mg but less than 250mg	-7.5 +5

Drug uniformity:[40]

Five tablets were chosen at random from each formulation, crushed in a mortar, and the average tablet's weight was obtained from the crushed mixture. Once the sample had been crushed, a phosphate buffer with a pH of 7.4 was added to it, and it was left there overnight to completely dissolve the medication. After filtering, the appropriate dilution was performed. UV-Visible spectroscopy was used to determine the amount of medication in each tablet.

Fourier Transform Spectroscopy Analysis:[44]

On FTIR, the infrared spectra of the improved formulations and pure ornidazole were captured between 400 and 4000 cm. Then, using an FTIR spectrometer and the KBr disc method, IR spectra for the test materials were acquired.

Differential Scanning Calorimetric Analysis ;[45]

Comparative Scanning Using a DSC Q2000 V24.2Build 107 apparatus, calorimetric analysis of ornidazole, m beta-CD, physical mixes, and inclusion complexes was performed. For the purpose of calculating heat flow, the mass of the reference pan and the empty pan were both considered. The mass of the sample, which was put in sealed aluminium pans, ranged from 3 to 10 by 0.5 metres. the liquid nitrogen's cooling agent. From 20° to 300°, the samples were scanned at 10°/min.

In Vitro drug release study in simulated gastric and intestinal fluid:[46]

A rotating dissolution tester model USP-23 was used to conduct an in vitro release study. At a speed of 100 rpm and a temperature of 37.00.5, the dissolving was conducted. The medication was released from the tablet over the course of two hours in a 900 ml solution of pH 0.1N HCl, and the remaining hours of the research were spent in a pH 7.4 phosphate buffer solution. In order to maintain steady state, 5 ml samples were removed at the current time intervals and replaced with an equivalent volume of fresh solution. A UV-Visible spectrophotometer operating at 320 nm was used to analyse the medication emitted. To determine which release kinetics model best fits the acquired profiles, the drug release data were fitted to multiple models.

In Vitro drug release in Rat ceacal content fluid :[30]

For the investigation, male albino rats were employed, weighing 200–250gm and kept on a typical diet.

The caeceums were traced, ligated at both ends, and dissected when the abdomens were opened. They were then immediately placed in a pool of pH 6.8 phosphate buffer saline that was suspended in PBS. The dissolution equipment was operated at 37.05 and 50 rpm for the drug release investigation, and phosphate pH 6.8 with 4% rat caecal content was used as the dissolution media. The dissolution was carried out in a pH 0.1N HCL dissolution medium for the following three hours, and on the fifth hour the medium was changed to a phosphate buffer with a pH of 6.8 and 45 rat caecal content until the end of the study. Five millilitres of sample solution were withdrawn from the solution at predetermined intervals. After the test sample was removed, an equal amount of brand-new dissolving medium was added. A 0.4meter membrane filter was used to separate the supernatant, and a UV-visible spectrometer was used to evaluate the filtrate at 320nm.

In Vivo Roentgenographic study:[31]

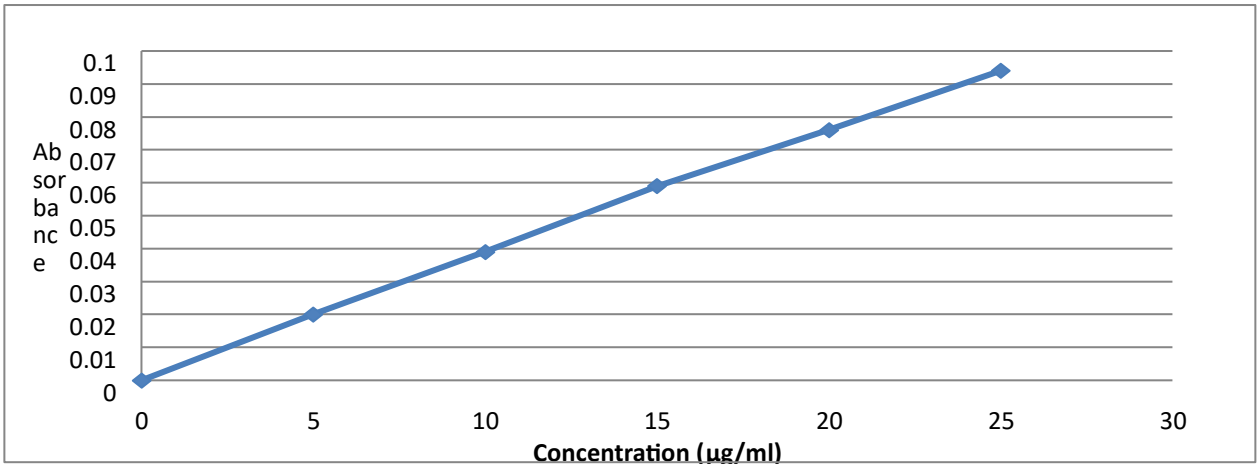
For the investigation, a healthy rabbit weighing between 4 and 5 kg was employed. To scan the location of the tablet in the GIT, the optimal formulation was made with the radio-opaque substance barium sulphate. Prior to the trial, the rabbit was allowed to drink water after a 12hour fast. The oral feeding tube was used to administer the test formulation orally. The form, integrity, and location of the tablet in the GIT were captured on X-Ray images at intervals of 1, 3, 5, 7, 9, 11, and 15 hour

7. RESULT:

SPECTROMETRIC DATA FOR THE ESTIMATION OF ORNIDAZOLE IN 0.1N HCl

Sr. NO.	CONCENTRATION	ABSORBANCE(nm)
1	0	0.00
2	5	0.02
3	10	0.039
4	15	0.059
5	20	0.076
6	25	0.094

CALIBARATION CURVE

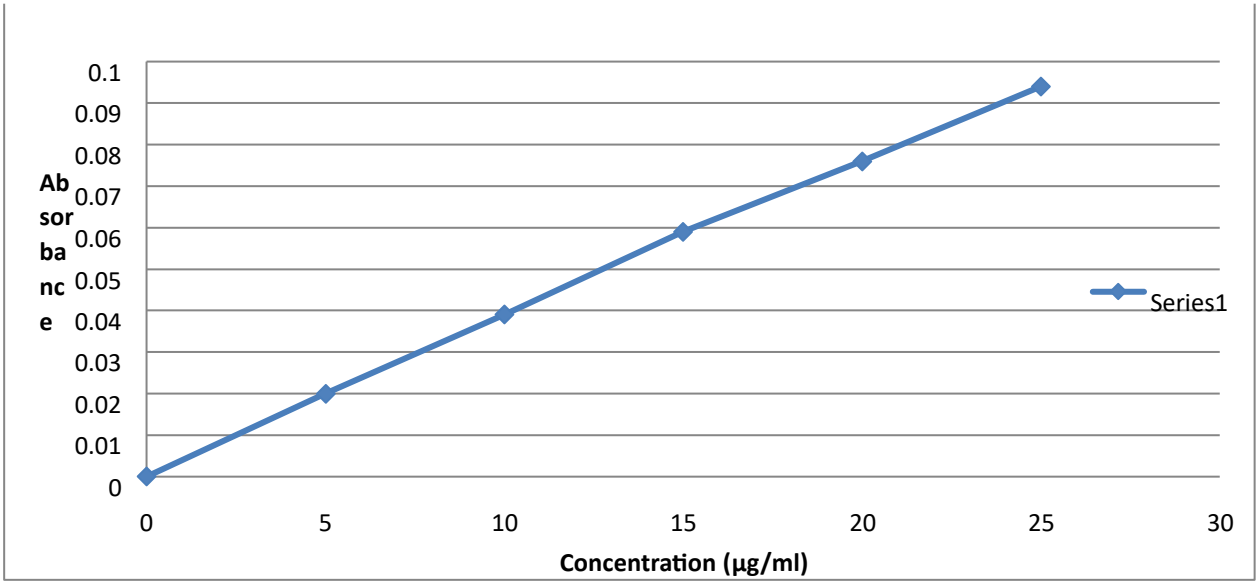


Standard Calibaration curve of Ornidazole in 0.1N

SPECTROMETRIC DATA FOR THE ESTIMATION OF ORNIDAZOLE IN PHOSPHATE BUFFER pH 6.8

Sr. NO.	CONCENTRATION	ABSORBANCE(nm)
1	0	0.00
2	5	0.208
3	10	0.420
4	15	0.616
5	20	0.817
6	25	1.014

CALIBARATION CURVE

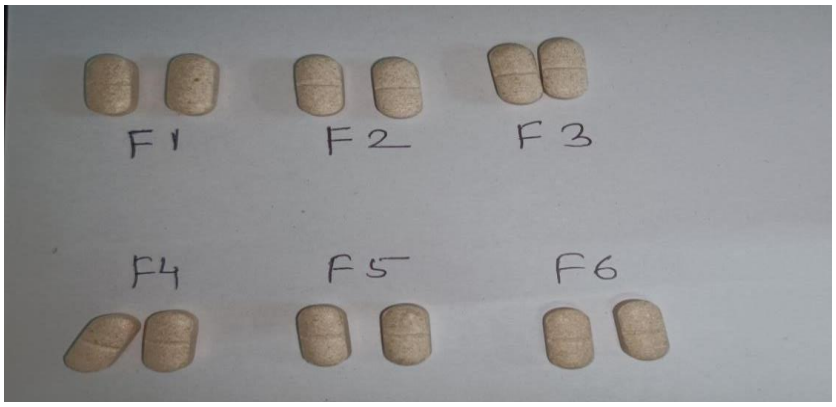


Standard Caliberation curve of Ornidazole in Phosphate buffer pH 6.8

POST COMPRESSION EVALUATION OF ORNIDAZOLE MATRIX TABLET

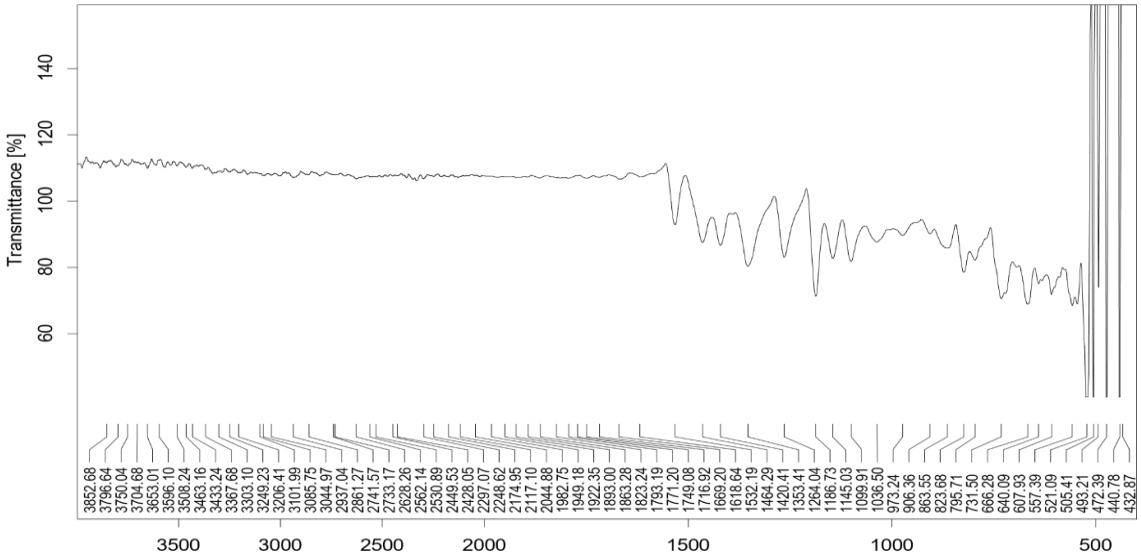
Formulation	Weight (Mg)	Bulk Density	Tapped Density	Hardness (Kg/Cm2)	Friability (%)	Thickness	Drug Content
F1	403	0.351	0.405	5.2	0.29	3.4	97.62
F2	400	0.311	0.368	5.7	0.16	3.5	98.59
F3	407	0.321	0.398	5.3	0.11	3.5	97.42
F4	405	0.343	0.412	5.4	0.32	3.4	98.16
F5	402	0.298	0.354	5.3	0.18	3.5	s98.90
F6	402	0.295	0.382	5.7	0.24	3.4	97.50

Manufactured tablets of Formulations



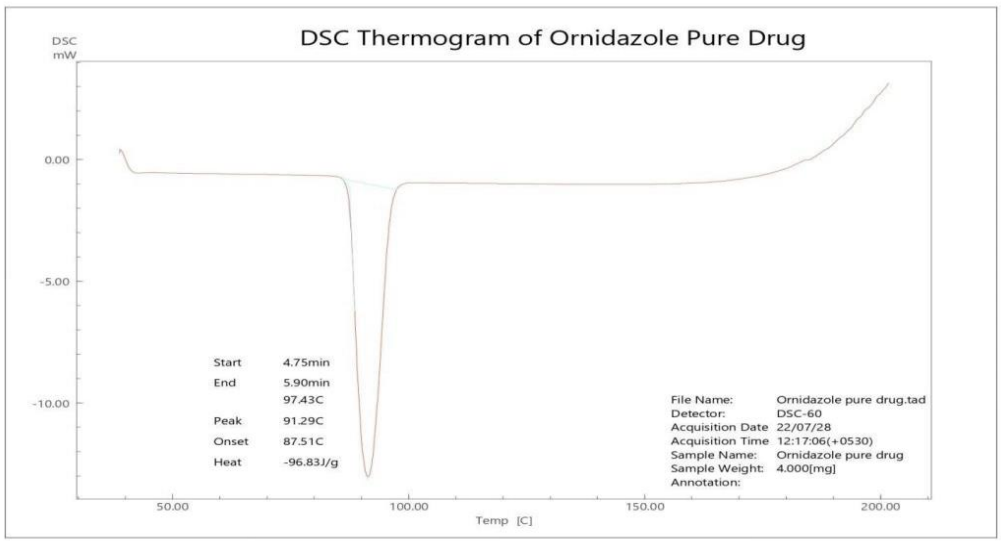
FTIR:-

FTIR SPECTRA FOR PURE DRUG ORNIDAZOLE



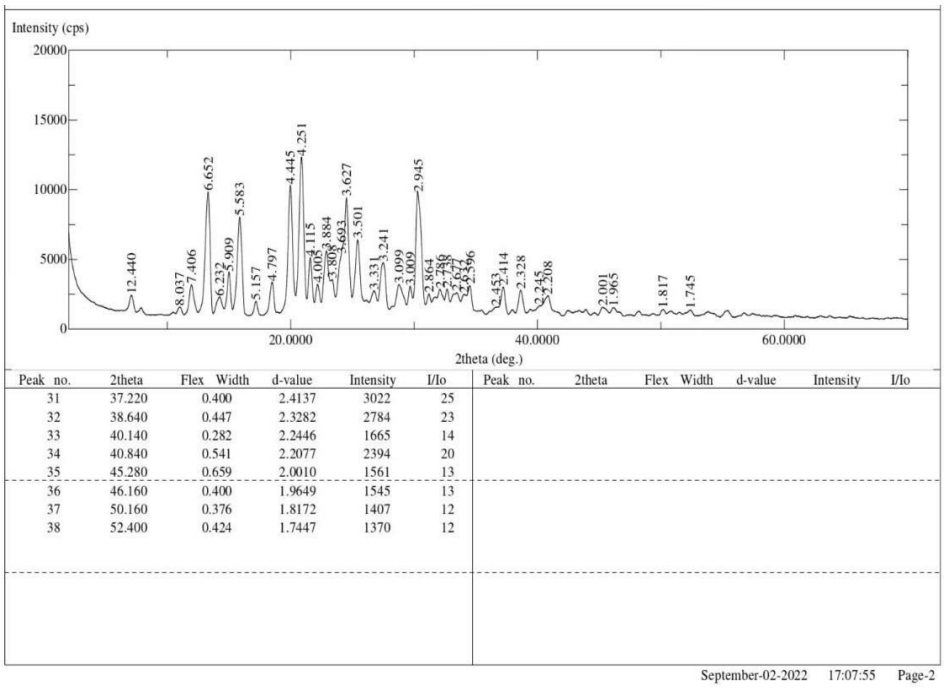
DSC

DSC OF ORNIDAZOLE DRUG



XRD

XRD OF PURE DRUG ORNIDAZOLE



Peak no.	2theta	Flex	Width	d-value	Intensity	I/Io	Peak no.	2theta	Flex	Width	d-value	Intensity	I/Io
31	37.220		0.400	2.4137	3022	25							
32	38.640		0.447	2.3282	2784	23							
33	40.140		0.282	2.2446	1665	14							
34	40.840		0.541	2.2077	2394	20							
35	45.280		0.659	2.0010	1561	13							
36	46.160		0.400	1.9649	1545	13							
37	50.160		0.376	1.8172	1407	12							
38	52.400		0.424	1.7447	1370	12							

KINETIC VALUES OF ORNIDAZOLE RELEASE FROM TABLETS

Formulation code	Regression coefficient value			Slope value(n)	
	Zero order	Higuchi	Peppas	Higuchi	Peppas
F1	0.893	0.316	0.603	14.20	1.110
F2	0.925	0.321	0.638	15.18	1.110
F3	0.918	0.355	0.591	16.14	1.104
F4	0.930	0.331	0.568	15.90	1.172
F5	0.839	0.474	0.639	19.75	0.493
F6	0.928	0.369	0.587	17.33	1.012

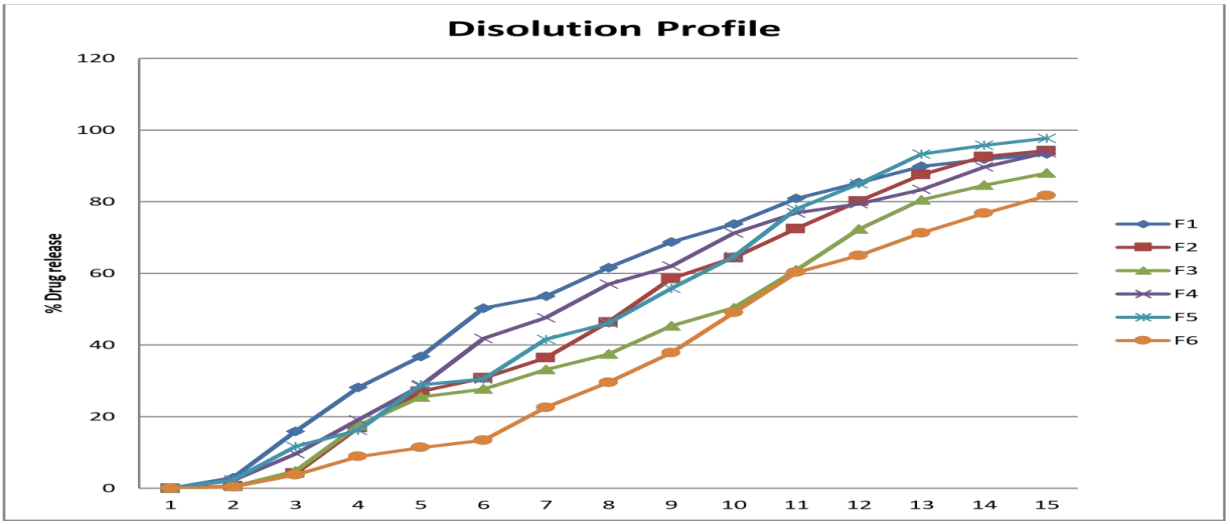
In Vitro Drug Release Profile Of Ornidazole From Colon Targeted Tablets In Gastric And Intestinal Fluids (F1, F2, F3)

IN VITRO % DRUG RELEASE DATA OF ORNIDAZOLE

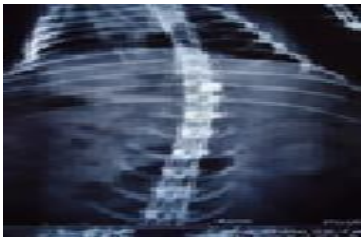
SR.NO	TIME (hour)	F1	F2	F3	F4	F5	F6
1	0	0	0	0	0	0	0
2	0.5	2.93	0.62	0.46	2.17	2.32	0.31
3	1	15.86	4.19	4.81	9.62	11.64	3.72
4	1.5	28.12	16.91	17.54	19.09	16.15	8.84
5	2	36.77	27.02	25.47	28.58	28.89	11.34
6	3	50.25	30.77	27.67	41.80	30.47	13.37

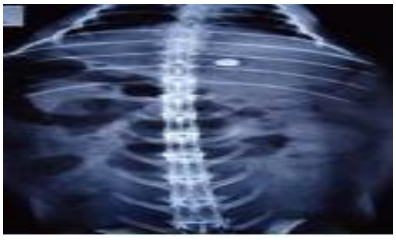
7	4	53.58	36.39	33.13	47.59	41.53	22.54
8	5	61.56	46.37	37.42	56.95	46.07	29.54
9	6	68.69	58.52	45.31	61.98	55.74	37.80
10	7	73.76	64.33	50.33	71.21	64.65	49.02
11	8	80.90	72.47	60.94	76.87	77.91	60.24
12	9	85.29	80.15	72.33	79.44	84.98	64.96
13	10	89.86	87.53	80.48	83.41	93.30	71.24
14	11	91.85	92.59	84.60	89.70	95.73	76.75
15	12	93.32	94.25	87.96	93.68	97.70	81.65

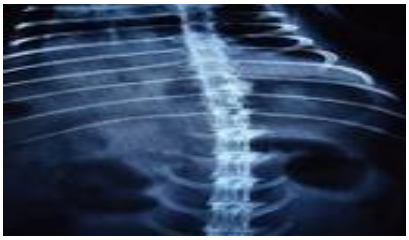
In Vitro Drug Release Profile Of Ornidazole From Colon targeted Tablets In Gastric And Intestinal fluids



ABDOMINAL X-RAY PHOTOGRAPHS OF RABBIT TAKEN AT DIFFERENT TIME INTERVALS AFTER ADMINISTRATERED WITH COLON TARGETED TABLET



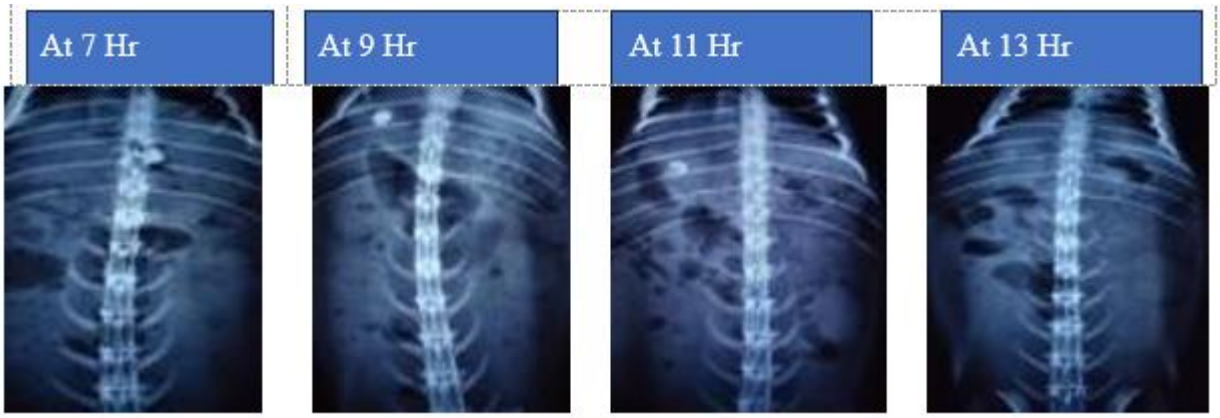




At 1 Hr

At 3 Hr

At 5 Hr



8. DISCUSSION

The primary objective of this effort was to create a matrix tablet for the delivery of ornidazole, an antiprotozoal drug used to treat Crohn's disease and ulcerative colitis, to the colon. For colontargeted medication delivery, ornidazole tablets were made utilising the dry granulation process using a variety of polymers, including locust bean gum, inulin, and pectin in varying ratios. Due to the angle of repose values being less than 300, the granule evaluation results indicate that all of the granules have satisfactory flow characteristics. Both the Carr's Index and the Hausner's Ratio demonstrated that granules had good packing ability. All of the tablets' weights and medication contents were discovered to be consistent. The hardness ranged from 4.3 to 4.7 kg/cm2 and the friability from 0.35 to 0.60 percent, indicating that the core tablet has good mechanical strength. The drug content ranged from 96% to 98.7%, and the thickness ranged from 3.4 to 3.5. By using FTIR analysis, the drug polymer interaction was investigated, and the results are shown in the figure. The distinctive peaks of ornidazole's spectrum were 3486 cm-1, 2933 cm-1, 1831 cm-1, 1695 cm-1, 1545 cm-1, and 1296 cm-1. Contrarily, in the spectra of the formulation, the same ornidazole-related features peak was seen with only very modest variations. This shows that there is no drug-polymer interaction and that the drug is stable.

The DSC of ornidazole in both its pure and polymerized forms was carried out and represented in figure. The pill with the medication within displayed an endothermic peak at 1700C. The melting point of the pure ornidazole medication caused a pronounced endothermic peak to appear at 2910C. However, pills that contain drugs do not exhibit this peak. This particular substance was uniformly distributed and amorphous. The XRD of unloaded and drug-loaded polymer tablets containing ornidazole is shown in the figure, and ornidazole exhibits a distinctively intense peak between 100 and 200 because it is crystalline. As opposed to drug- loaded pills, which did not produce an explosive peak. This demonstrates the drug's amorphous dispersion. Dissolution rate test equipment was used in simulated stomach fluid and intestinal fluids for the in vitro drug release study. The drug release from tablets in simulated stomach and intestinal fluids was 93.32%, 94.25%, 87.96%, 93.68%, 97.70%, and 81.65% of drug released from formulations, respectively, according to the ornidazole medication's dissolution profile, which is shown in table no. The tablets failed to delay the drug release in the environment of the stomach and small intestine after five hours, and the majority of the medication was released in the upper section of the digestive system. Therefore, tablets that were further tuned were picked. The optimised F5 demonstrated maximum drug release at 5 hours and the remaining drug release, or 97.70%, was demonstrated in the colonic region. The colon-targeted medication should release and sustain drug release in the colon as well as safeguard drug

release in the stomach and small intestine. As a result, experiments on in vitro drug release were conducted in phosphate buffer 6.8 pH with 4% rat caecal contents. For this study, the improved F5 formulation has been used. The zero order release, Highuchi equation, and Korsmayers equations were used to fit the tablet release data, and Peppa's equation was used to determine the drug release mechanism. Table No. — contains the calculated n values together with the corelation coefficient. The n values rise when polymer concentration grows as well. The computed n value indicates that non-fickian transport was used for the drug release mechanism. The tablet was still present in its whole in the stomach and small intestine, according to the roentgenography scan. The position of the tablet in the rabbit after administration is indicated by the X-Ray images acquired at 0, 1, 3, 5, 7, 9, 11, and this. The tablet's intactness had decreased, and it was bloated. The image, which was taken 15 hours after administration, shows how the tablet has vanished. This suggests that colonic bacteria are responsible for the tablet's breakdown.

9. SUMMARY

In this effort, the colon is being carefully investigated as a potential medication delivery site. Due to its close to neutral pH, prolonged transit time, low activity of proteolytic enzymes, and high reactivity to absorption boosters, the colon is an advantageous location for medication administration. Ornidazole is insoluble in acidic environments and poorly absorbed from the upper GIT. But in alkaline settings, it dissolves and is almost totally absorbed through the colon Oral administration of ornidazole might also aggravate the lining of the stomach. A drug that is poorly absorbed from the upper GIT and may be utilised for colonic sickness is the greatest candidate for colon cancer treatment.

The tested tablets were weighed, examined for weight variation, hardness, thickness, friability, drug content, time of disintegration, and underwent an in vitro dissolving test. All of these parameters were found to be within normal bounds. According to ICH rules, the formulation F5 was treated as a confirmatory trial and was put through stability studies up to two months of accelerated stability since it gives more core protection under acidic conditions while still showing the quickest drug release under intestinal pH.

10. CONCLUSION

Physical observation and FTIR tests were used in the preformulation studies to determine the composition of the API and its compatibility with the excipients. The findings demonstrated that there was no interaction between any of the chosen Excipients and the API.

The dry granulation method was used to successfully create the ornidazole matrix tablets using the chosen excipient amounts. According to pre-requisites of standards, the developed tablets were assessed for both pre- and post-compression parameters. And the outcomes matched the pharmacopoeia's requirements. The enteric polymer Eudragit S100 was pan coated onto the ornidazole matrix tablets that were created. Since it offers more protection to the site from core damage in acidic conditions and at the same time exhibits the fastest drug release under intestinal pH, formulation F5 outperformed all other batches with a 97.70% drug release at 12 hours. Therefore, the trial F5 was deemed to be the optimum formulation. The formulation F5 incorporating enteric coated matrix tablet of ornidazole can be inferred from the results. It would be a potential formulation to meet the goal of curing ulcerative colitis and Crohn's disease without causing gastrointestinal irritation or ulcers, which is helpful for individuals who have a prior history of ulcerative colitis and Crohn's disease.

REFERENCE

1. N SS, Irfan M, Hasnain M, Khan GJ, Ahmad S. FORMULATION , OPTIMIZATION AND EVALUATION COLON TARGATED DRUG DELIVERY SYSTEM FOR.
2. 2018;05(04):3168–76.
3. Patel MM. Micro/nano-particulate drug delivery systems: a boon for the treatment of inflammatory bowel disease. Expert Opin Drug Deliv. 2016;13(6):771–5.
4. Chourasia MK, Jain SK. Pharmaceutical approaches to colon targeted drug delivery systems. J Pharm Pharm Sci. 2003;6(1):33–66.
5. Kumar R, Patil MB, Patil SR, Paschapur MS. Polysaccharides based colon specific drug delivery: A review. Int J PharmTech Res. 2009;1(2):334–46.
6. Das M, Ghosh L. Evaluation of polymers for compression coating oaminosalicylic acid matrix tablets for colon targeting. Int J Pharm Pharm Sci. 2013;5(SUPPL 3):122–5.
7. Grewal AS, Bhardwaj SK, Patro SK, Kanungo SK. Visible spectrophotometric estimation of ornidazole in pure and pharmaceutical formulation. Int J ChemTech Res. 2012;4(3):1044–8.
8. Neha S, Harikumar SL. Polymers for Colon targeted drug delivery: A review. Int J Drug Dev Res. 2013;5(1):21–31.
9. Gopinath H, Kapudasi R, Shanmuga D, Bhowmik D, Bada PK, Sankar K. Review on , colon specific drug delivery Strategies and in-vitro in-vivo evaluation. 2015;(May).
10. Jain V, Shukla N, Mahajan SC. Polysaccharides in colon specific drug delivery. 2015;1(1):3–11.
11. Laxmi GRP, Srikanth G. Formulation and Evaluation of Colon Specific Drug Delivery of Press Coated Esomeprazole Tablets. J Drug Deliv Ther. 2019;9(1):9–16.
12. b manjula, v aishwarya, vinod beulah sudheer kumar. Formulation and Evaluation of Ornidazole matrix tablets for colon specific drug delivery. world J Pharm Pharm Sci. 2016;5(4):2440–9.
13. Kumar, S. Pradeep, Prathibha, D., Parthibarajan, R., Reichal CR. Colon Specific Drug Delivery System : a Review. 2014;2(2):75–85.
14. Dangi AA, Ganure Ashok L, Divya J. Formulation and evaluation of colon targeted drug delivery system of levetiracetam using pectin as polymeric carrier. J Appl Pharm Sci. 2013;3(1).
15. Vemula SK, Kebamo S, Mosisa B, Paulos B. Effect of time-dependent polymer on the dissolution rate of flurbiprofen: Formulation and evaluation of colon-specific matrix tablets. Thai J Pharm Sci. 2016;40(1).
16. Amidon S, Brown JE, Dave VS. Colon-Targeted Oral Drug Delivery Systems: Design Trends and Approaches. AAPS PharmSciTech. 2015;16(4):731–41.
17. Mura P, Maestrelli F, Cirri M, González Rodríguez ML, Rabasco Alvarez AM. Development of enteric-coated pectin-based matrix tablets for colonic delivery of theophylline. J Drug Target. 2003;11(6):365–71.
18. Gupta VK, Gnanarajan G, Kothiyal P. A review article on colonic targeted drug delivery system. Phama Innov. 2012;1(7):14–24. Basit AW. Advances in colonic drug delivery. Drugs. 2005;65(14):1991–2007.
19. Philip AK, Philip B. Colon targeted drug delivery systems: A review on primary and novel approaches. Oman Med J. 2010;25(2):70–8.
20. Singh B. Modified-Release Solid Formulations for Colonic Delivery. Recent Pat Drug Deliv Formul. 2008;1(1):53–63.

21. Ren Y, Jiang L, Yang S, Gao S, Yu H, Hu J, et al. Design and preparation of a novel colontargeted tablet of hydrocortisone. Brazilian J Pharm Sci. 2017;53(1):1–11.
22. Asane GS, Rao YM, Bhatt JH, Shaikh KS. Optimization, characterisation and pharmacokinetic studies of mucoadhesive oral multiple unit systems of ornidazole. Sci Pharm. 2011;79(1):181–96.
23. Reddy PS, Bose PSC, Saritha D, Sruthi V. Formulation and Evaluation of Colon Targeted Matrix Tablet Using Natural Tree Gums. Int J Pharm Pharm Sci. 2018;10(9):92.
24. Asghar LFA, Chandran S. Design and evaluation of matrices of Eudragit with polycarbophil and carbopol for colon-specific delivery. J Drug Target. 2008;16(10).
25. Anusha K, Krishna Sailaja A. Preparation and evaluation of mefenamic acid loaded microspheres using synthetic and natural polymers. Der Pharm Lett. 2016;8(1):197–205.
26. Samaha D, Shehayeb R, Kyriacos S. Modeling and comparison of dissolution profiles of diltiazem modified-release formulations. Dissolution Technol. 2009;16(2):41–6.
27. Veerareddy SRM and PR. Effect of Formulation Variables on the Release of Aceclofenac From Hpmc Matrix Tablets. Int J Pharm Sci Res. 2011;2(11):2901–7.
28. Patel P, Roy A, Vinod Kumar SM, Kulkarni M. Formulation and evaluation of colon targeted tablets of Ornidazole for the treatment of amoebiasis. Int J Drug Dev Res. 2011;3(1):52–61.
29. kinage krishna, nandgude tanaji, bhise khan deshmukh pradeep. studies on development of oral colon targeted drug delivery system of locust bean and xanthan gums. Int J green Pharm. 2007;33–4. 30. Krishnaiah YSR, Indira Muzib Y, Srinivasa Rao G, Bhaskar P, Satyanarayana V. Studies on the development of colon targeted oral drug delivery systems for ornidazole in the treatment of amoebiasis. Drug Deliv J Deliv Target Ther Agents. 2003;10(2):111–7.
30. Patil CC, Naikwadi A, Jorapur P, Samiullah S, Karajgi S. In-vivo, in-vitro analysis of formulated colon targeted ornidazole matrix tablet. Int J Drug Deliv Technol. 2021;11(3):777–81.
31. h. rajpurohit, p. sharma s. sharma. Polymers for colon targeted drug delivery. Indian J Pharm Sci. 2010;689–96.
32. Shravani E AD. Design and development of Ciprofloxacin colon specific drug delivery system. 2011;3(2):383–95.
33. Sulthana A, Ramu B, Srikanth G, Rajkamal B. Formulation and evaluation of colon specific tinidazole matrix tablets. Res J Pharm Dos Forms Technol. 2016;8(3).
34. Kumar D V, Mishra A, Easwari TS. Formulation and Development of Acrycoat-Coated Chitosan Beads of Ornidazole for Colon Targeting. Eur J Appl Sci. 2013;5(2):47–52.
35. Leontiev D, Bevz O, Volovyk N, Gella I, Georgiyants V. The synthesis and study of profiles of the ornidazole impurities. Sci Pharm Sci. 2018;0(1 (11)):4–11.Ansori.. Pap Knowl Towar a Media Hist Doc. 2015;3(April):49–58.
36. M S, S P. Development and Evaluation of a Novel Time and Ph-Dependent Colon Targeted Drug Delivery of Ornidazole. Asian J Pharm Clin Res. 2021;14(6):108–11. rowe rc, sheskey p quinn m. handbook of pharmaceutical excipients. 2009.
37. Indira Muzib Y, Kurri PS. Formulation and evaluation of gum olibanum-based sustained release matrix tablets of Ambroxol hydrochloride. Int J Pharm Pharm Sci. 2011;3(2):195–
38. 9.
39. Deshmukh R. Development and in-vitro evaluation of colon specific indomethacin matrix tablet for the treatment of inflammatory bowel disease. Res J Pharm Technol. 2021;14(5).

40. Vemula SK. Colon specific drug delivery: Effect of Eudragit enteric coating on hydroxypropyl methylcellulose matrix tablets of flurbiprofen. J Young Pharm. 2015;7(4).
41. Pawar PS, Saleem MA. Formulation and evaluation of oral colon targeted tablet of budesonide. Der Pharm Lett. 2013;5(3):1–12.
42. Sirisha B, Ajitha M. Formulation and in vitro evaluation of oral colon targeted tablet of pyrantel pamoate. Int J Pharm Biol Sci. 2018;8(4):91–102.
43. Fenin V, Kachawa VS, Jain CP. Optimization of Colon Specific Drug Delivery System for Ornidazole using Modified Gum. Int J Pharm Sci Drug Res. 2020;13(02):176–82.
44. Kaur S, Singh K, Swami G, Sharma AK. Preparation and evaluation of matrix tablets of indomethacin for colon specific delivery. Der Pharm Lett. 2014;6(1).
45. Chemical book available from https://www.chemicalbook.com/product/chemical propertiesCB.htm Accessed 14th July 2020.
46. Raymond C Rowe, Paul J Sheskey & Marian E Quinn:Handbook of Pharmaceutical
47. Excipients. 6th edition. Available at Library of BLDEA's SSM College of Pharmacy, Vijayapur.