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INFLUENCE OF ABELMOSCHUS ESCULENTUS, HIBISCUS ROSASINENSIS AND TAMARINDUS INDICA MUCILAGES ON NIZATIDINERELEASE FROM FLOATING TABLETS

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ABSTRACT

The aim of present research work is to formulate and evaluate controlled release floating tablet of Nizatidine using natural polymers such as *Abelmoschus esculentus, Hibiscus rosasinensis and Tamarindus indica kernel mucilage* and to study the influence of natural polymers on controlled release of the Nizatidine in view to enhance bioavailability and therapeutic action. The tablets were formulated by employing wet granulation method using PVP K 30 as binder and isopropyl alcohol as granulating fluid. The granules were evaluated for flow properties. All the formulations showed values within the prescribed limits for tests like hardness, friability and weight variation which indicate that the prepared tablets are of standard quality. All the tablets were formulated using sodium bicarbonate as effervescent agent. All the prepared formulations floated immediately after placing into the beaker and the floating was maintained more than 14 h. It was observed that the carbon dioxide generated from sodium bicarbonate in presence of dissolution medium (0.1N HCl) was trapped in the polymer gel matrix formed by the hydration of polymer which decreases the density (<1) and makes the tablet buoyant. The correlation coefficient values (r) revealed that the dissolution profiles followed Zero order kinetics and the mechanism of drug release was governed by Peppas model. The n values are found to be more than 0.5 (n>0.5) indicted that the drug release was predominantly controlled by nonfiction diffusion. The order of drug release with respect to selected polymers was found as *Abelmoschus esculentus* >*Hibiscus rosasinensis* >*Tamarindus indica.* The optimized formulation (FTF5) offered best controlled release along with floating lag time of 1min and total floating time of >12 h. Good stability was observed for 3 months during accelerated stability studies.

INTRODUCTION

Nizatidine (NIZ) is histamine H_2- receptor antagonists widely prescribed in active duodenal ulcers, gastric ulcers, Zollinger-Ellison syndrome, *Helicobacter pylori*eradication, gastro esophageal reflux disease and erosive esophagitis. The recommended adult oral doses of NIZ are 150 mg twice daily [1].

A traditional oral sustained release formulation releases most of the drug at the colon. Thus it is suitable only for the drugs having absorption window either in the colon or throughout the gastrointestinal tract. NIZ has a short biological half-life of approximately 2–3 h, an absolute bioavailability of only 50%, and it is absorbed only in the initial part of the small intestine[2-3]. These attributes like stomach as site of action, short half life and low oral bioavailability make it a suitable candidate for floating drug delivery system. All these factors highlight the need to develop sustained release dosage forms of NIZ.It is also reported that oral treatment of gastric disorders with an H_2- receptor antagonist like NIZ, used in combination with antacids, promotes local delivery of these drugs to the receptor of the parietal cell wall. Local delivery of these drugs also increases the stomach wall receptor site bioavailability and increases the efficacy of drugs to reduce acid secretion. This principle may be applied for improving systemic as well as local delivery of NIZ, which would efficiently reduce gastric acid secretion.It is also reported that oral treatment of gastric disorders with an H_2- receptor antagonist like NIZ, used in combination with antacids, promotes local delivery of these drugs to the receptor of the parietal cell wall. Local delivery of these drugs also increases the stomach wall receptor site bioavailability and increases the efficacy of drugs to reduce acid secretion[4]. This principle may be applied for improving systemic as well as local delivery of NIZ, which would efficiently reduce gastric acid secretion. The gastroretentive drug delivery system can be retained in the stomach and assist in improving the oral sustained delivery of drugs. There is a need to investigate a number of indigenously available retardant materials to make the concept of controlled release drug delivery more viable for the drug industry at more economical way. In the present study, natural polymers such as *Abelmoschus esculentus* gum and *Hibiscus rosasinensis*, *Tamarindus indica* kernel mucilage were selected for the preparation of floating tablets of NIZ. Sodium bicarbonate was used as gas generating agent. Tablets were prepared by wet granulation method using these polymers.

MATERIALS AND METHODS

NIZ was obtained as a gift sample from Hetero labs, Hyderabad. *Abelmoschus esculentus* gum, *Hibiscus rosasinensis*gum and *Tamarindus indica* kernel mucilage were extracted as per the procedure. PVP K 30, Isopropyl alcohol and Sodium bicarbonate were purchased from Qualigens fine chemicals, Mumbai. All other ingredients were of analytical grade.

PREPARATION OF NIZFLOATING TABLETS

NIZ was mixed with required quantities of *Abelmoschus esculentus* gum, *Hibiscus rosasinensis*, *Tamarindus indica* kernel mucilage, Sodium bicarbonate and Citric acid by geometric mixing. The tablets were formulated by employing wet granulation method using PVP K 30 as binder and isopropyl alcohol as granulating fluid. Magnesium stearate and talc were used as lubricant and glidant respectively. The final blend was compressed into tablets using 12 mm punches and corresponding dies on rotary tablet compression machine [6].The composition of each formulation was given in Table 1.

Evaluation of pre-compression parameters:

Flow properties of granules: The granules were evaluated for the following parameters [7].

a) **Bulk density:** A 5 gm of blend was weighed and transferred to a measuring cylinder.

Ingredients	**NA F1**	**NA F2**	**NA F3**	**NA F5**	**NA F5**	**NH F1**	**NH F2**	**NH F3**	**NH F4**	**NH F5**	**NT F1**	**NT F2**	**NT F3**	**NT F4**	**NT F5**
Nizatidine	150	150	150	150	150	150	150	150	150	150	150	150	150	150	150
Tamarind kernel powder	37.5	75	150	225	235	-	-	-	-	-	-	-	-	-	-
Hibiscus Rosasinensis leaves mucilage	-	-	-	-	-	37.5	75	150	225	235	-	-	-	-	-
Abelmoschus esculentus gum	-	-	-	-	-	-	-	-	-	-	37.5	75	150	225	235
Micro crystalline cellulose	202.5	165	90	10	5	202.5	165	90	10	5	202.5	165	90	10	5
PVP	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Isopropyl alcohol	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s	q.s
Sodium bicarbonate	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50
Citric acid	25	25	25	25	25	25	25	25	25	25	25	25	25	25	25
Magnesium stearate	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Talc	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Total weight	500	500	500	500	500	500	500	500	500	500	500	500	500	500	500

Table 1: **Composition (mg) of NIZ floating tablets formulated with different natural polymers**

Then bulk volume was noted. Bulk density was calculated by using the following formula

$$\text{Bulk density} = \frac{Mass\ of\ the\ powder}{Bulk\ volume}$$

b) **Tapped density:** A 5 gm of blend was weighed, transferred to a measuring cylinder and subjected to 100 tapings. Then volume was noted as tapped volume. Tapped density was measured by using the following formula

$$\text{Tapped density} = \frac{Mass\ of\ the\ powder}{Tapped\ volume}$$

c) **Carr's index:** Carr's index was calculated by using the following formula

$$\text{Carr's index} = \frac{Tapped\ density - Bulk\ density}{Tapped\ density} \text{ X } 100$$

d) **Hausner's ratio**

Hausner's ratio was calculated by using the following formula

$$\text{Hausner's ratio} = \frac{Tapped\ density}{Bulk\ density}$$

e) **Angle of repose:** 5 gm of blend was taken and poured into a hollow cylinder which was placed on a graph sheet. Then the cylinder was slowly lifted. Then height and diameter of the heap formed were noted down. The angle of repose (θ) was calculated by the formula

$$\text{Angle of repose, } \theta = \text{Tan}^{-1}\frac{h}{r}$$

Evaluation of NIZfloating tablets

a) **Hardness**: The hardness of the tablet was measured by Monsanto hardness tester. The lower plunger was placed in contact with the tablet and a zero reading was taken. The plunger was then forced against a spring by tuning a threaded bolt until the tablet fractured. As the spring was compressed a pointer rides along a gauge in the barrel to indicate the force [8]. The hardness was measured in terms of kg/cm^2.

b) **Weight variation**: Formulated tablets were tested for weight uniformity, 20 tablets were weighed collectively and individually. From the collective weight, average weight was calculated [8].

c) **Friability**: The Roche friability test apparatus was used to determine the friability of the tablets. Thirteen pre-weighed tablets were placed in the

apparatus and operated for 100 revolutions and then the tablets were reweighed. The percentage friability was calculated according to the following formula [8].

$$\text{Friability} = \frac{\text{Initial Weight - Final Weight}}{\text{Initial Weight}} \times 100$$

d) **Swelling Index**: Formulated tablets were weighed individually (W_0) and placed separately in Petri dish containing 50 mL of 0.1N HCl. The Petri dishes were placed in an incubator maintained at 37±0.5°C. The tablets were removed from the Petri dish, at predefined intervals of time and reweighed (Wt), and the % swelling index was calculated using the following formula [9]: % W_U = (Wt-Wo/Wo) × 100, where, W_U iswater uptake, Wtis weight of tablet at time t and Wo is weight of tablet before immersion.

e) **In vitro buoyancy study**: This test is characterized by floating lag time and total floating time. The test was performed using USP-Type II paddle apparatus using 900 mL of 0.1N HCl at paddle rotation of 100 rpm at 37 ± 0.5° C. The time required for tablet to rise to surface of dissolution medium and duration of time the tablet constantly float on dissolution medium was noted as floating lag time and total floating time [10].

f) Drug content: 20 tablets were weighed and powdered the powder weight equivalent to 150mg ofNIZ was dissolved in 100 mL of 0.1N HCl and filtered. 5 mL of this was diluted to 50mL with water and drug content was estimated at 315 nm by UV spectrophotometer [11].

g) **In vitro dissolution test**: The release of NIZ from the tablet was studied using USP-Type II paddle apparatus. Drug release profile was carried out in 900 mL of 0.1N HCl maintained at 37 ± 0.5°C temperatures at 100 rpm. 5 mL of samples were withdrawn at regular time intervals. The samples was replaced by its equivalent volume of dissolution medium and was filtered through 0.45 µm Whatman filter paper and analyzed at 315 nm by UV spectrophotometer [12].

Statistical analysis Statistical analyses were performed on dissolution profiles for each group of formulations by one-way analysis of variance (One-way ANOVA) using VassarStats online software (http://vassarstats.net/). In this experiment, the one-way ANOVA was used to determine whether there are any statistically significant differences between the means of five independent (unrelated) groups consisting of dissolution data.Student t-test was conducted on drug content and floating lag time.

Similarity factor (f_2): The similarity factor (f_2) given by SUPAC guidelines for a modified release dosage form was used as a basis to compare dissolution profile. The dissolution profiles are considered to be similar when f 2 is between 50 and 100. The dissolution profiles of products were compared using an f 2 which is calculated from the following formula,

$$f_2 = 50 \times \log \{[1 + (1/n) \sum_{j=1}^{n} | R_j - T_j |^2]^{-0.5} \times 100\}$$

Where, n is the dissolution time and Rj and Tj are the reference and test dissolution values at time t. The similarity factor (f_2) was calculated for comparison of the dissolution profile before and after stability studies in the present study[13].

Kinetic modelling studies: To analyze the mechanism of release and release rate kinetics of the dosage form, the data obtained were fitted into Zero order, First order, Higuchi and Korsmeyer-Peppas equations. Based on the obtained R^2 values, the best-fit model was selected.

Drug Excipient Compatibility Studies: Fourier Transform Infrared (FTIR) Spectroscopy studies were used for the evaluation of physicochemical compatibility and interactions, which helps in the prediction of interaction of the drug with polymers used in the study. The FTIR

spectra (400 to 4000 cm^{-1} and resolution of 4 cm^{-1}) of the pure NIZ and polymers were measured by preparing dispersion in dry KBr using a fourier transform infrared spectrophotometer (Bruker Alpha, UK). The recorded spectrum was further subjected to analysis by Opus FT-IR software V 6.5 software, Bruker UK**.** The transmission minima (absorption maxima) in the spectra obtained with these polymers were compared. The presence of additional peaks corresponding to the functional groups was noted[14].

Stability studies of optimized floating matrix tablets: The optimized floating matrix tablets were separated in to two groups. Each group of formulations were placed separately in stability chamber which is maintained at 25±5ºC/60% RH and 40±5ºC/75% RH respectively for three months and every month the formulations from each group were subjected to dissolution studies and % drug release was calculated[15].Significance of difference for floating lag time, assay values and dissolution profiles of the optimized formulation before and after accelerated stability testing was calculated based on Student's t-test. The table value of 2.57 at 95% confidence limits is used for determining the level of significance. The possible significance of difference between the dissolution profiles of selected formulation before and after accelerated stability testing was assessed.

RESULTS AND DISCUSSION

Floating tablets of NIZ were prepared by varying the concentration of *Abelmoschus esculentus* gum (FAF1-FAF5), *Hibiscus rosasinensis*(FHF1-FHF5) and *Tamarindus indica* kernel mucilage (FTF1-FTF5). The formulated granules were evaluated for various flow properties. The bulk density for all the formulations ranged from 0.514±0.87 to 0.527±0.98 gm/cm^3. The angle of repose for all the formulations was found to be in the range of 25.03±1.10º to 26.94±1.96º. The Carr's index for all the formulations ranged from 14.65% to 15.87%. The value of bulk density indicates good packing characters. The value of angle of repose (25-30º) for all the formulations indicates good flow property. The value of Carr's index (10-16%) indicates free flowing material. The values of Hausner's ratio were found to be between 1.170 and 1.184. The powder blend with Hauser's ratio of 1.25 has good flow properties. So the values indicate that the granules had acceptable flow properties. The flow properties were shown in Table 2.

Table 2: Pre-compression flow properties of powder blends (n=6)

Formulation	Density of Bulk (gm/cm^3)	density of Tapped (gm/cm^3)	Carr's Index	Hausner's Ratio	Angle of repose (°) ±SD
NAF1	0.520±0.98	0.616±0.67	15.58	1.184	26.72±1.16
NAF2	0.523±0.99	0.617±1.98	15.23	1.180	25.90±1.01
NAF3	0.527±0.98	0.619±2.90	14.86	1.170	25.41±0.16
NAF4	0.516±1.98	0.611±1.98	15.54	1.184	27.32±2.16
NAF5	0.519±0.90	0.613±1.45	15.49	1.183	26.94±1.96
NHF1	0.521±0.70	0.615±0.43	15.28	1.180	26.31±0.13
NHF2	0.514±0.87	0.611±2.23	15.87	1.188	27.64±1.14
NHF3	0.519±0.85	0.614±1.78	15.49	1.183	26.93±0.16
NHF4	0.521±0.45	0.616±0.09	15.08	1.177	25.09±1.59
NHF5	0.518±0.53	0.614±2.56	14.75	1.173	25.03±1.10
NTF1	0.521±0.09	0.611±2.56	14.65	1.171	25.71±1.18
NTF2	0.524±0.12	0.608±0.90	15.54	1.184	25.08±1.76
NTF3	0.516±0.53	0.613±1.45	15.49	1.183	26.94±1.96
NTF4	0.519±0.09	0.615±0.43	15.30	1.180	26.31±0.13
NTF5	0.523±0.12	0.611±2.23	14.82	1.185	27.52±1.14

The post compression parameters of prepared tablets were summarized in Table 3. Floating matrix tablets were evaluated for hardness and friability. The hardness was found to be in between 4.5 – 4.8 $kg.cm^{-2}$. The tablets satisfied friability requirement, as the % friability values were less than 1%. The drug content estimations showed values in the range of 99.54 to 100.14%, which reflects good uniformity in drug content among different formulations. All the tablets passed weight variation test as the % weight variation dioxide generated from sodium bicarbonate in presence of dissolution medium (0.1N HCl) was trapped in the polymer gel matrix formed by the hydration of polymer which decreases the density (<1) and makes the tablet buoyant. The results of various physical properties was within the Pharmacopoeia limits of ±5% of the weight. All the formulations showed values within the prescribed limits for tests like hardness, friability and weight variation which indicate that the prepared tablets are of standard quality.

All the tablets were formulated using sodium bicarbonate as effervescent agent. All the prepared formulations floated immediately after placing into the beaker and the floating was maintained more than 12 h. It was observed that the carbon

and *in vitro* buoyancy studies were tabulated in Table 3.The swelling index studies showed a gradual increase with increase in concentration of natural polymer and were summarized shown in Table 4.

Table 3: **Post-compression physicochemical evaluation of NIZ floating tablets** (**n=3**)

Formulation	Hardness (kg/cm^2)	Weight variation (mg)	Friability (%)	Uniformity of drug content (%)	Floating Lag time (min)	Total floating time (h)
NAF1	4.8±0.15	501.32±0.24	0.40±0.01	100.14±0.13	1.15	>12
NAF2	4.5±0.01	500.65±0.28	0.34±0.01	99.78±0.15	1.19	>12
NAF3	4.2±0.12	499.83±0.39	0.25±0.02	99.56±0.11	1.23	>12
NAF4	4.3±0.19	500.61±0.02	0.58±0.01	99.07±0.86	2.12	>12
NAF5	4.3±0.08	501.51±0.66	0.72±0.02	97.45±0.76	2.2	>12
NHF1	4.5±0.06	500.23±0.13	0.45±0.01	99.54±0.12	1.45	>12
NHF2	4.4±0.01	501.12±0.18	0.36±0.02	99.68±0.11	1.50	>12
NHF3	4.6±0.05	499.66±0.23	0.28±0.01	99.73±0.17	1.52	>12
NHF4	4.3±0.02	498.18±0.16	0.56±0.02	99.72±1.21	2.17	>12
NHF5	4.6±0.09	499.05±0.85	0.54±0.01	99.25±0.85	2.36	>12
NTF1	4.8±0.07	500.21±0.15	0.64±0.06	99.78±0.13	1.50	>12
NTF2	4.4±0.05	500.18±0.12	0.49±0.012	99.83±0.10	1.72	>12
NTF3	4.5±0.01	499.86±0.13	0.38±0.01	99.92±0.13	1.89	>12
NTF4	4.6±0.04	500.78±0.14	0.58±0.02	99.50±0.94	2.21	>12
NTF5	4.2±0.15	499.16±0.18	0.65±0.018	98.97±0.80	2.34	>12

Table 4: Swelling index values of NIZfloating tablets formulated with different concentrations of natural polymers

Formulation	Swelling index (%)		
	After 1 h	After 2h	After 8h
NAF1	22.75±0.01	30.47±0.23	80.28±0.85
NAF2	22.84±0.05	45.83±0.42	90.99±0.96
NAF3	28.87±0.08	58.82±0.52	98.19±0.74
NAF4	33.05±0.07	58.91±0.39	97.49±0.41
NAF5	37.71±0.04	62.84±0.86	98.61±0.52
NHF1	26.77±0.07	28.61±0.41	58.62±0.63
NHF2	33.19±0.06	45.61±0.15	73.17±0.14
NHF3	37.61±0.12	48.31±0.63	75.29±0.25
NHF4	34.52±0.16	60.82±0.45	99.12±0.36
NHF5	39.54±0.18	72.81±0.46	99.10±0.51
NTF1	19.18±0.14	29.11±0.59	70.51±0.62
NTF2	15.39±0.18	41.67±0.47	82.66±0.61
NTF3	19.26±0.04	43.88±0.25	83.61±0.43
NTF4	26.72±0.32	48.71±0.36	93.19±0.62
NTF5	35.66±0.48	56.74±0.69	97.14±0.42

The characteristics peaks in FT-IR studies confirmed the structure of NIZ (Table 5). The same peaks were also reported in all drug loaded matrix tablet. There were no change or shifting of the characteristic peaks in matrix tablets suggested that there was no significant drug polymer interaction which indicates the stable nature of the drug in all formulations.

Table 5: FTIR of NIZ with three natural polymer

S.No.	Formulation	Peak characteristics		
		N–H bond inprotonated tertiary amine group	Stretching vibrationof C=N in aci-nitro group of nitronic acid	Stretching vibration of nitro group attached to saturated carbon
1	Pure NIZ	2853.82	1688.18	1483.95
2	NIZ+*Tamarindus indica* mucilage	2853.72	1688.17	1483.59
3	NIZ +*Hibiscus rosasinensis* leaves mucilage	2827.88	1612.69	1484.29
4	NIZ +*Abelmoschus esculentus* gum	2846.41	1613.06	1483.33

In vitro dissolution studies of all the formulations of floating matrix tablets were carried out in 0.1N HCl. The study was performed for 12 h and the cumulative drug release was calculated. All the formulations remained floating and intact throughout the dissolution studies. The formulations (FAF1-FAF5) containing *Abelmoschus esculentus* gum showed decrease in drug release with increase in concentration of *Abelmoschus esculentus* gum (Fig. 1). The results of dissolution profiles of all formulations were statistically analysed by using one-way ANOVA and were found to be statistically different ($p< 0.05$).The *f*-ratio value was

3.85772, the*p*-value was0.010644 and the result was significant at $p < .05$. The drug release from formulation FAF5 containing drug and natural polymer in 1:1.5 ratio showed a maximum drug release at end of 12h. The dissolution profile for the formulations FHF1- FHF5 was shown in Fig. 2.The formulations (FHF1-FHF5) containing *Hibiscus rosasinensis*showed decrease in drug release with increase in concentration of *Hibiscus rosasinensis*. The results of dissolution profiles of all formulations were statistically analysed by using one-way ANOVA and were found to be statistically different ($p < 0.05$). The *f*-ratio value was 4.34062, the *p*-value was 0.00341 and the result was significant at $p < .05$. The formulations (FTF1-FTF5) showed an increase of drug release with an increase in concentration of *Tamarindus indica* kernel mucilage. The drug release from formulation FTF5 containing drug and natural polymer in 1:1.5 ratio showed a maximum drug release at end of 11.5 h.The results of dissolution profiles of all formulations were statistically analysed by using one-way ANOVA and were found to be statistically different ($p < 0.05$). The *f*-ratio value was 3.40695, the *p*-value was .013257 and the result was significant at $p < .05$.The dissolution profile for the formulations FTF1- FTF5 was shown in Fig. 3.The order of drug release with respect to selected polymers was found as *Abelmoschus esculentus* >*Hibiscus rosasinensis* >*Tamarindus indica.* To ascertain the mechanism of drug release, the dissolution data was analyzed by zero order, first order, and Higuchi and Peppas equations. The correlation coefficient values (r) revealed that the dissolution profiles followed Zero order kinetics and the mechanism of drug release was governed by Peppas model. The n values are found to be more than 0.5 (n>0.5) indicted that the drug release was predominantly controlled by non fickian diffusion. The in-vitro drug release kinetic data was shown in Table 6.

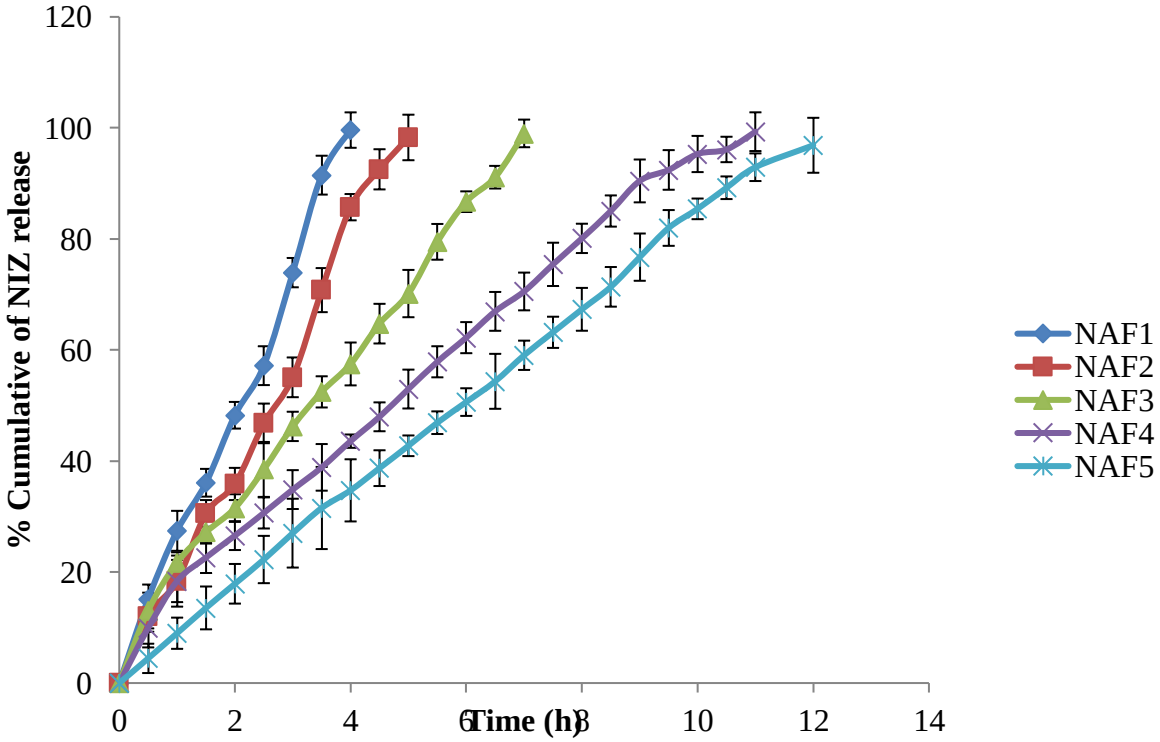

Fig. 1: **Comparative *in vitro* drug release profile of NIZfloating tablets formulated with different concentrations of *Abelmoschus esculentus* gum**

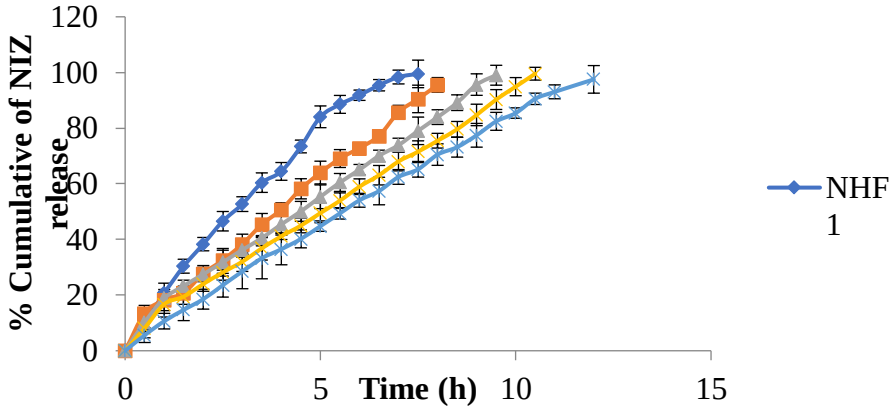

Fig. 2: Comparative *in vitro* drug release profile of NIZfloating tablets formulated with different concentrations of *Hibiscus rosasinensis*

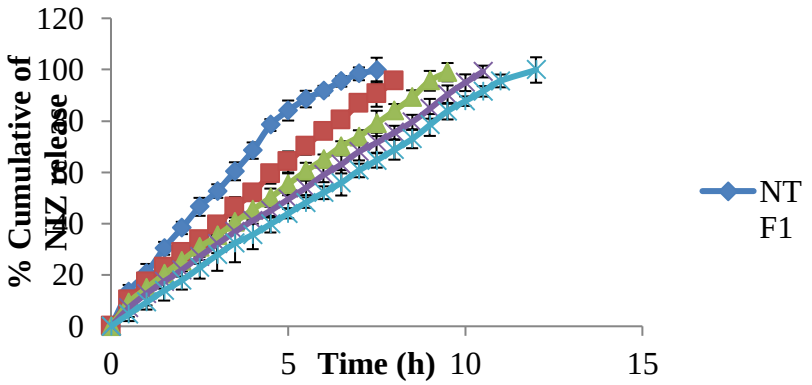

Fig. 3: Comparative *in vitro* drug release profiles of NIZfloating tablets formulated using *Tamarindus indica*

Table 6: *In vitro* drug release kinetic data of NIZ floating tablets formulated with different natural polymers

Formulation	T_{50} (h)	T_{90} (h)	Zero order		First order		Higuchi	Korsmeyer Peppas	
			R^2	K_0 ($mg.h^{-1}$)	R^2	K_1 (h^{-1})	R^2	R^2	N
NAF1	2.5	3.5	0.9932	24.720	0.6717	1.051	0.9031	0.9906	0.9096
NAF 2	3	4.5	0.9876	20.274	0.9461	0.682	0.9876	0.9861	0.9614
NAF 3	3.5	6.5	0.9794	13.396	0.8823	0.456	0.9734	0.9889	0.7722
NAF 4	5	9	0.9965	8.853	0.8141	0.280	0.9965	0.9948	0.7495
NAF 5	6	11	0.9921	8.303	0.9934	0.232	0.9933	0.9923	0.9728
NHF1	3	6	0.9744	13.587	0.8495	0.593	0.9677	0.9924	0.8415
NHF2	4	7.5	0.9766	11.492	0.9862	0.317	0.9766	0.9451	0.7643
NHF3	4.5	9	0.9950	9.822	0.9712	0.332	0.9950	0.9791	0.7597
NHF4	5.5	9.5	0.9993	8.968	0.9382	0.311	0.9993	0.9989	0.7923
NHF5	6	10.5	0.9980	8.519	0.8893	0.298	0.9980	0.9931	0.9675
NTF1	3	6	0.9713	13.522	0.8298	0.615	0.9688	0.9944	0.7832
NTF2	4	7.5	0.9823	11.721	0.9692	0.326	0.9823	0.9908	0.8271
NTF3	4.5	9	0.9991	10.054	0.9805	0.335	0.9991	0.9992	0.8242
NTF4	5.5	9.5	0.9994	9.135	0.9380	0.301	0.9994	0.9990	0.8629
NTF5	6	10.5	0.9992	8.523	0.9249	0.316	0.9992	0.9989	0.9675

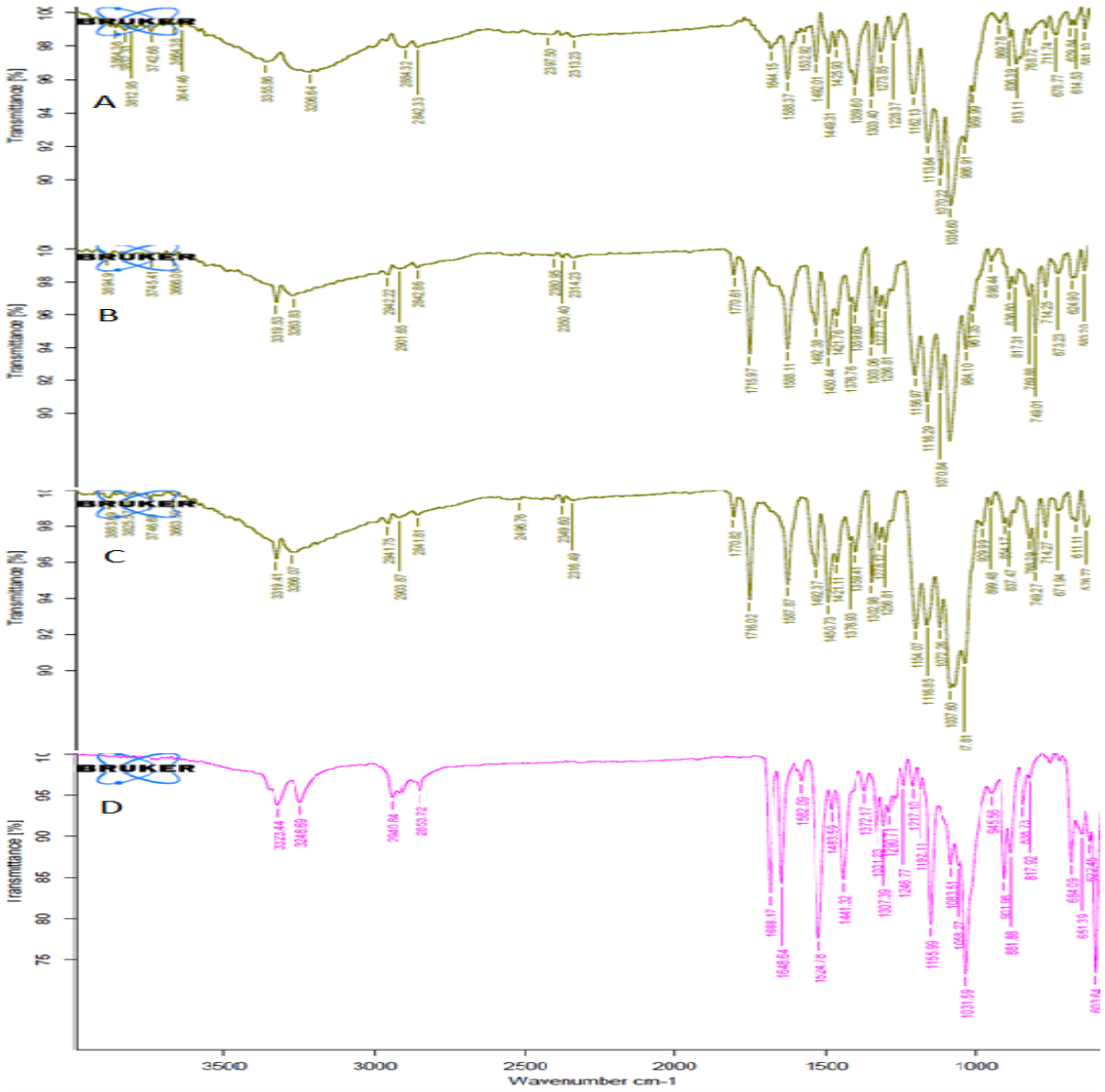

Fig. 4: FTIR spectrum of (A) pure NIZ, floating tablets of NIZ prepared using(B) *Abelmoschus esculentus* gum, (C) *Hibiscus rosasinensis and* (D)*Tamarind kernel Powder mucilage*

Based on floating lag time, floating time and *in vitro* drug release kinetics data, the formulation NTF5 was optimized. The tablets of batch NTF5 were packed in an aluminium pouch and subjected to accelerated stability studies at 40°C and 75% RH for 3 months in a humidity chamber. The drug content, floating lag-time and drug dissolution profile of the exposed samples were determined. The similarity factor (f_2) was calculated for comparison of the dissolution profile before and after stability studies.Student t-test was conducted on drug content and floating lag time and the values obtained were 1.74 and 1.09 respectively which were lesser than the table value of 2.57 at 95% confidence limits. There was no significant difference observed in the drug content uniformity and floating lag-time before and after the stability studies.

Similarity factor (f_2) for NTF5 optimized formulations compared before and after

stability testing was found to be88.64, which was between 50 and 100. This indicates existing of a close similarity between the dissolution profiles of the tested formulation before and after stability studies.Hence, these results confirm that the developed NTF5 formulation was stable under tested conditions.

From the above results, it is clearly evident that the *in vitro* release of NIZ from the floating tablet was influenced by nature of natural polymer. Based on the release rate constant and % of drug release the formulations prepared with *Tamarindus indica* kernel mucilage shown prolonged retarding nature compared with the formulations prepared with *Abelmoschus esculentus*, *Hibiscus rosasinensis*. Among all the formulations, FTF5 formulation containing drug and *Tamarindus indica* kernel mucilage in 1: 1.5 ratio was found to be optimized formulations.

CONCLUSIONS

This study discusses the preparation of floating tablets of NIZ using natural polymers of different *Abelmoschus esculentus, Hibiscus rosasinensis andTamarindus indica* in different ratios (1: 0.5; 1: 1; 1: 5 and 1: 2) respectively as drug-retarding polymers along with sodium bicarbonate and citric acid in 1: 0.76ratio as gas generating agents. The type of polymer affected the drug release rate and the mechanism. Polymer swelling was crucial in determining the drug release rate flotation. A lesser FLT could be achieved by increasing the concentration and increasing the viscosity grade of the polymer. The order of drug release with respect to selected polymers was found as *Abelmoschus esculentus >Hibiscus rosasinensis >Tamarindus indica.* The optimized formulation (FTF5) offered best controlled release along with floating lag time of 1min and total floating time of >12 h. Good stability was observed for 3 months during accelerated stability studies. Since the formulation showed sufficient release for prolonged period, the dose could be reduced and the possible incomplete absorption of the drug could be avoided.

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