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CURRENT STUDY WAS EVALUATING THE FAMOTIDINE FLOATING TABLET- By FTIR & HPLC

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ABSTRACT

A controlled drug delivery system (CDDS) should primarily be designed to increase bioavailability of drugs and make them more predictable. Several physiological challenges, however, preclude the development process, including a lack of physical restraint and localization of CDDS within the appropriate GI tract regions, and highly variable gastric emptying patterns. As a result, drug release from the CDDS can be incomplete, reducing its efficacy. These systems help in continuously releasing the drug before it reaches the absorption window, thus ensuring optimal bioavailability. HPLC is an accurate and precise method in terms of analytical performance (with a relative error of less than 2%).

Key Words: FTIR, Gastric, Famotidine, Floating Tablet, HPLC

INTRODUCTION

The most widely utilized route of administration for delivering drugs through pharmaceutical products of different dosage forms is oral drug administration [1]. Due to its ease of administration, patient acceptance, and cost-effective manufacturing process, the oral route is considered the most natural, easiest, convenient, and safe route [2]. The majority of pharmaceutical products designed for oral administration are immediate release or conventional drug delivery systems, which release the drugs quickly for rapid absorption [3].

Gastroretentive Drug Delivery Systems:

A gastroretentive drug delivery system (GRDDS) is a dosage form that can be retained in the stomach. Continuously releasing drugs for a prolonged period of time before they reach their absorption site can improve controlled delivery of drugs that have an absorption window, ensuring optimal bioavailability [4].

APPROACHES TO GASTRIC RETENTION

The following approaches have been used to increase the retention of oral dosage forms in the stomach over the last three decades:

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- Bio/ Muco adhesive systems.
- Expanding systems.
- High-density systems.
- Floating systems.

Providing digestible polymers or fatty acid salts to the stomach that will charge its motility pattern to a fed state reduces gastric emptying rate and permits considerable prolongation of drug release are another delayed gastric emptying approach of interest [5].

Methodology

Preformulation Study

The purpose of preformulation studies is to examine the physicochemical properties of a drug sample which may affect its performance and formulation. In the process of developing dosages, it is the first step through preformulation studies; we establish a kinetic rate profile and investigate compatibility with other excipients to develop a stable, effective, and safe dosage form [6].

Physicochemical Properties and Identification Of Drug

IR Spectroscopy for Identification Of Drug

For the identification of given drug, the IR spectra of drug samples (Famotidine) was compared with the standard IR spectra of pure drug.

Physicochemical properties of drug

General appearance

Drug was tested for colour, odour and taste.

Solubility of drug

Solubility test was conducted to determine its solubility in the dissolution medium and other solvent.

Drug –excipient compatibility

IR spectroscopy method was used for carried out drug–excipient compatibility study. FT-IR spectra of pure drug and drug + HPMC were recorded. Characteristic peaks of pure drug were compared with peaks of drug + HPMC.

Calibration Curve for Famotidine

From the stock solution, a concentration of various dilutions gives 5, 10, 15, 20, 25, 30 µg/ml concentration of duloxetine respectively. The absorbance was measured using UV spectrophotometer.

Precompression parameters of powder blends

Bulk and Tapped density

10gm of powder was weighed. Weighed amount of given powder was introduced into 100ml measuring cylinder. After transferred of powder into a measuring cylinder the initial volume was observed for bulk density and then cylinder was tapped continuously until no further change in volume was observed. Record the final volume for tapped density. Then bulk and tapped density were calculated by using the given formula

Bulk density = weight of powder / initial volume

Tapped density = weight of powder / tapped volume

Carr's index

Carr's index is also known as compressibility index. It is significant number that can be obtained from bulk and tapped density. The compressibility of raw material and blend was determined by Carr's compressibility index by using given formula

Carr's index (%) = {(tapped density)- (bulk density)/ (tapped density} × 100

Hausner's ratio

The Hausner's ratio is a number that indicates flowability of a powder. Hausner's ratio is calculated by given equation

Hausner's ratio = Tapped density / Bulk density

Angle of repose

Maximum angle possible between the surface of a pile of powder and the horizontal plane are refer as angle of repose. Angle of repose used to measure frictional force leads to improper flow. Funnel stand method was used for determined the angle of repose. The average value is taken and angle of repose was calculated by using the given equation

$$\tan \theta = h/r$$

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

Where θ = Angle of repose h = height of the heap r = radius of the heap

Compression of Tablet

Floating tablets of famotidine were prepared by direct compression method using different ingredient. Famotidine and other ingredients were passed through sieve no# 80 individually. According to different formulation required amount of ingredient was weighed by using digital balance.

Drug, HPMC K4M, HPMC K15M, MCC, Dibasic calcium phosphate and sodium bicarbonate were blended geometrically in mortar and pestle and then powder blends were lubricated with talc and magnesium stearate. Final mixing was done by using poly bag. The punching machine dye was adjusted to get 300mg tablet with hardness 4-6 kg/cm2. Tablets were collected and evaluated. 6 formulations of (F1 to F6) floating tablets of famotidine were prepared using variable concentration of HPMC K4M & HPMC K15M as shown in table 1.

Post Compression Parameter (Evaluation)

The prepared floating tablets were evaluated for general appearance, thickness, hardness, friability, weight variation, *In vitro* buoyancy, *In vitro* dissolution studies, and short-term stability study.

General appearance

Organoleptic properties (General appearance) of tablet is the first most important quality for the acceptance of tablet. Its play a major role for the consumer acceptance. Prepared tablets were evaluated for organoleptic properties (colour, odour, taste and shape)

Thickness

6 tablets from each formulation were randomly selected and thickness was measured by using vernier calipers and then average value was calculated.

Hardness

Hardness of tablet refer to the ability of a tablet to withstand for mechanical shocks. Hardness testing is used to test the breaking point of tablet. Hardness was expressed in Kg/cm^2.

Friability

20 tablets were taken, initially weighed (W initial). Preweighed selected tablets were placed in the friabilator which revolves at 25 rpm (100 revolutions) for 4 min. Then tablets were removed from the chamber de-dusted and weighed again (W final). The % friability was then calculated by

F= {(W initial)- (W final)/ (W initial)} ×100

Weight variation

Average weight was calculated and percentage deviation from the average weight was determined by using given formula.

% deviation = {(Average weight – initial weight) /Average weight} X 100

In vitro buoyancy/ floating study

In vitro buoyancy studies were performed for all the formulations. The randomly selected tablets from each formulation were kept in a 100 ml beaker containing 0.1N HCL pH 1.2. The time taken for the tablet to rise to the surface and float was floating lag time and the duration of time the dosage form constantly remained on the surface of medium was determined as total floating time (TFT)

In vitro dissolution studies

In vitro dissolution studies of famotidine floating tablets were carried out by using USP type II apparatus (paddle type). Dissolution vessel was filled with 900ml 0.1 N HCL pH 1.2 and then temperature of the medium was adjusted to 37±0.50C.

Rotational speed of paddle was set at 50 rpm and then one tablet was introduced in each dissolution vessel. 10ml solution were withdrawn from the dissolution vessels at every hour for 8 hrs and the samples were replaced with 10ml fresh dissolution medium. Absorbance of this solution was measured at 218 nm using a UV spectrophotometer [7].

HPLC-UV Method

The pharmaceutical sample was prepared by grinding 10 tablets and homogenizing them, then dissolving the mass equivalent to one tablet in 5 mL methanol, 1 mL HCL 20%, and 100 mL distilled water. Filtration was performed on the solution. Experimental data were recorded at 267 nm with methanol (A) or acetic acid (B) at a flow rate of 0.4 mL/min at +25°C. In two mL of HCl aqueous solution 20%, two mL of methanol, and 0.2 mL of distilled water, 0.01 g famotidine was dissolved in 0.2 mL of HCl aqueous solution 20%.

Drug release kinetics

In order to understand the exact mechanism of drug release from the dosage form, result of *in vitro* dissolution study of formulation which show good parameters was analysed according to various kinetics equation (zero order, first order, Higuchi model and korsmeyer Peppas) [8].

Short term stability study

Ideal formulation for stability studies was selected on the basis of cumulative % drug release and floating time. Stability studies was performed according to ICH guideline at 400°C and 75% RH. The formulation was sealed in aluminium packing and introduced in humidity chamber maintained at 400°C/75% RH for three months. After 3 months formulation was analysed for various parameters [9].

RESULTS

Famotidine is a histamine H2 receptor antagonist. It is widely used in condition where inhibition of gastric acid secreation may be beneficial such as heart burn associated with acid reflux, duodenal and gastric ulcer, gastroesophagal reflux diseases and hyper-secretory syndrome such as Zollinger –Ellision's. Floating tablets of cimetidine were developed to increase the gastric residence time of the drug; hence they could be retained in stomach for prolong time and drug is releases lowly at the desired rate.

Preformulation studies were conducted for drug and concluded that famotidine is white to pale yellow crystalline powder, bitter in taste, odourless and soluble in water, 0.1N HCL but not in organic solvents. FTIR spectra obtained indicated that there is no interaction between drug and polymer and sample is also identify by the characteristic peak of famotidine.

Preparation of calibration curve

Concentration of various dilutions 5, 10, 15, 20, 25, 30 µg/ml concentration of famotidine has done. The regression values were also calculated to be $r^2 = 0.9937$, and the calibration values have been shown in table 3 as well as the image has been shown in figure 6.

Precompression parameters of powder blends

Bulk and Tapped density

The bulk density and tapped density for all the batches varied from 0.427 to 0.470 g/mL and 0.502 to 0.549 g/mL mentioned in the table 4.

Carr's index

Carr's index values were found to be in the range of 13.25 to 13.86, which is satisfactory for the powders as well as implies that the blends have good compressibility.

Hausner's ratio

Hausner's ratio values obtained were in the range of 1.149 to 1.169, which shows a passable flow property for the powder blend based on the USP. The result has shown below table 6.

Angle of Repose

Table provides the data obtained for the angle of repose for all the batches prepared. The values were found to be in the range of 21.23 to 21.67, which indicates good flow property for the powder blend according to the USP.

Raw materials and prepared powder blend of all formulations were evaluated for their flow properties such as the angle of repose, bulk density, tapped bulk density,

Hausner's ratio and Carr's index. The Carr's index, Hausner's ratio and angle of repose were ranged between 13.25 to 13.86, 1.149 to 1.169 and 21.23 to 21.67 respectively. It could be concluded from the result that the powder blend with different formulations components were having good flow properties, good compressibility, which allow these formulations to be directly compressed into tablets.

Post Compression Parameter (Evaluation)

The prepared floating tablets were evaluated for general appearance, thickness, hardness, friability, weight variation, *In vitro* buoyancy, *In vitro* dissolution studies, and short-term stability study.

General appearance

The prepared tablets of all formulations remained off white, smooth, flat faced circular with no visible cracks.

Hardness and Thickness

The results for tablet thickness for all batches were found to range from 3.2 to 3.5 mm, respectively. Hardness or breaking force of tablets for all batches was found to range from 4.5±1.90 to 4.5±1.90 N. Tablet formulations must show good mechanical strength with sufficient hardness in order to handle shipping and transportation.

Weight variation

The values were obtained in the range of 301.3±2.35to 303.3±2.35 mg for weight variation.

Friability

All the tablets passed friability test and was found to be 0.61±0.24 to 0.74±0.30%

In vitro buoyancy/ floating study

All the formulation showed good buoyancy parameters, floating lag time was found to be 12.35±0.3 to 14.57±0.12 sec and total floating time was between 11 to 13 hr. The formulations containing HPMC 4KM showed good buoyancy parameters when compared to formulations containing HPMC15KM. Among all the formulation F3 showed better result.

***In vitro* dissolution study**

From the *in vitro* dissolution result it can be concluded that floating tablets prepared with HPMC K4M showed better sustained drug release than floating tablets prepared with HPMC K15M. Formulation containing HPMC K4M showed drug release within the range 76.40% to 92.05% on other hand formulations containing HPMC K15M was found between 75.40% to 89.71%. HPMCK4M containing gastroretentive formulation F3 exhibited 92.03% cumulative drug release and good buoyancy and was chosen for drug release kinetic studies. F3 follow zero order kinetics and mechanism of release is non-fickian diffusion.

LOQ AND LOD ANALYSIS

The LOQ and LOD values were found to be 0.00145 mg mL-1 and 0.00041 mg mL-1

Table 1: Composition of different ingredients of famotidine floating tablet

Ingredients	F1 mg/tablet	F2 mg/tablet	F3 mg/tablet	F4 mg/tablet	F5 mg/tablet	F6 mg/tablet
Famotidine	30	30	30	30	30	30
HPMC K4M	90	75	60	-	-	-
HPMC K15M	-	-	-	90	75	60
MCC	47	63	77	47	63	77
Sodium Bicarbonate	78	78	78	78	78	78
DCP	35	35	35	35	35	35
Magnesium stearate	7	7	7	7	7	7
Talc	3	3	3	3	3	3

Table 2: Physicochemical properties of cimetidine

Colour	Crystalline white or pale yellow colour
Taste	Bitter in nature
Odour	Odourless
Solubility	Soluble in water, 0.1N HCl, but not soluble in organic solvent

Table 3: Calibration data of famotidine

S. No	Concentration (µg/ml)	Absorbance (nm)
1	5	0.1081
2	10	0.2931
3	15	0.4087

4	20	0.5798
5	25	0.6912
6	30	0.7891

Table 4: Bulk density and tapped density of famotidine powder

Formulation	Density (g/ml)	
	Bulk density	Tapped density
F1	0.440±0.002	0.520±0.001
F2	0.430±0.001	0.504±0.002
F3	0.441±0.001	0.510±0.002
F4	0.446±0.001	0.524±0.005
F5	0.470±0.001	0.549±0.001
F6	0.427±0.001	0.502±0.002

Table 5: Carr's index of powder

Formulation	Flow properties	
	Carr's index	As per USP
F1	13.30±1.15	Pass
F2	13.86±1.20	Pass
F3	13.25±1.32	Pass
F4	13.64±1.51	Pass
F5	13.67±0.851	Pass
F6	13.77±1.30	Pass

Table 6: Hausner's ratio of powder.

Formulation	Flow properties	
	Hausner's ratio	As per USP
F1	1.17±0.02	Pass
F2	1.168±0.02	Pass
F3	1.149±0.03	Pass
F4	1.169±0.01	Pass
F5	1.15±0.02	Pass
F6	1.16±0.01	Pass

Table 7: Angle of repose of powder

Formulation	Flow properties	
	Angle of repose	According to USP
F1	21.45±0.28	Good
F2	21.23±0.79	Good
F3	21.26±0.36	Good
F4	21.67±0.86	Good
F5	21.46±0.95	Good
F6	21.56±1.04	Good

Table 8: Hardness and Thickness of floating tablets

Formulation	Thickness (mm)	Hardness (N)
F1	3.4±0.05	4.3±3.57
F2	3.3±0.03	4.1±5.02
F3	3.5±0.04	4.5±1.90
F4	3.4±0.04	4.3±1.96
F5	3.2±0.03	4.2±1.77
F6	3.4±0.02	4.1±8.52

***Table 9: Weight variation of floating tablet**

Formulation	Weight variation[α] (mg)
F1	303.2±3.09
F2	301.4±1.20
F3	303.3±2.35
F4	301.4±1.19
F5	302.3±1.79
F6	301.9±1.09

Table 10: Friability test of famotidine tablet

Formulation	Friability test (%)
F1	0.66±0.17
F2	0.71±0.28
F3	0.60±0.21
F4	0.74±0.30
F5	0.61±0.24
F6	0.68±0.11

Table 11: In vitro buoyancy/ floating study of famotidine tablet

Formulations	Floating lag time(sec)*	Total floating time(h)
F1	13.22±0.5	11
F2	13.20±0.9	11
F3	12.35±0.3	11
F4	14.57±0.12	13
F5	13.44±0.6	11
F6	12.54±0.2	11

Table 12: Kinetic release data of F3

Formulation	Correlation Coefficient r^2 Values				
	Zero order	First order	Higuchi's	Peppas's	
				R^2	N
F3	0.9902	0.825	0.895	0.973	0.80

Table 13: Stability study of F3

Parameters	1st month 40°C ± 2°C/ 75% RH ± 5%	2nd month 40°C ± 2°C/ 75% RH ± 5%	3nd month 40°C ± 2°C/ 75% RH ± 5%
Physical appearance	Off white, flat faced	Off white, flat faced	Off white, flat faced
Hardness (kg/cm2)	4.5±1.90	4.5±1.78	4.5±1.85
Weight variation (mg)	303.3±2.35	303.28±0.15	303.33±0.16
Friability	0.60±0.21	0.60±0.19	0.60±0.18
Floating lag time (sec)	12.35±0.3	12.25±0.3	12.27±0.3
In vitro release (%)	92.02%	92.15%	92.41%

Figure 1: Drug absorption in the case of (a) Conventional DF (b) GRDDS

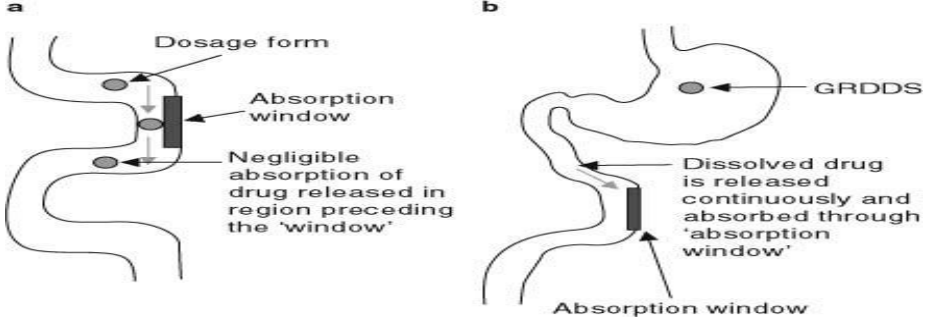


Figure 2: FTIR of Famotidine

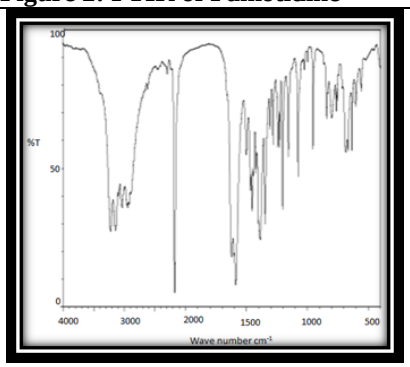


Figure 3: FTIR of Famotidine + HPMC

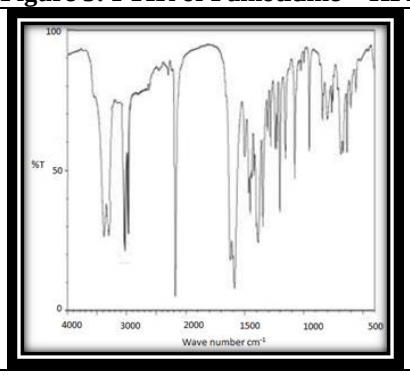


Figure 4: Calibration curve of Famotidine

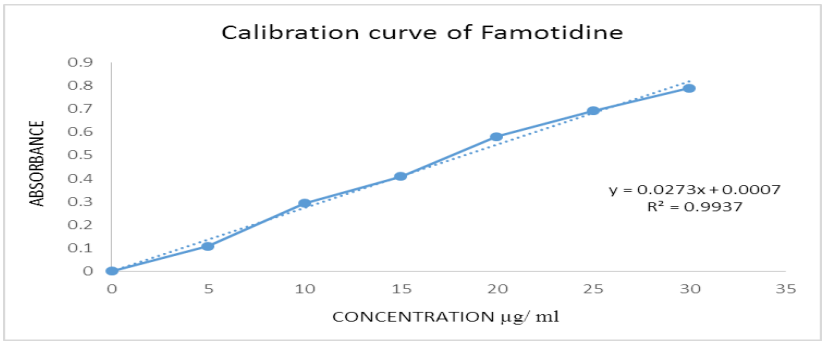


Figure 5 : HPLC CHROMATOGRAM OF FAMOTIDINE TABLETS

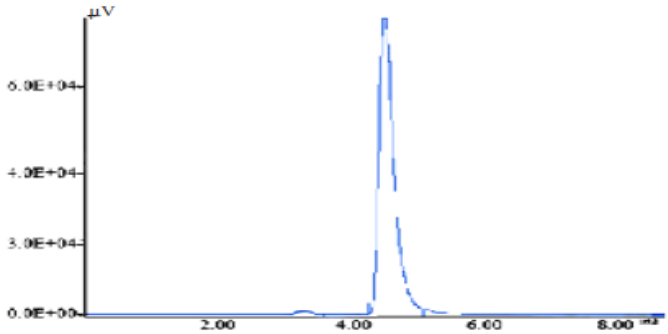


Figure 6: In vitro dissolution study

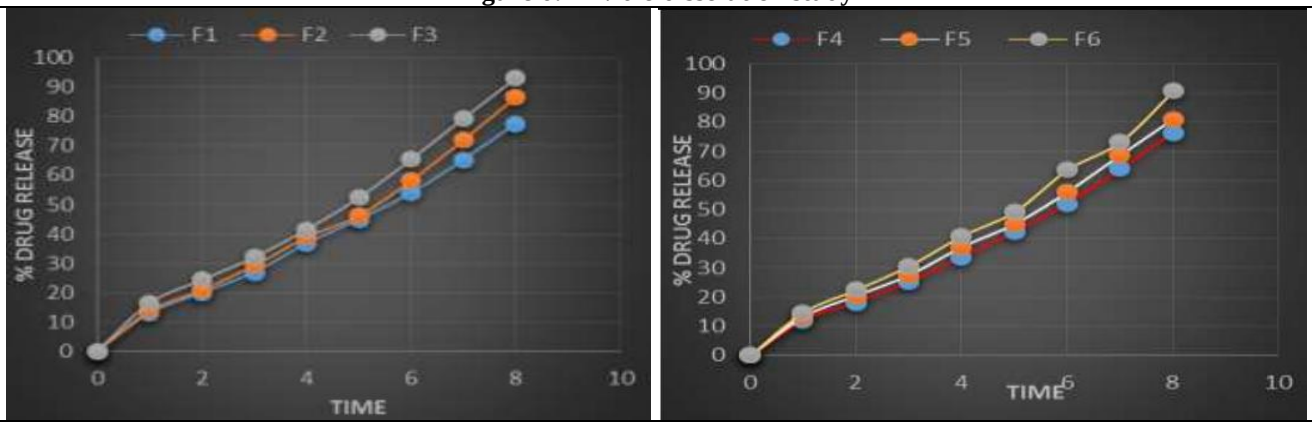


Figure 7: Zero order kinetic study of F3

Figure 8: Higuchi model study of F3

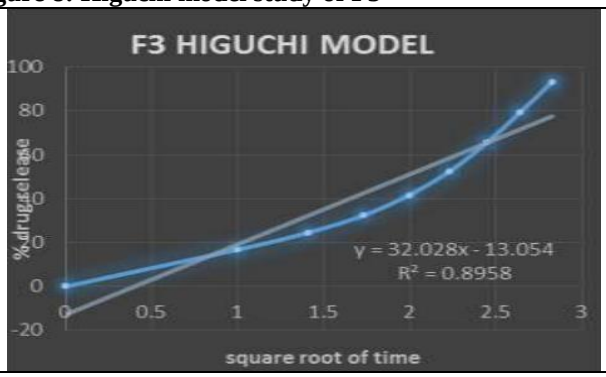
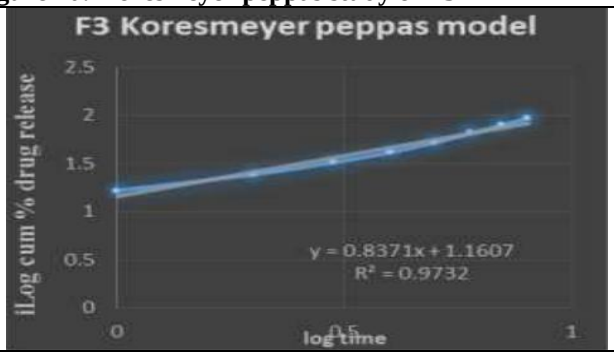


Figure 9: First order kinetic study of F3

Figure 10: Koresmeyer peppas study of F3



CONCLUSION

There has been extensive exploration of gastro-retentive drug delivery technologies in recent years. For drugs with a narrow absorption window, gastro retentive drug delivery systems are the best choice. Several drug delivery devices aimed at releasing drugs into the stomach are being developed nowadays. Despite the fact that these drug delivery systems have several advantages. As well as their advantages, they have disadvantages, such as a very low correlation between their *in vitro* and *in vivo* results. Designing appropriate formulation strategies considering the physiological events in the GIT, selecting the correct combinations of drugs and excipients, and considering the physiological events in the GIT.

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