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FORMULATION AND EVALUATION OF STOMACH - SPECIFIC NOVEL GASTRO-RETENTIVE FORMULATIONS OF 5-FLUOROURACIL FOR TARGETING GASTRIC CANCER

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ABSTRACT: Intravenous administration of 5-Fluorouracil (5FU) produces severe systemic, dose-related side effects due to its cytotoxic nature, additionally, 5FU is rapidly absorbed from the stomach after oral administration. Therefore a combined floating-bioadhesive tablet (FBT) of 5FU has been developed in order to reduce the dose and associated side effects in other sites of the body. The tablets were prepared by direct compression technique. Hydroxy propyl methyl cellulose (HPMC) K15M was used as a release retardant polymer while carbopol-971P, guar gum and sodium alginate were used as bioadhesive polymer. The pre-compression characteristics shown fair flow behaviour and core tablet properties were within the Pharmacopoeia limit. All formulation batches reported satisfactory floating lag time in a range of 125 - 500 sec and remained buoyant for more than 6 h. Kinetics of dissolution data demonstrated that formulation batch FB4, FB9 and FB10 follow Korsmeyer-Peppas model, FB11 follows first-order kinetics; and FB1, FB2, FB3, FB5, FB6, FB7, FB8, FB12 and FB13 follows Higuchi Matrix model. Analysis of the data revealed that formulation batch FB4 containing HPMC K15M and sodium alginate in the ratio of 4:1 produced the most favourable formulation to develop sustained-release gastroretentive drug delivery system (GRDDS) with optimum drug release pattern and satisfactory physicochemical characteristics. Hence, the formulation batch FB4 was selected as optimized formulation and was kept for further studies.

INTRODUCTION: In the era of therapeutic advancement, the oral route still has respect for drug administration pertaining to its suitability and wide acceptability [1].

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Several efforts have been crafted in order to develop an oral controlled drug delivery system (CDDS) that can produce a steady-state plasma drug concentration for a longer period of time by releasing the drug in a controlled and reproducible manner and thereby decreasing the dosing frequency [2]. Since, the majority of drugs are absorbed in upper gastrointestinal tract (GIT) and some are degraded in an alkaline environment; gastric retention for them is highly desirable. Moreover, the rapid gastrointestinal transit reduces the efficacy of some drugs by preventing their

complete absorption from the absorption zone (stomach/ upper GIT) [1]. Thus, development of a gastroretentive drug delivery system (GRDDS) with unique characteristics of gastric retention and controlled drug release may have numerous advantages for these categories of medications. Furthermore, literature advocates that GRDDS can be used as targeted therapy for certain diseases related to stomach or upper GIT (stomach ulcers/cancers); as GRDDS may provide selectivity and effective localization of pharmacologically active moiety at pre-identified target(s) at a therapeutic concentration [3]. Several approaches have been developed including floating drug delivery systems (FDDS), bio/mucoadhesive systems, swelling or expanding systems, modified-shape systems, high-density systems and other delayed gastric emptying devices, in order to improve the gastric residence of drugs or pharmaceutical agents [1].

The 5-fluorouracil (5FU) is a major antimetabolite used in the treatment of several solid cancers, such as stomach, colon, lung and breast cancer [4]. Generally, 5FU is administered intravenously; however, pertaining to its cytotoxic nature, 5FU produces severe systemic, dose-related side effects [3]. Moreover, 5FU is rapidly absorbed from the stomach after oral administration, and peak levels in the blood are reached between 15 and 60 min after ingestion [3].

In the present study, a combined floating-bioadhesive tablet (FBT) of 5FU by using various polymers has been developed in order to reduce the dose of the drug, and associated side effects in other sites as well. The objective of the study was to formulate and evaluate a stomach-specific targeted therapy containing 5FU as a model drug for the treatment of gastric cancer.

MATERIALS AND METHODS: The drug (5FU) was received from Intas Pharmaceutical Ltd., Gujarat as a gift sample. Sodium bicarbonate, citric acid and carbopol 971 P were obtained from Loba Chem. Pvt. Ltd., Guar gum was obtained from Noveon chemicals. Microcrystalline cellulose (MCC), hydroxy propyl methyl cellulose (HPMC) K15M and sodium alginate were brought from Signet chemical corporation, Mumbai. All other reagents are of analytical or pharmaceutical grade and deionized water was obtained by reverse osmosis. The HPMC K15M was used as a release retardant (primary) polymer. Carbopol 971 P, guar gum and sodium alginate were used as bioadhesive (secondary) polymer. Sodium bicarbonate and citric acid were used as the gas generating agent. The other excipients used were MCC for its diluent property and polyvinylpyrrolidone (PVP) K30 for its binding property.

Pre-compression Characteristics of Drug and Polymers: Micromeritic characterization of pharmaceutical ingredients plays a vital role in determining the quality of a dosage form. In order to improve the flow-property of the ingredients (drug and polymer), the bulk and true density, the angle of repose, carr's compressibility index and hausner's ratio were calculated [5].

Formulation of Floating-Bioadhesive Tablets of 5-fluorouracil: The FBT containing 5FU were prepared by direct compression technique [6]. The ingredients along with their quantities used for the preparation of the tablet have been illustrated in **Table 1**.

TABLE 1: FORMULATION CHART OF FLOATING- BIOADHESIVE TABLETS OF 5-FLUOROURACIL

Ingredients/ Formulation bathes	5FU	HPMC K 15M	Guar gum	SA	Carbopol 971P	SB	CA	PVP K30	MCC	Talc and MS
FB1	100	48	12	-	-	40	10	50	30	10
FB2	100	45	15	-	-	40	10	50	30	10
FB3	100	40	20	-	-	40	10	50	30	10
FB4	100	48	-	12	-	40	10	50	30	10
FB5	100	45	-	15	-	40	10	50	30	10
FB6	100	40	-	20	-	40	10	50	30	10
FB7	100	48	-	-	12	40	10	50	30	10
FB8	100	45	-	-	15	40	10	50	30	10
FB9	100	40	-	-	20	40	10	50	30	10
FB10	100	40	10	10	-	40	10	50	30	10
FB11	100	40	10	-	10	40	10	50	30	10
FB12	100	40	-	10	10	40	10	50	30	10
FB13	100	30	10	10	10	40	10	50	30	10

CA- Citric acid, HPMC-Hydroxy propyl methyl cellulose, 5FU- 5-Fluorouracil, MCC– Microcrystalline cellulose, MS- Magnesium stearate, PVP- Polyvinylpyrrolidone, SA- Sodium alginate, SB- Sodium bicarbonate

All ingredients (except talc and magnesium stearate) were sieved properly, accurately weighed and blended homogeneously in a mortar. Then the mixture was passed through sieve no. 30 to get uniform size particles. The requisite amount of talc and magnesium stearate was added to the mixture for their good anti-sticking property that supportsin the easy ejection of the tablet from the dies [7].

Subsequently, the homogeneously blended mixture was compressed on a rotary tablet press (RIMEK, 10 stations, KEL) with 10 mm concave punch with a compression force of 250 kg/cm^2. The tablet hardness was maintained in the range of 5 - 6 kg/cm^2.

Evaluation of the Prepared Tablets: All the tablets were evaluated for core tablet properties (hardness, friability, weight variation, thickness, and content uniformity), floating behaviour, swelling characteristics, mucoadhesion property, and dissolution studies. The entire evaluation test was done in compliance with Indian Pharmacopoeia (IP) and United State Pharmacopoeia (USP) [8 - 9].

Core Tablet Properties: Tablet hardness was evaluated by using Monsanto hardness tester for five tablets in each batch [10]. Similarly, friability was determined with the help of Roche friabilator after randomly selecting ten tablets from each batch [11]. In order to determine the weight variation, twenty tablets were randomly selected from each batch and then accurately weighed by using an electronic balance (Shimadzu, AUW-D, Japan) [12]. Similarly, thethickness was also determined for each tablet form all batches [13].

To evaluate the content uniformity, a powder of a tablet that is equivalent to 300 mg (one tablet) was dissolved in 500 ml of 0.1N HCl, and the samples were analysed spectrophotometrically (SHIMAZU, UV-1800) at 266 nm. All the data have been recorded as the mean ± standard deviation (SD) [14].

Floating Behaviour: The floating behaviour of the tablet from each batch was determined in 500 ml of 0.1N HCl that was maintained at 37 ± 0.5 °C. The floating lag time *i.e.* time required for the tablet to reach the surface; and the floating duration *i.e.* the time which the tablet remains afloat) were recorded [7].

Swelling Characteristics: The swelling behaviour was measured in terms of percentage weight gained by the tablet. The swelling characteristics of the tablets containing the drug were determined by placing the pre-weighted tablet in the dissolution test apparatus (Lab India, Disso 2000, 8 stations) in 500 ml of 0.1N HCl and maintained for 8 h at 37 ± 0.5 °C, without rotation [15]. At the end of the prespecified interval (1, 2, 4, 6 and 8 h), the tablets were removed from the dissolution medium, wiped with a tissue paper to remove free water then weighted. The swelling index (S_w) was calculated according to the equation (Eq. 1).

$$S_w = \frac{W_t - W_o}{W_o} \qquad (1)$$

Where W_0 is the initial weight of the dry tablet and W_t is the weight of the swollen tablet at time t.

***In-vitro* Bioadhesion Study:** The bioadhesion study determines the tensile strength of the tablet. The study was conducted by using modified physical balance method. One pan of the balance was replaced with a metal shaft which was 5 g heavier in weight than the pan [16]. A fresh piece of goat mucosa was obtained from a local slaughter house, washed with distilled water and 0.1N HCl, and thawed to room temperature immediately before use. At the time of testing a section of tissue was transferred, keeping the mucosal side out, to the upper glass vial using a rubber band and an aluminium cap. The diameter of each exposed mucosal membrane was 1.1 cm. The vials with the goat funds tissue were stored at 37 °C for 10 min. Next, one vial with a section of tissue was connected to the balance and the other vial was fixed on a height-adjustable pan.

A tablet was applied to the lower vial with the help of two pieces of adhesive tape. The height of the vial was adjusted so that the tablet could adhere to the mucosal tissues of the vial. A constant weight (10 g) was placed in the upper vial and applied for 2 min, after which it was removed, and the upper vial was then connected to the balance. Weights were added at a constant rate to the pan on the other side of the modified balance of the device until the two vials were separated [6].

The bioadhesive force, expressed as the detachment stress in N/M^2, was determined from the minimum weight required to detach the two vials using the following equation (Eq. 2).

Force of adhesion = Mucoadhesion in gram × 0.0981

***Ex-vivo* Mucoadhesive Time:** *Ex-vivo* residence time provides a clear picture regarding the efficiency of bioadhesive polymers that remains to stick to gastric mucosa for a prolonged period of time. In this study, a modified USP disintegration apparatus (ESICO, Model 901) was used to determine the *ex-vivo* residence time. The medium was constituted of 900 ml (pH 1.2) of 0.1N HCl maintained at 37 ± 0.5 ℃. A piece of goat gastric mucosa was tangled to the tip of a glass slab and allied vertically to the disintegration apparatus. The tablet was moistened and then linked with the mucosal membrane. Subsequently, the glass slide was moved up and down position such that the tablet was completely dipped in the buffer solution at the lowest point and was out at the highest point. The time taken for complete displacement of the tablet from the mucosal surface was noted [6, 17].

***In-vitro* Drug Release Study:** The drug release from the FBT matrices was determined in triplicate for all formulations by the USP dissolution apparatus II (Lab India, Disso 2000, 8 stations) [7]. The test was conducted using 900 ml 0.1N HCl maintained at 37 ± 0.5 ℃ with a shaft rotation of 50 rpm. Aliquot of 5 ml was withdrawn at predetermined time intervals (every 1-h interval up to 4 h, then 2 h interval up to 12 h; then after every 4 h up to 24 h) and an equivalent amount of fresh dissolution fluid equilibrated at the same temperature was replaced [3]. The samples were filtered through Whatman filter paper (no. 41), suitably diluted using 0.1N HCl and analysed at 266 nm using UV-Visible spectrophotometer (Shimazu, UV-1800).

Kinetics of Drug Release: To determine the drug release kinetics, the dissolution data of all formulation were fitted to different models like Zero order, First-order, Higuchi and Korsmeyer-Peppas [18].The model having the highest correlation coefficient (R^2) was considered to be the best fit for the designated kinetic release [19].

Zero-order (Eq. 3) data were plotted as cumulative percentage of drug released against time

$$C_t = C_o + k_o t \quad (3)$$

First-order (Eq. 4) data were plotted as the log cumulative percentage of the released drug against time

$$log\ C_t = log\ C_o - (k_1 t/2.303) \quad (4)$$

Higuchi's equation (Eq. 5) data were plotted as the cumulative percentage released drug against the square-root of time

$$Ct = K_H\, t^{1/2} \quad (5)$$

Moreover, for better characterization of the drug release mechanisms, the Korsmeyer-Peppas (Eq. 6) was applied

$$C_t / C_\infty = K_k\, t^n \quad (6)$$

Where C_0 is the concentration, C_t is the concentration at time t, C_∞ is the concentration at infinitive time, k_0 is the zero-order rate constant expressed as concentration/time, and t is time in hours, k_1 is the first order rate constant, K_H represents the constant of the system, K is a constant incorporating structural and geometric characteristic of the drug dosage form and n is the release exponent, indicative of the drug release mechanism [7, 16].

RESULTS AND DISCUSSION:

Pre-compression Parameters: The pre-compression parameters such as densities, the angle of repose, carr's compressibility index and hausner's ratio for drug and polymers indicated fair flow behaviour. The data has been depicted in **Table 2**.

TABLE 2: MICROMERITIC CHARACTERIZATION OF DRUG AND POLYMERS

Parameters	5FU	Carbopol -971P	HPMC K15M	Guar gum	Sodium alginate
Loose bulk density (g/cm^3)	0.4 1± 0.03	0.217± 0.021	0.304 ± 0.020	0.363 ±0.017	0.454 ± 0.021
Tapped density (g/cm^3)	0.49± 0.03	0.312± 0.019	0.478 ± 0.029	0.572 ±0.151	0.666 ± 0.021
Carr's compressibility index	16.3± 0.014	30.60± 0.024	36.40 ± 0.012	36.34 ±0.011	31.98 ± 0.023
Hausner's ratio	1.19± 0.01	1.43± 0.02	1.57 ± 0.04	1.57 ± 0.03	1.46 ± 0.07
Angle of repose	25± 1.3^0	29 ± 1.2^0	32 ± 1.3^0	31 ± 0.3^0	30 ± 1.5^0

All the values represent mean ± standard deviation (n=3); 5FU- 5-fluorouracil, HPMC-Hydroxy propyl methyl cellulose

Core Tablet Properties: Examination of tablets from all batches exhibited a flat circular shape with no cracks. The hardness was found to be in the

range of 4.7 ± 0.1 to 5.3 ± 0.4 kg/cm^2. A thickness in the range of 3.11 ± 0.02 to 3.42 ± 0.03 mm was reported. Tablet from all batches passed the weight variation test as per USP specification. The percentage friability was found to be <0.9%. The percentage drug content was up to 98% with some variability observed between formulation batches **Table 3**.

TABLE 3: STANDARD PHYSICAL TESTS FOR 5-FLUOROURACIL FLOATING- BIOADHESIVE TABLETS

Formulation bathes	Hardness (kg/cm^2)	Friability (%)	Content uniformity (%)	Weight variation	Thickness (mm)
FB1	4.7 ± 0.1	0.81 ± 0.02	92.2	passes	3.27 ± 0.03
FB2	5.3 ± 0.4	0.66 ± 0.02	91.3	passes	3.15 ± 0.02
FB3	5.0 ± 0.1	0.72 ± 0.03	95.4	passes	3.23± 0.05
FB4	4.8 ± 0.2	0.72 ± 0.05	94.2	passes	3.11 ± 0.02
FB5	4.9 ± 0.1	0.41 ± 0.01	83.3	passes	3.21 ± 0.04
FB6	5.1 ± 0.5	0.82 ± 0.07	87.4	passes	3.11 ± 0.05
FB7	5.2 ± 0.5	0.87 ± 0.02	98.1	passes	3.42 ± 0.03
FB8	5.1 ± 0.1	0.67 ± 0.08	89.2	passes	3.12 ± 0.03
FB9	5.0 ± 0.7	0.78 ± 0.01	87.5	passes	3.23 ± 0.06
FB10	5.1 ± 0.7	0.39 ± 0.03	88.2	passes	3.21 ± 0.02
FB11	5.3 ± 0.1	0.83 ± 0.06	85.9	passes	3.34 ± 0.05
FB12	5.2 ± 0.6	0.42 ± 0.02	91.6	passes	3.12 ± 0.03
FB13	5.1 ± 0.4	0.78 ± 0.03	94.2	passes	3.26 ± 0.02

All the values represent mean ± standard deviation (n=6)

Literature suggests that tablet hardness has a great role in the tablet friability, dissolution and floating time and duration [20 - 22]. Hardness limits the tablet friability and may prolong the tablet floating lag-time [21 - 22]. Evidence reported that this effect might be due to the abridged rate and extent of dissolution medium penetration into the tablet core [7].

Floating Behaviour: The tablet from all formulation batches reported satisfactory floating lag time in a range of 125-500 sec and remained buoyant for more than 6 h in the dissolution medium with rotation **Table 4**. Floating time for the all formulation was found to be increasing with the increasing amount of polymer.

TABLE 4: FLOATING BEHAVIOR OF FORMULATED BATCHES

Formulation batches/ Characteristics	Floating lag-time (sec)	Duration of floating (h)
FB1	153 ± 0.2	8 ± 0.2
FB2	274±0.3	8 ± 0.7
FB3	217 ±0.2	7 ± 0.3
FB4	125 ±0.3	10 ± 0.8
FB5	195±0.8	6 ± 0.1
FB6	450 ±0.7	7 ± 0.6
FB7	175 ±0.5	10 ± 0.2
FB8	321 ±0.5	11 ± 0.3
FB9	347 ± 0.2	6 ± 0.9
FB10	500 ±0.3	7 ± 0.4
FB11	378 ±0.6	9 ± 0.3
FB12	412 ±0.5	12 ± 0.2
FB13	365 ±0.8	7 ± 0.1

Values are mean ± standard deviation, if not indicated

The floating lag time varies on the amount of sodium bicarbonate and citric acid used in the CO_2 formation and the concentration of polymers. Furthermore, the ideal matrix or coating material should be highly porous to dissolution medium in order to initiate rapid generation of CO_2 and allow its release to start floating [7]. In addition, the higher water content might be the cause of reduction of floating lag-time as it could lead to greater penetration of the gastric fluid into the tablet leading to faster CO_2 generation [23].

Swelling Characteristics: The study found that the maximum liquid uptake and swelling of the polymer was achieved up to 8 h and then gradually decreased due to erosion. Formulation batch FB13 reported more swelling (108.13%) after 8 h and batch FB1 reported less swelling (75.76%) among the formulations **Fig. 1**.

Water uptake capacity has a major role in the floating, dissolution, bioadhesion and swelling [7]. Furthermore, the water uptake capacity depends upon the type and amount, and viscosity of polymer used in the formulation. In this study, formulations containing more concentrations of bioadhesive polymer reported additional swelling compared to other formulations. Further, formulation batches with a mixture of bioadhesive polymer revealed extraordinary swelling as compared to other batches.

Sodium alginate and carbopol containing formulations reported more swelling than guar gum containing formulations. This might be due to the quick conversion of sodium alginate to alginic acid in acidic pH that swells upon hydration [24] and matrix-forming properties carbopol that easily hydrated and thereby produced more swelling [25].

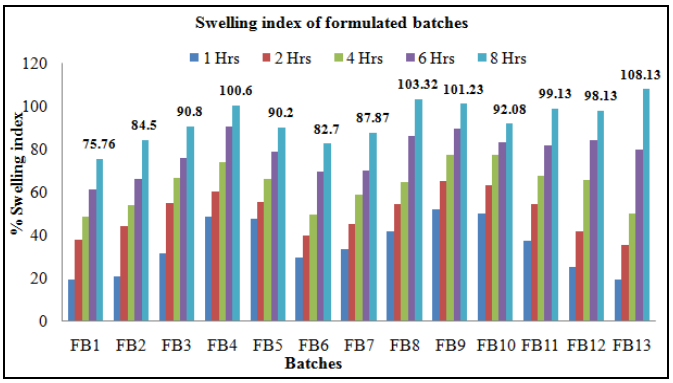


FIG. 1: SWELLING BEHAVIOUR OF FORMULATED BATCHES

Bioadhesion Characteristics: The force of bioadhesion was reported in a range of 0.07 ± 0.02 to 0.13 ± 0.08 N/m^2. Formulation batch FB9 (HPMC and carbopol 971 P) reported highest bioadhesion (0.13 ± 0.08 N/m^2) while batch FB2 (HPMC and guar gum) reported lowest bioadhesion strength (0.07 ± 0.02 N/m^2) among all the formulations. Similarly, mucoadhesion residence time was found to be more with batch FB9 and FB13 (up to12 h), which contains carbopol 971P and a mixture of other three bioadhesive polymers respectively **Table 5**.

TABLE 5: ADHESION CHARACTERISTICS OF FORMULATED TABLETS

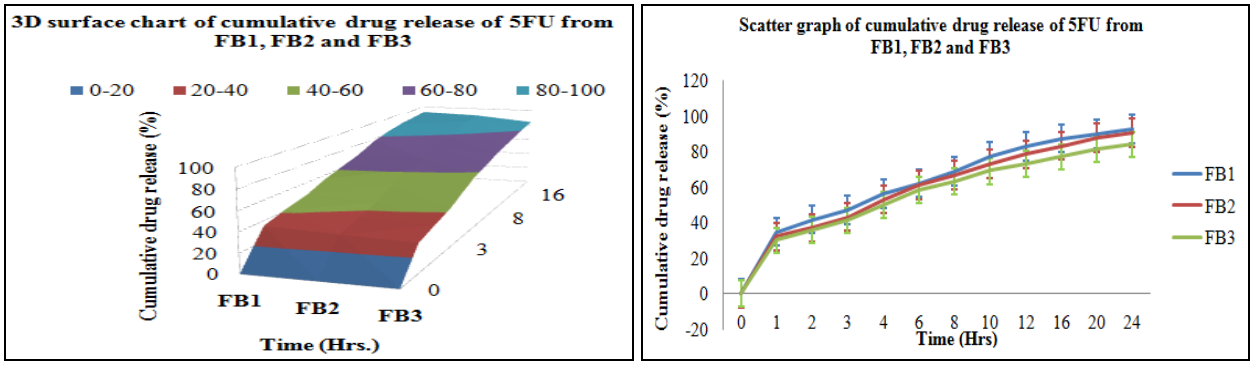
Formulation batches/ Characteristics	*In-vitro* bioadhesion strength (N/m^2)	*Ex-vivo* mucoadhesion time (h)
FB1	0.08 ± 0.03	6 ± 0.3
FB2	0.07 ± 0.02	7 ±0.5
FB3	0.09 ± 0.05	10 ±0.1
FB4	0.09 ±0.03	5 ± 0.2
FB5	0.11 ± 0.03	7 ± 0.2
FB6	0.11 ±0.09	8 ±0.6
FB7	0.08 ±0.02	9 ±0.4
FB8	0.1 ± 0.02	11±0.2
FB9	0.13 ±0.08	12 ± 0.5
FB10	0.07 ±0.05	10 ±0.4
FB11	0.11 ± 0.02	10 ± 0.8
FB12	0.12 ±0.02	11 ± 0.3
FB13	0.11 ± 0.07	12 ± 0.6

All values are mean ± standard deviation

From this study, it was found that with increasing the concentration of polymer the strength and time of adhesion increases. Gangurde HH *et al*., reported that the detachment force was increased with the increase in polymer concentration after evaluating the sustained release GRDDS tablets of ofloxacin. This could be due to the availability of more adhesive sites and polymer chains for inter-penetration with mucin, resulting consequently in the increase of bioadhesive strength [26]. Recently Kar K *et al*., also demonstrated the similar results and concluded that hydrophilic polymers are the good candidate for preparation of bioadhesive tablet [27].

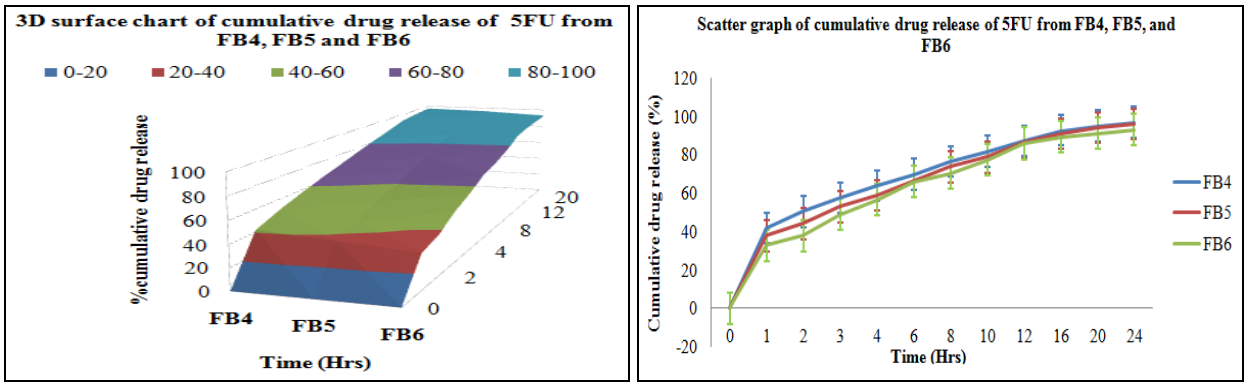
***In-vitro* Dissolution Study:** The *in-vitro* dissolution study was carried out using USP dissolution apparatus II (Lab India, Disso 2000, 8 stations). Formulation batches (FB1-FB3) containing HPMC K15M and guar gum **Fig. 2** reported only up to 80% drug release in 24 h period. Among all the batches, formulation batch FB4 containing HPMC K15M and sodium alginate in the ratio of 4:1 reported more and sustained drug release (97% at 24 h) compared to other formulation batches **Fig. 3**. Formulation batches (FB7-FB9) that contain the mixture of HPMC K15M and carbopol 971P reported up to 90% drug release in 24 h **Fig. 4**. Formulation batches (FB10-FB13) containing the mixture of polymers resulted in less drug release at the specified time compared to other batches **Fig. 5**. It has been also observed that the drug release was hampered by an increase in the polymer concentrations.

By varying the type and concentration of polymer (s) in the current study, varied drug release profiles were accomplished. The similar results have been reported in literature [3, 7, 27]. The hydrophilic nature of the polymer allows gradual hydration of the tablet matrix, leading to swelling of the tablets. Subsequently, the glass transition temperature of the polymers decreases and the glassy polymer is transformed into a rubbery state. It leads to enhancement of polymeric chains mobility. This phenomenon supports ease transportation of water into the tablet and consequently transports the dissolved drug from tablet core to the dissolution medium [3, 7, 27].



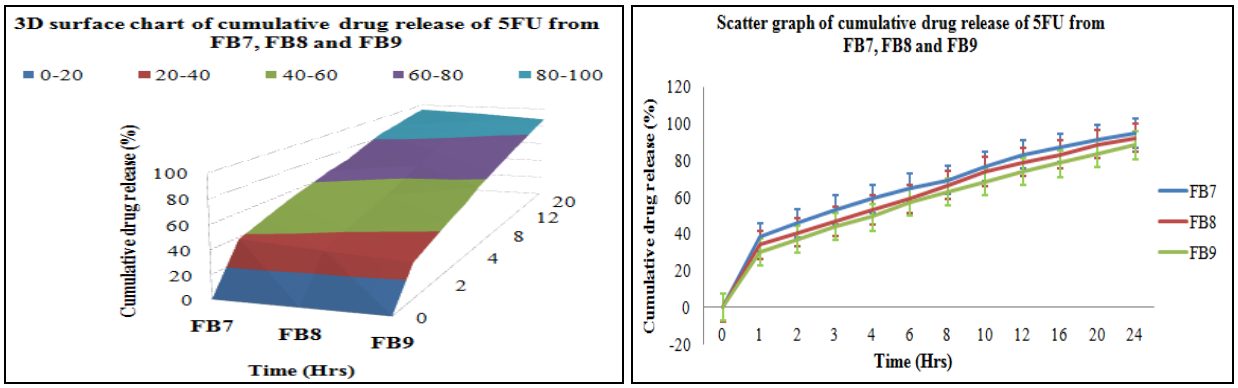
A **B**

FIG. 2: DISSOLUTION PROFILE OF FORMULATION BATCHES FB1 TO FB3



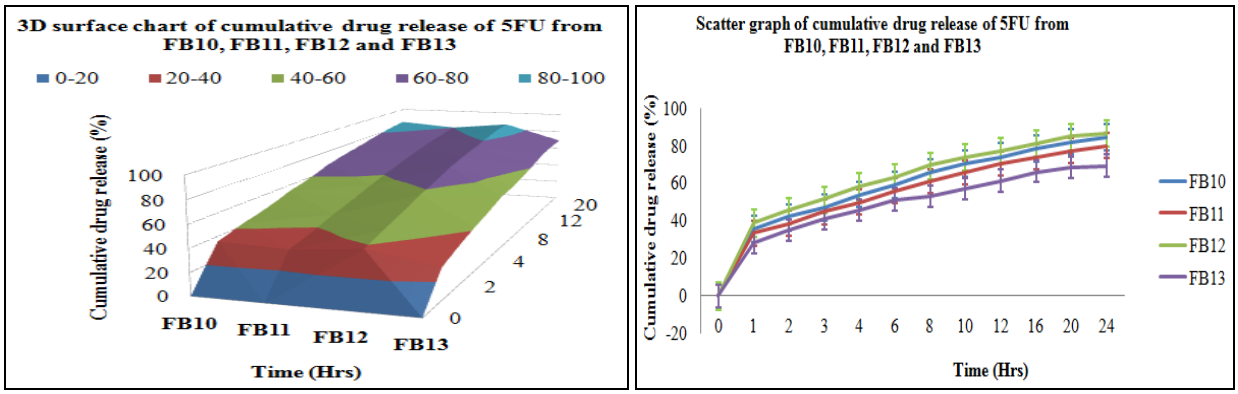
A **B**

FIG. 3: DISSOLUTION PROFILE OF FORMULATION BATCHES FB4 TO FB6



A **B**

FIG. 4: DISSOLUTION PROFILE OF FORMULATION BATCHES FB7 TO FB9



A **B**

FIG. 5: DISSOLUTION PROFILE OF FORMULATION BATCHES FB10 TO FB13

Kinetics of Drug Release: The result of drug release kinetics was presented in **Table 6**. Regression values (R^2) were found to be between 0.724 and 0.998 for different formulations. Formulation batches FB4, FB9 and FB10 follow Korsmeyer-Peppas model. This indicates that the release mechanism is not known or more than one type of release phenomenon could be involved. However, batch FB1, FB2, FB3, FB5, FB6, FB7, FB8, FB12 and FB13 follows Higuchi Matrix model, which indicates that the drug release is controlled by diffusion of drug through the pores. The mean diffusion exponent value (n) was found to be ranged from 0.3727 to 0.4864.

TABLE 6: KINETIC DATA OF FORMULATED BATCHES

Formulation batches	Zero-order (R^2)	First order (R^2)	Matrix model (R^2)	Korsmeyer-Peppas model (R^2)
FB1	0.8537	0.9655	0.9968	0.9778
FB2	0.8786	0.9725	0.9977	0.9879
FB3	0.8686	0.9628	0.9978	0.9910
FB4	0.7543	0.9554	0.9883	0.9945
FB5	0.8253	0.9699	0.9968	0.9945
FB6	0.8626	0.9669	0.9964	0.9911
FB7	0.8336	0.9413	0.9923	0.9907
FB8	0.8581	0.9723	0.9952	0.9867
FB9	0.8924	0.9766	0.9968	0.9987
FB10	0.7827	0.9148	0.9910	0.9931
FB11	0.8025	0.9947	0.9936	0.9903
FB12	0.7241	0.9036	0.9869	0.9935
FB13	0.7612	0.8834	0.9912	0.9962

CONCLUSION: From the study, it was concluded that HPMC K15M and sodium alginate might be a promising combination for the formulation of GRDDS. Among all formulation batches, FB4 reported good drug release pattern with appropriate swelling index and comparable bioadhesion strength. Hence, the formulation batch FB4 was selected as optimized formulation and was kept for further studies. Moreover, the FBT containing 5FU is feasible and may help in reducing the unwanted dose-dependent side effects at other sites by targeted drug delivery to gastric tumours. Furthermore, it could serve as an alternative option to painful intravenous therapy.

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CONFLICT OF INTEREST: Nil

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