DOI: 10.22270/jmpas.2021.V10I6.1632 ISSN NO. 2320–7418

International peer reviewed open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com CODEN: JMPACO

Research articles

Formulation, development and optimisation of ph. dependent drug delivery system containing proton pump inhibitor

Ghugarkar Prasad Gorakshanath*, Khulbe Preeti

Suresh Gyan Vihar University, Jaipur, India.

ABSTRACT

The present study was involving the targeting the Rabeprazole formulation at site specificity. Peptic ulcer mostly occurs in the lower part of the gastrointestinal tract. Proton pump inhibitors category drugs mainly used to cure peptic ulcer. As most of proton pump inhibitors degrades in acidic condition in stomach, the present study mainly focus on targeting site specificity without degradation of drug in stomach. Rabeprazole and selected excipients was tested for reformulation study as well as for analytical techniques like Ultra Violet Visible Spectroscopy, Fourier Transform Infrared Spectroscopy and Differential Scanning Calorimetry. Core pellet formulation of Rabeprazole was formulated using extruder and spheroniser. After core pellet preformulation seal coating of pellet was completed. As seal coating mainly helps the core pellet from interaction between another coating polymer. Seal coating was completed by using Opadry coat. At the top of the pellet polymer coat was applied. Polymer coat was helps to deliver the formulation in appropriate pH only. Polymer coat also protects the formulation from degradation in stomach where acidic condition presents. Evaluation parameters like dissolution test, Ultra Violet Visible Spectroscopy, Fourier Transform Infrared Spectroscopy and Differential Scanning Calorimetry, optimisation parameter applied to optimised formulation. Stability study was performed on optimised formulation.

Keywords: Ulcer, Gastrointestinal tract, Polymer, Coating.

Received – 08/08/2021, Reviewed - 02/10/2021, Revised/ Accepted- 16/11/2021

Correspondence: Ghugarkar Prasad Gorakshanath* ✉ ghugarkarp@gmail.com

Gyan Vihar School of Pharmacy, Suresh Gyan Vihar University, Jaipur, India.

INTRODUCTION

Due to good patient acceptance, ease of administration, such as tablets, capsules, liquid solutions, etc., oral administration of drugs has been the most common and preferred route of administration for most therapeutic agents. As the absorption rate differs from stomach to stomach, compared to gastric capillaries, it increases the surface area of the capillaries that pass through the intestine (approximately 4,500 cm^2), the intestinal mucosa and a greater blood flow (1000 ml / min). Some drugs with pH-dependent stability are also known to be unstable in an acidic environment (stomach) [1]. Various techniques have been developed to overcome this stability problem. One of them is the development of enteric-coated or polymer coated products. These enteric coated as well as polymer coated formulation forms resist the acidic environment of the stomach where in acidic condition formulation not show a drug release and allow drug release in the basic pH environment of basic intestinal condition [2]. The biggest advantage of enteric coating as well as polymer coated pellet is improving the appearance of the product and the core is pharmaceutical elegance.

The granulation provides flexibility for formulation design and development. It Reduces the local concentration of irritating drugs. Improve the safety and effectiveness of drugs. The particles provide reduced gastric emptying rate and changes in transit time. The particles are scattered freely in G.I.T. And they always maximize drug absorption and reduce peak plasma fluctuations. Pellets ensure improved fluidity during formulation development. The particles can be coated with different polymers to control the release of the drug with different pH condition. In the case of immediate release products, the larger pellet surface allows for better distribution [3]. Chemically incompatible products can be formulated and administered in a single and multi-dose by palletisation them.

MATERIAL AND METHOD

Rabeprazole, Mannitol, PVP K-30, HPMCP, Talc, Opadry coat, Eudragite FS 30-D, PEG obtained from Modern chemical.

Melting Point determination

Melting point of the selected drug was checked by using capillary tube process.

Preformulation parameter

Preformulation parameters such as density as well as compressibility factors were carried out.

FTIR study

FTIR study of the plain drug as well as mixture of Drug and excipients selected for formulation was carried out with FTIR spectrometer. Drug FTIR study carried out to check the purity of drug. Drug and excipient FTIR study was carried out to determine the compatibility between selected drug and excipient.

UV determination

Accurately weigh rabeprazole (100 mg) and dissolve in 100 ml of 0.1 N HCl to form a stock solution (1000 µg / ml). The stock solution was further diluted appropriately with 0.1 N HCl to obtain a working standard solution with a concentration of 100 µg / ml. The working standard solution is adequately diluted to a concentration of 20 µg / mL and then scanned in the UV range. This shows that there is an absorption maximum at 292 nm. [4].

DSC study

DSC study was performed on selected drug and formulation. The differential scanning calorimetry study was performed to check the variation occurred in physicochemical parameter of drug through thermal effect [5].

Pellet Preparation

Compaction with the help of extruder and spheroniser and drug layering with coating are the most widely used palletisation techniques in pharmaceutical industry. From this the compaction techniques, by using extruder and spheroniser is the most popular and high yield technique. Recently, however, melt palettization has been used frequently in making compaction pellets using a different type of equipment, e.g., is high-shear mixer, pellet preparation by extrusion and spheronization. The process involves initially making the extrudes with cylindrical rod shaped from the powder material and then converting the extrudes into beads using the spheronizer technique. The powder material could be any type of powder but mostly of the drug powder. After formulation of pellet by extruder and spheroniser, second step was to coat the rabeprazole core pellet [6]. Seal coat helps to protect the core pellet from interaction between another coat. Initially mixture of methylene di chloride and iso propyl alcohol completed. After that Opadry coat polymer was mixed thoroughly in previously mixed solvent solution. The mixture was continuously stirred till it get fully dissolved. Seal coating process was performed in Glatt coater. After seal coating last step was to coat the formulation with polymer coat. For targeted drug delivery system polymer coat mostly used. Eudragit FS 30D was used for polymer coat. Initially polyethylene glycol and talc mixed. After mixing the previous mixture Eudragit FS 30D was mixed in previously prepared mixture. Polymer coating process was performed in Glatt coater.

Table 1: Formulation of core pellet

Ingredient	Quantity (mg)					
	F1	F2	F3	F4	F5	F6
Rabeprazole	20	20	20	20	20	20
Mannitol	7	7	8	11	12	13
PVP K-30	3	4	5	6	7	8
HPMCP	2	3	4	5	6	7
Talc	3	3	4	4	5	5
Alcohol	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.

Table 2: Composition of seal coating

Ingredient	Quantity %
Opadry coat	24
MDC	50
IPA	50

Table 3: Composition of Polymer coating

Ingredient	Quantity (mg)
Eudragite FS 30-D	46
PEG	11.25
Talc	09

RESULT AND DISCUSSION

Physicochemical Characters

Table 4: Organoleptic characters

Test	Observation
Appearance	Amorphous
Colour	White to off white
Odour	Characteristic
Melting Point	139-141^{0}C.

Preformulation parameter: Preformulation parameters of the prepared mixture was carried out. Result obtained was given in below table [7].

Table 5: Pre formulation result

Batch	Angle of repose (Θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Compressibility index (%)	Hausnar's ratio
F1	20.41±0.07	0.75	0.86	12.79	1.14
F2	42.26±0.11	0.79	0.85	07.05	1.07
F3	24.27±1.12	0.74	0.85	08.70	1.14
F4	25.92±0.08	0.76	0.86	11.62	1.13
F5	31.61±0.06	0.71	0.83	14.45	1.16
F6	32.97±0.08	0.72	0.85	15.29	1.18

FTIR Study

The FTIR spectrum of the preparation shows that the drug exists in an active form, and its chemical structure has not changed. Hence from the received FTIR spectrum it was observed that API-Excipients compatible to each other [8].

UV Determination

From the obtained result of UV spectra, it was found that lambda max of the mixture was 292 nm. When different aliquots prepared scanned under given lambda max the obtained result was plotted under the graph as mean absorbance vs. concentration. And the graph shows linear result also R^2 value was within limit [8].

Figure 3. Calibration curve of Rabeprazole

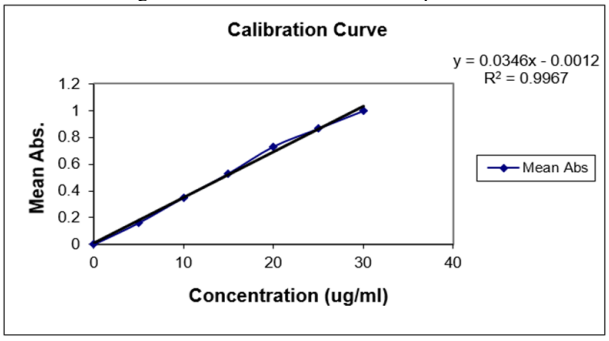


Figure 1. FTIR Study of API

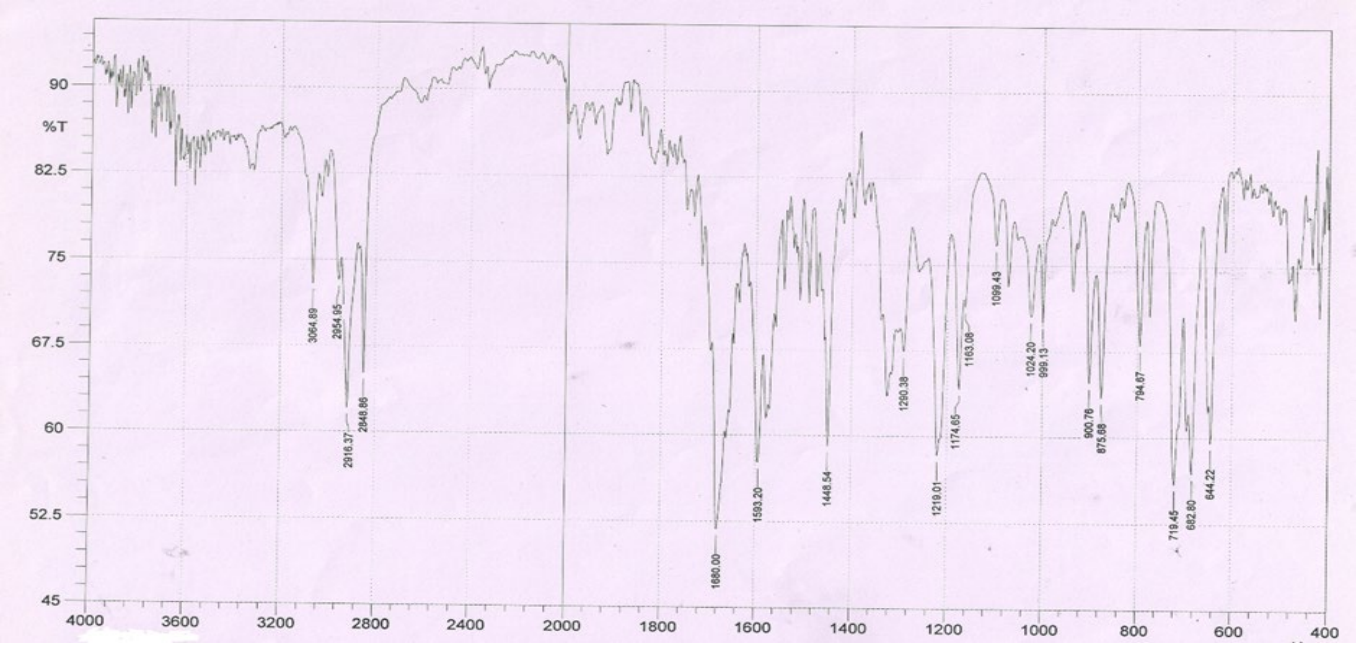


Figure 2. FTIR Study of API and excipient

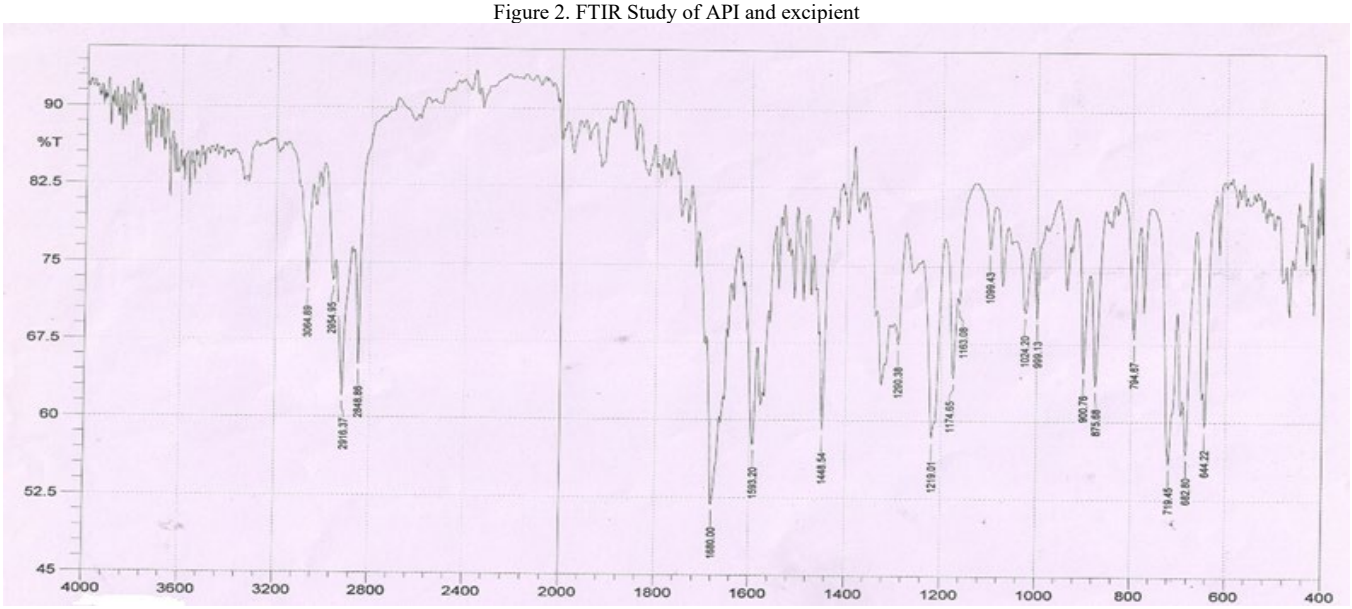
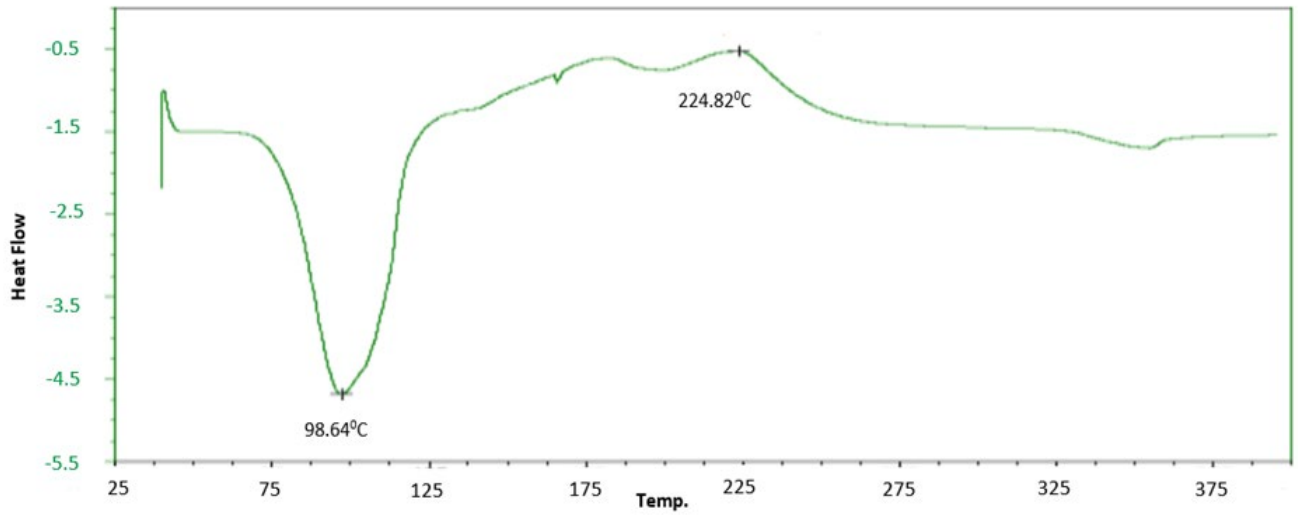


Figure 4. DSC study of Formulation



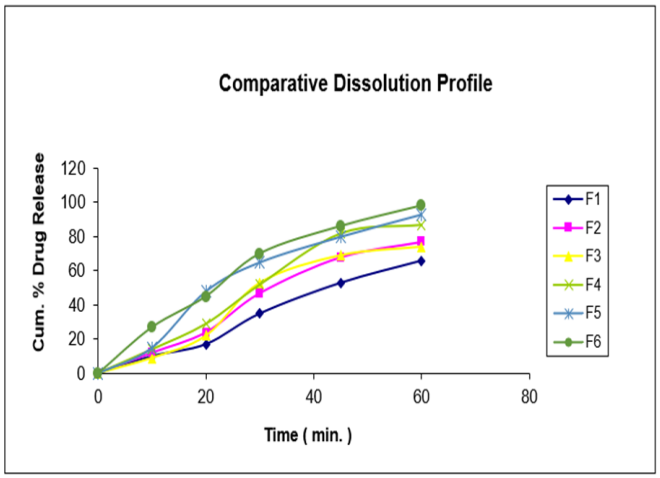
DSC Result

From the received thermal study of the formulation it was observed that there was no any change in the thermogram of the formulation. Hence it was observed the there was no any change in the formulation with effect of using different excipients and with thermal effects [9].

In-vitro drug release study

In vitro dissolution studies for initial two hours was carried out in acidic medium that is in 0.1 N HCL and had revealed the acid resistance capacity of formulation. After that dissolution behaviour of formulation was carried out in basic medium that is in phosphate buffer pH 7.4 medium revealed the in vitro drug release characteristics, batch 6 has shown the optimised release characteristics [9].

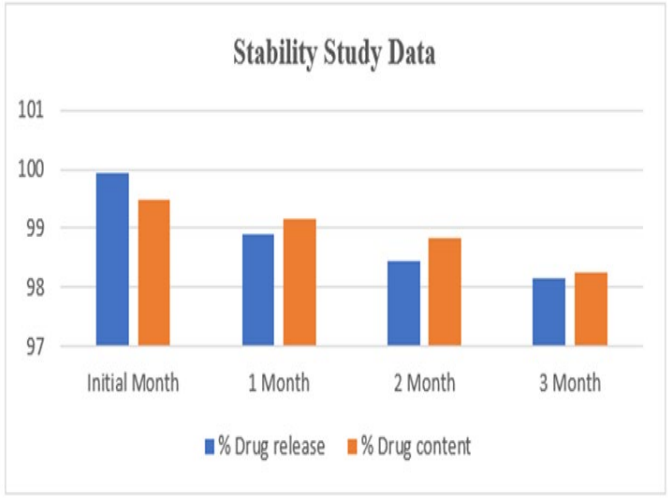
Figure 5. In-vitro dissolution comparative study



Stability Study

There were no changes in % drug release as well as in % drug content of formulation stored at different temperature for drug remaining vs. time at 25°C/60% RH, 30°C/65% RH and 40°C/75% RH. Formulation was kept in stability chamber for 3 months. Result was checked at initial, one, two- and three-month intervals. Stability data result was with in limit. Data was shown in below figure [10].

Figure 6. Stability Study Data



Response Surface Plot and Overlay contour plot

Many optimisation studies are performed for determining better production conditions and can obtain the benefits of continuous experiments. These studies can benefit from response surface methods as well as overlay contour plot method. We have explained this method and some methods through informed research. The goal is to use experiments aimed at improving drug delivery systems for a class to optimise the formulation at best level by using optimized formulations. It is expected that such formulations will provide benefits by enhancing the ability to target the activity of molecules in the targeted site. However, some efforts have produced methods that are not commercially viable, mainly because of the important critical quality attributes (CQA), and the packaging efficiency is too low. In this technique, the experimental mainly focused on different parameters for optimization: the percentage of release, the percentage of polymer coating, and the percentage of plasticizer in the coating. It also conducted a risk analysis to determine which process factors to study and compiled a list of parameters [11].

Figure 7. Response surface plot

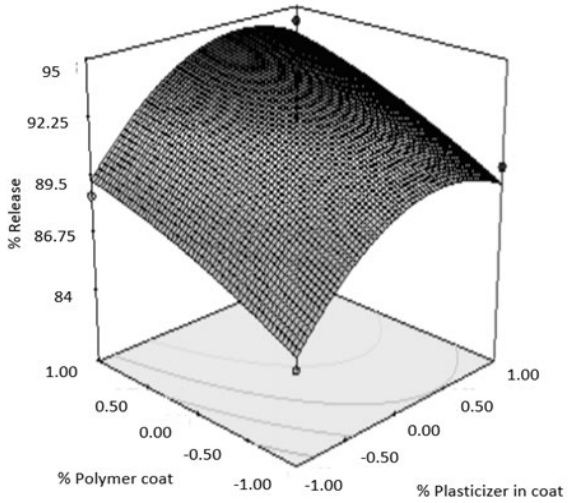
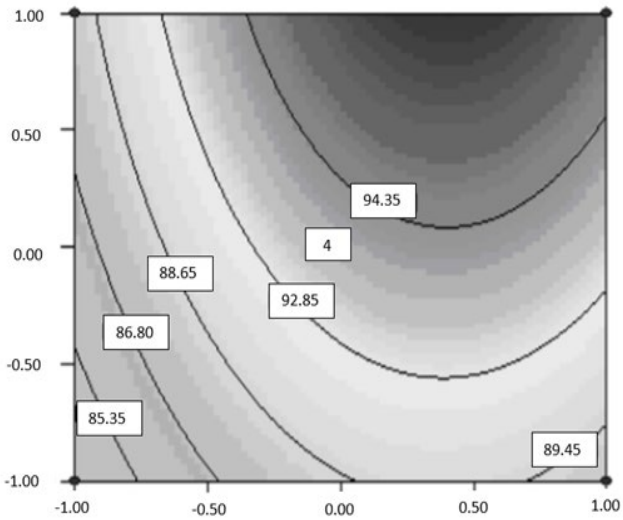


Figure 8. Overlay Contour Plot



CONCLUSION

The present study was to develop, evaluate and optimise the formulation containing proton pump inhibitor. Initially pellete formulation was prepared by using extruder and spheonisation technique. Main advantage of the pelete formulation was to increase surface area of formulation. Seal coating was applied on core pellete by using Opadry polymer. At the top of the formulation it was coated with Eudragit FS 30D polymer. Polymer coat helps the formulation to release drug in appropriate pH condition only. Coating was performed in Glatt coater. From 6 batches batch no. 06 shows optimised batch as it shows best result among all batche. Stability study was performed on optimised batch. Hence Formulation, optimisation of Rabeprazple was carried out.

REFERENCE

1. Narwal S, Saini V, 2016. Formulation, development and evaluation of fast disintegrating thin film of esomeprazole magnesium trihydrate, Am J Pharm, Tech Res, 6,520.
2. Balakrishna T, Vidyadhara S, Murthy Tegk, Rmu A, Sasidhar R, 2018. Formulation and evaluation of esomeprazole fast dissolving buccal films, Asian J Pharm Clin Res, Vol 11, Issue 10, 193-199.
3. Bouhussein DM, El-Bary AA, El Nabarawi SH, 2016. Chitosan mucoadhesive buccal films effect of different casting solvents on their physicochemical properties, Int, J Pharm, Pharm Sci, 8,13.
4. Yassina BG, Abassb HA, 2016. Design and evaluation of fast dissolving oro-dispersible films of metoclopramide hydrochloride using 32 multifactorial designs, Int J Pharm, Pharm Sci, 8, 218-22.
5. Sumio C, Megumi M, Katsuki N, and Ryoya K, 2016. Ingestibility and Formulation Quality of Lansoprazole Orally Disintegrating Tablets, Hindawi Publishing Corporation Journal of Pharmaceutics, Volume 16,16.
6. Balakrishna T, Vidyadhara S, Sasidhar R, Satya P, and Murthy T, 2017. Formulation and evaluation of lansoprazole oro-dispersable tablets, IJPSR, Vol 8(2):804-812.
7. Ramu S, Chandra P, Gopal R, Srinivasa R and Ramakrishna G, 2015. Formulation and evaluation of Lansoprazole delayed release pellets, IJPCBS, 5(4).
8. Swathi P, 2017. Formulation and Evaluation of Rabeprazole Sodium and Domperidone Pellets, Indo American Journal of Pharmaceutical Research, 7(07).
9. Kumari M, Jain NP, 2019. Formulation Development & Evaluation of Buffered Tablet of Proton Pump Inhibitors Drug Rabeprazole Sodium, Journal of Drug Delivery and Therapeutics, 9(4-s),315-321.
10. Sachin C, Nidhi N, Tanuja B, and Saharan V, 2018. An investigation of in-vitro release of rabeprazole sodium from pulsatile release tablets containing hpmc-ec blend as time lagged press coating, IJPSR, Vol 9(7): 2825-2831.
11. Murali KG, Ravilla D, and Ramesh P, 2018. Formulation, development and in-vitro evaluation of rabeprazole sodium delayed release enteric coated tablets, WJPPS, Volume 6, Issue 8, 1121-1134.

How to cite this article

Ghugarkar Prasad Gorakshanath, Khulbe Preeti, 2021. Ulcer, Gastrointestinal tract, Polymer, Coating, Jour. of Med. P'ceutical & Allied. Sci. V 10 - I 6, 1632, P- 3878 - 3882. doi: 10.22270/jmpas. 2021.V10I6.1632