CODEN [USA]: IAJPBB ISSN : 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

SJIF Impact Factor: 7.187

https://doi.org/10.5281/zenodo.14523335

https://www.iajps.com/volumes/volume11-december-2024/46-issue-12-december-24/

Available online at: http://www.iajps.com *Research Article*

FORMULATION & EVALUATION OF ENTERIC-COATED CAPSULES FOR THE TREATMENT OF ULCERATIVE COLITIS

K.Tejaswini[1], D.Raj kumar[2]

[1]Mother Teresa College of Pharmacy, N.F.C Nagar, Ghatkesar, Medchal, Telangana.

Article Received: October 2024 Accepted: November 2024 Published: December 2024

Abstract:

As part of this investigation, budesonide sustain-release micro tablets in capsule form were created and refined to treat ulcerative colitis. Cross povidone and HPMC K4 M were used as release retardants in the direct compression method used to create Budesonide micro tablets. FTIR spectroscopy indicates that the generated formulations do not exhibit any indication of drug-excipient interaction. The constructed micro pills' physicochemical characteristics were good. It was discovered that formulation BF4 was the best optimized when all of the formulas were examined. As per the previously reported results, capsules are able to withstand acidic pH levels and retain their structural integrity. It was shown that capsules were the most effective choice for enteric drug delivery systems.

Keywords: *Budesonide, Sustain-release, Ulcerative colitis, Enteric-coated, Capsules.*

Corresponding author:

Devara Raj kumar,

Mother Teresa College of Pharmacy,

N.F.C Nagar, Ghatkesar, Medchal, Telangana.

QR code

Please cite this article in press **Devara Raj kumar** *et al.,* ***Formulation & Evaluation Of Enteric-Coated Capsules For The Treatment Of Ulcerative Colitis.,****Indo Am. J. P. Sci, 2024; 11 (12).*

INTRODUCTION:

Inflammation and ulcers (sores) in the digestive system are symptoms of the inflammatory bowel disease (IBD) known as ulcerative colitis. The innermost lining of your large intestine, often known as the colon and rectum, is impacted by ulcerative colitis [1]. In the majority of people, symptoms typically appear gradually rather than abruptly. Draining and perhaps life-threatening consequences are possible with ulcerative colitis. Although there is no known cure, many innovative treatments can significantly lessen the disease's signs and symptoms and result in long-lasting remission [2]. Typically, either drug therapy or surgeries are used as treatments. The treatment of ulcerative colitis may be successful with various drug classes. Some individuals may not respond adequately to some drugs. The initial line of treatment for ulcerative colitis is frequently anti-inflammatory drugs, which are suitable for the majority of patients with this condition [3].

The enteric-coated drug-delivery technology (ECDDT), which offers complete enteric protection without the need for a separate enteric coating, is described in recent technical research. ECDDT can provide quicker development timelines and decrease program risk by doing away with the preparation and application stages required for enteric coating [4]. It has been demonstrated that this cutting-edge technology makes it possible to develop products that require enteric protection and/or targeted release to the upper gastrointestinal tract by enabling the oral delivery of sensitive molecules and acting as a valuable tool for product development.

MATERIALS AND METHODS:

Budesonide was obtained as a gift sample from MSN Labs Pvt. Ltd. Crospovidone, HPMC K4M were purchased from S.D. Fine Chem. Ltd, Mumbai, India.

METHODOLOGY:

Formulation of Mini-Tablets:

Each ingredient was independently run through #60mesh after being weighed by the amounts listed in Table 1. After that, an "8-station rotary mini press tablet machine with a 5mm punch" was used to compress the contents into 40 mg tablets in a geometrical arrangement [5]. Enteric-coated capsules of size #0 were filled with compressed tablets. One mini-tablet is contained in each capsule. Each capsule has a dosage of 3 mg.

Table 1: Formulations of Budesonide Mini-Tablets

S.No	Ingredient (mg)	BF1	BF2	BF3	BF4	BF5	BF6	BF7	BF8	BF9
1.	API	4	4	4	4	4	4	4	4	4
2.	HPMC K4M	0.8	1.6	2.4	0.8	1.6	2.4	1.6	0.8	2.4
3.	Crospovidone	0.8	2.0	1.2	2.0	1.2	2.0	0.8	1.2	0.8
4.	Microcrystalline Cellulose	43.8	41.8	41.8	42.6	42.6	41	43	43.4	42.2
5.	Magnesium Stearate	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2	0.2
6.	Talc	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4
Entire Tablet Mass (mg)		50	50	50	50	50	50	50	50	50

Evaluation

Pre-compression

Bulk Density (ρb)

A measuring cylinder was filled with the weighed powder, and the primary weight was noted. The original volume is known as the bulk volume [6].

$$\rho b = M / Vb$$

Where,

M and Vb are the powder mass and powder bulk volume, correspondingly.

Tapped Density (ρt)

It is calculated by dividing the powder's weight by its tapped volume. With the help of a funnel, the powder was added to a measuring cylinder, and the volume reached is the tapped volume after 500 taps using a Tap Density tester [7].

$$\rho t = M / Vt$$

here, Vt are the Tapped volume of the powder

Angle of Repose (θ)

A funnel was placed such that its bottom tip was precisely 2.0 cm above the hard surface, and the medication and blend were poured through the walls to determine it.

$$\theta = \tan\text{-}1(h/r)$$

Where, h = height of pile in cm, r = radius of pile in cm.

Carr's Index (or) % Compressibility

Powder flow qualities are indicated. The purpose of measuring it is to ascertain the relative significance of interparticulate interactions [8].

$$CI = \rho t - \rho b / \rho t \text{ X } 100$$

here, ρt and ρb are tapped and bulk density individually.

Hausner's Ratio

An indirect measure of the ease of powder flow is Hausner's ratio. It is computed using the formula below.

$$HR = \rho t / \rho b$$

Post-compression:

Uniformity of Weight:

Weighing each tablet separately, twenty were chosen at random. The weight average was determined [9]. A comparison was made between the tablets' percentage deviation and the standard parameters.

Thickness

The homogeneity of size and shape was assessed by measuring the thickness. Using vernier callipers, the tablets' thickness was determined [10].

Hardness

In a diametric compression test, tablet hardness is determined by a Monsanto hardness tester [11].

Friability

Using Roche friability, the produced formulations' friability was assessed. The tablets were dedusted and weighed again after the pre-weighed sample was put in the friability tester and spun for 25 revolutions for 4 minutes [12].

$$\% \text{ Friability } = \frac{\text{Initial weight of tablets} - \text{Final weight of tablets}}{\text{Initial weight of tablets}} X\ 100$$

Drug content uniformity:

A 100 ml volumetric flask was filled with precisely weighed powder that contained 10 mg of medication after five little tablets were weighed and pulverised into a mortar using a UV visible spectrophotometer [13]. The drug's homogeneity of content was measured at a wavelength of 247 nm.

In-Vitro Drug Release:

The integrity of enteric-coated capsules at acidic pH was evaluated. Table 5 and Figure 8 show the results of the release profile after 6 units containing 3 mg of medication in each capsule were dissolved [69] for 2 h in 1000mL of 0.1N hydrochloric acid at 75RPM and 37°±5°C for 2 hours, and then 7.5 pH phosphate buffer at 1000mL and 75RPM and 37°±5°C for 8 hours. After two hours, NMT 5% release is the limit [14].

Compatibility Study using FTIR

With FTIR spectra acquired on a Bruker Alpha II, the compatibility between the pure medication and excipients was identified [15]. To determine the likelihood of any interaction between the formulation's constituent parts, the FT-IR spectrophotometer was employed.

Stability Studies:

The stability study is a useful technique for determining the recommended storage conditions at 40°C ± 2°C/75% RH ± 5% RH and the retest period for the drug substance or shelf life [16].

RESULTS AND DISCUSSION:

Table 2: Evaluation Criteria for Budesonide Powder Blend Precompression

Formulations	BF1	BF2	BF3	BF4	BF5	BF6	BF7	BF8	BF9
Angle of repose (°)	27.52	25.30	28.54	25.31	25.48	26.22	27.42	24.14	29.38
Bulk density (gm/cc)	0.74	0.87	0.75	0.81	0.75	0.77	0.85	0.83	0.70
Tapped density (gm/cc)	0.84	0.90	0.82	0.85	0.86	0.83	0.93	0.85	0.81
Compressibility Index (%)	8.23	6.47	10.74	6.94	11.73	7.12	10.54	4.61	12.30
Hausners proportion	1.08	1.06	1.10	1.07	1.12	1.07	1.12	1.05	1.14

The findings in Table 2 demonstrated good flow characteristics for every formulation and were confirmed to be within the bounds.

Table 3: Post compression Parameters

Formulation	Weight Variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug Content (%)
BF1.	38.53	2.06	1.7	0.16	98.68
BF2.	38.78	1.94	2.2	0.14	97.37
BF3.	40.35	1.77	2.7	0.16	101.9
BF4.	39.33	2.60	2	0.15	99.65
BF5.	40.0	1.63	2.4	0.18	99.31
BF6.	39.21	2.01	2.5	0.12	98.67
BF7.	38.36	2.1	3.0	0.20	98.80
BF8.	39.67	2.36	2.3	0.14	99.60
BF9.	41.63	1.68	3.2	0.16	100.01

Friability and weight fluctuation results in Table 3 were judged to be within acceptable bounds. The range of thickness was 1.77-2.60 mm, the range of hardness was 1.8-2.8 kg/cm2, and the range of drug content was 97.37-101.9 % [17].

In-Vitro Drug Release Study

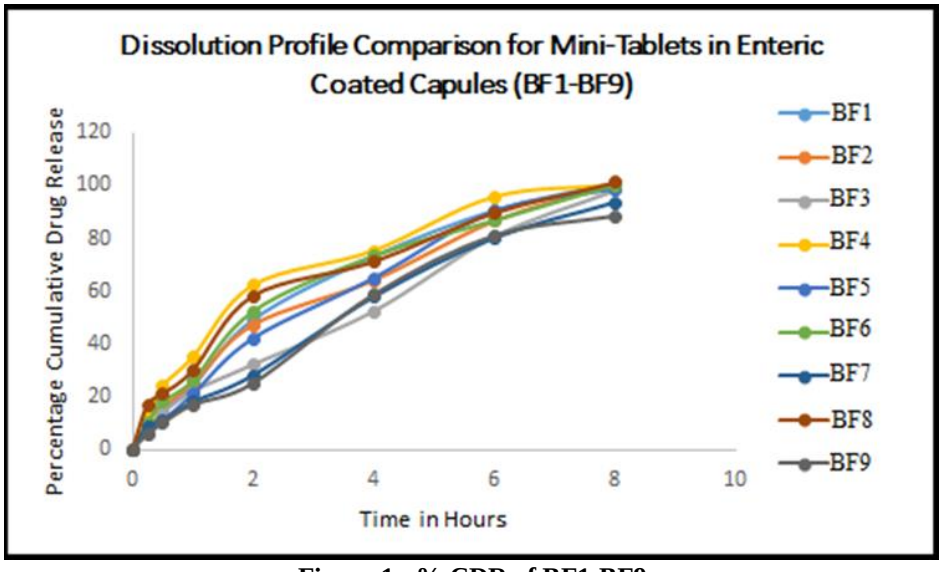

Figure 1: % CDR of BF1-BF9

FTIR:

Drug and polymer compatibility was further demonstrated by the fact that the primary peak of the FTIR spectra of the drug and excipients did not change, indicating that neither the drug's nor the excipients' qualities in the preparation changed [18].

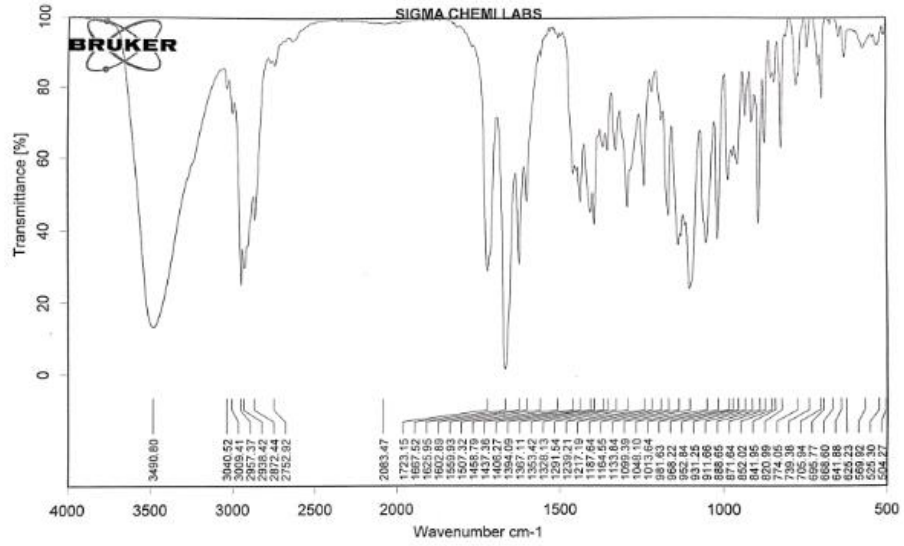

Figure 2: FTIR Spectroscopy of Budesonide Pure Drug

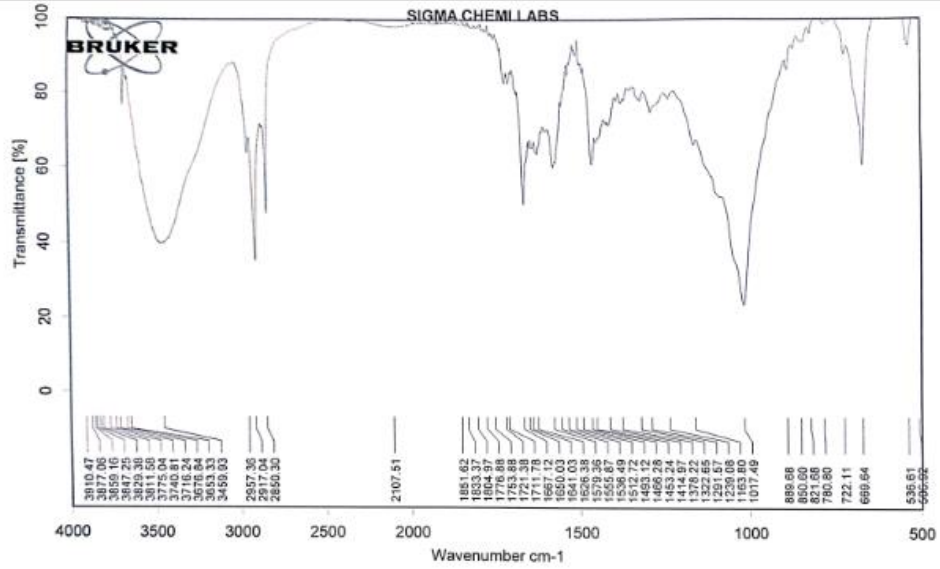

Figure 3: FTIR Spectroscopy of Preparation Blend

Table 4: FTIR Interpretation for Budesonide

	O-H Stretching	C-H Stretching	C=O Stretching
Pure Drug	3490.80	3040.52	1723.15
Formulation Mixture	3459.93	2957.36	1667.12

Since the bands' characteristics and locations in the formulation remain unchanged, it can be said that the medicine retains its identity without coming into contact with the excipients [19].

Stability studies:
All were found to be within acceptable bounds according to data acquired for optimized formulation (BF4).

Table 5: Stability data of Budesonide Mini-Tablets in Enteric Coated Capsules

Time (h)	Cumulative Drug Release	
BF4 -40°C ± 2°C/75% RH ± 5% RH%		
	0 month	After 3 months
0	0.00	0.00
0.25	12.74	11.72
0.50	24.13	25.48
1	35.02	36.55
2	62.24	61.90
4	75.32	74.49
6	95.71	96.23
8	100.18	98.71
Average Drug Content %	99.34	99.21

Budesonide showed an endothermic peak at 250.25°C before stabilisation and at 250.19°C following stability. The DSC spectrum revealed that none of the examined substances had any potential interactions or degradation [20].

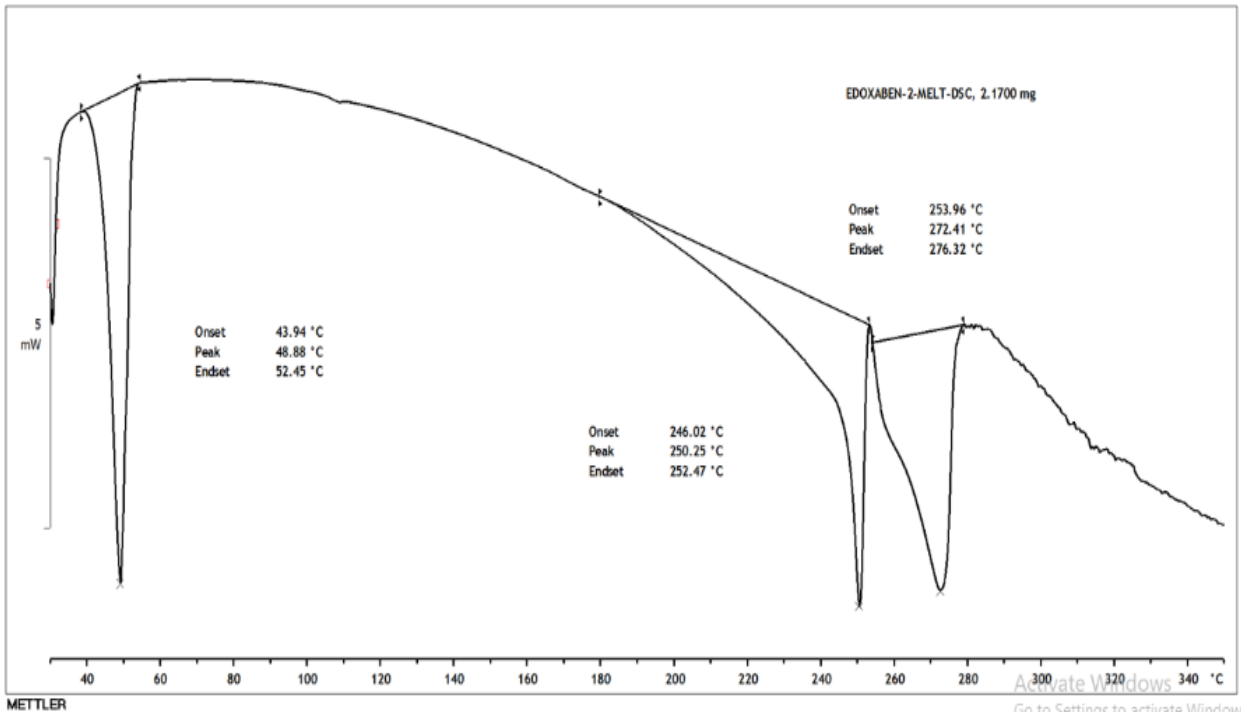

Figure 4: BF4's DSC studies before stability

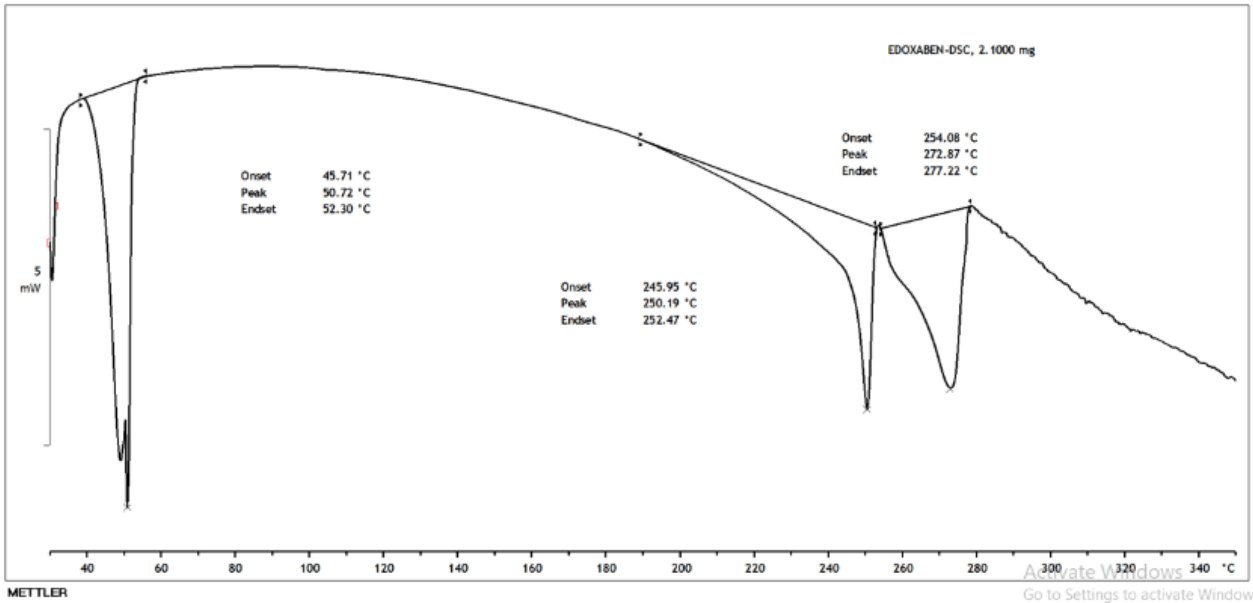

Figure 5: DSC analysis of BF4 following stability

CONCLUSION:

Budesonide sustain-release micro tablets in capsule form were developed and optimized as part of this study to treat ulcerative colitis. Budesonide mini tablets were made by the direct compression technique with the help of cross povidone and HPMC K4 M as release retardants. The produced formulations show no evidence of drug-excipient interaction, according to FTIR spectroscopy. The physico-chemical properties of the assembled mini tablets were satisfactory. When all of the formulations were compared, formulation BF4 was found to be the most optimized. DSC, in-vitro dissolution, and drug content were all found to be within acceptable bounds. Therefore, it can be claimed that the formulation is stable. The in vitro dissolving test was performed on small tablets in capsules, and samples were taken at the appropriate times and examined under a UV lamp. Two hours later, no traces of the substance were discovered. According to the aforementioned findings, capsules are resilient to acidic pH and maintain their integrity. It was discovered that the best option for enteric medication delivery systems was capsules.

REFERENCES:

1. Crohn's & Colitis Foundation of America. Surgery for Crohn's Disease and Ulcerative Colitis. (https://www.crohnscolitisfoundation.org/sites/default/files/legacy/assets/pdfs/surgery_brochure_final.pdf) Accessed 7/20/2020.
2. Rao KV, Venkatchalam VV. Dissolution kinetics of immediate release mini tablets of cefuroxime axetil. W J Pharm Res 2018;7:923-46.
3. Patel H, Shaikh SN. Formulation development optimization and evaluation of telmisartan mini tablets. Int J Pharm Bio Sci 2018;8:545-54.
4. Priyanka, Kumar K, Teotia D. A comprehensive review on pharmaceutical mini tablets. J D Delivery Ther 2018;8:382-90.
5. Singh S, Virmani T, Virmani R, Kumar P, Mahlawat G. Fast dissolving drug delivery systems: formulation, preparation techniques and evaluation. Universal J Pharm Res 2018;3:60-9.
6. Paul NAC, Ernest AAA, Jim WA. Design and evaluation of chronotherapeutic pulsatile drug delivery system of cilnidipine. Universal J Pharm Res 2017;2:18-22.
7. Honmane SM, Dange YD, Osmani RAM, Jadge DR. General consideration of design and development of dosage forms: pre-formulation review. Asian J Pharm 2017;11:479-85.
8. Ankush S., Kapil K., Amritpal S., Pooja and Anju, "A review on novel approaches for colon targeted drug delivery system." International journal of pharmaceutical chemical and biological sciences.2014, 4(2), 241-249.
9. Lorena, S., Paolo, M., Lorella, G., Susanne, M. and Franco, P., "Formulation and Coating of Alginate and Alginate-Hydroxypropyl cellulose Pellets Containing Ranolazine." Journal of Pharmaceutical Sciences. 2016, 12(5), 1-8.
10. Chen, K., Yinghua, S., Bing, Li. and Rui, Fan., "Preparation and evaluation of duloxetine hydrochloride enteric-coated pellets with

different enteric polymers." Asian Journal of Pharmaceutical Sciences. 2016, 2(5), 165-178.
11. Mastoi SM, Ali A, Aslam H, Niaz K. Comparision of antidyslipiemic potential of 80 milligrams of Fenofibrated with 8 grams of Nigella sativa seeds daily. Univ J Pharm Res. 2017; 2(6):50-52.
12. Saddam C Shaikh, Dnyaneshwar S, Dipak V Bhusari, Jain S, Pooja P Kochar, Vikram N Sanchati. Formulation and evaluation of Ibuprofen gastro-retentive floating tablets. Univ J Pharm Res. 2018; 3(4):20-25
13. Donepudi Pradyumna, Lankalapalli Srinivas, Nallamothu Krishna. In-vivo study of Budesonide mini-tablets in enteric coated capsules for the treatment of ulcerative colitis. Research Journal of Pharmacy and Technology.2024; 17(4):1758-2. doi: 10.52711/0974-360X.2024.00279
14. Viviane Doggwiler, Michael Lanz, Valeria Paredes, Georg Lipps, Georgios Imanidis. Tablet formulation with dual control concept for efficient colonic drug delivery. International Journal of Pharmaceutics.2023; 631,122499.
15. Shoaeb M. Syed, Pratiksha V. Rathi , Kiran G. Gawale , Dipali C. Hamde. Formulation and evaluation of pH activated dosage form as minitablets in capsule for delivery of fesoterodine. Journal of Taibah University Medical Sciences.2022;17(1):72-81,
16. Anita, Anil Singh and Ankit Dabra. A Review on Colon Targeted Drug Delivery System, IJPSR, 2019; Vol. 10(1): 47-56.
17. Mohd Abdul Hadi, Raghavendra Rao NG, Sunil Firangi. Mini-tablets technology: an Overview. American Journal of Pharm tech Research. April 2012; 2(2): 128-150.
18. Faiezah A. A. Mohamed, Matthew Roberts, Linda Seton, James L. Ford, Marina Levina, and Ali R. Rajabi-Siahboomi, Production of extended release mini-tablets using directly compressible grades of HPMC. Drug Development and Industrial Pharmacy, 2012, 1-8.
19. P. Sandhya, Sameera Khan Formulation and Evaluation of Repaglinide Biphasic Mini Tablets IOSR Journal of Pharmacy and Biological Sciences. Volume 9, Issue 1 Ver. II,Jan. 2014, 66-73
20. Honmane SM, Dange YD, Osmani RAM, Jadge DR. General consideration of design and development of dosage forms: pre-formulation review. Asian J Pharm 2017;11:479-85.