Design AND Evaluation OF Floating Drug Delivery System OF AN Nelfinavir MESYLATE Antiviral Drug USING Different Natural Polymers

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Abstract: In the present study, an attempt was made to formulate floating tablets of Nelfinavir mesylate by various synthetic and natural polymers by direct compression method to increase the gastric retention time of the drug and thus increases the bioavailability of the drug. Optimized formulations NFS4 utilized HPMC K4M and NFB3 used Bhara gum this led to prolonged retention in the gastric area, minimizing fluctuations in plasma concentration that often occur with conventional dosage forms. Among the natural polymers, Bhara gum performed exceptionally well, with NFB3 exhibiting the shortest lag time of 1.33 min. These formulations were further evaluated for stability and in vivo studies. Floating drug delivery systems offer significant future potential, including reducing fluctuations in drug plasma levels due to delayed gastric emptying and decreasing the need for frequent drug administration.

1.0 Introduction:

GRDDS tablets were prepared to remain in the stomach for a prolonged and predictable duration. Prolonged gastric retention enhances bioavailability, minimizes drug waste, and improves solubility for drugs poorly soluble at higher pH. It also enables targeted delivery to the stomach and upper small intestine[1-5].

Nelfinavir mesylate is an antiretroviral drug primarily used in the treatment of HIV/AIDS. It belongs to the class of medications known as protease inhibitors (PIs). HIV is a retrovirus that targets the immune system, specifically CD4+ T cells, which are crucial for the body's defense against infections. The virus uses these cells to reproduce and spread throughout the body. Nelfinavir mesylate exerts its antiviral effect by specifically binding to the active site of the HIV protease enzyme. This binding is competitive and reversible, meaning nelfinavir mesylate competes with the natural substrates of the protease for access to the enzyme.

The aim of the present work was to develop and evaluate the floating using antiretroviral drugs. Hence, in light of the above the present work was aimed to evaluate the natural polymers like Bhara gum, Grewia gum and Mesquite Gum for their properties like viscosity, swelling index, microbial load etc. and applications of these gums in the design of GRDDS tablets and compare with proved synthetic polymers (HPMC K4M, K15M, K100M).

2.0 Materials & Methods:

2.1 Materials

Nelfinavir Mesylate were procured from Gift Sample from Ajanta Pharma Ltd, Mumbai. HPMC K4M, HPMC K15 M, HPMCK 100M, Microcrystalline Cellulose Croscarmellose sodium, Sodium bicarbonate, Methanol, Magnesium stearate, Talc Albizia gum, Gum Bhara and Mesquite gum were procured from Yarrow chem, Mumbai, India.

2.2 Methods

2.2.1 Physico-Chemical Properties[6-7]:

In the present study, the gums were procured from Yarrow Chem. Products, Mumbai, and subjected to a series of evaluations including solubility, phytochemical screening, powder characterization, moisture content determination, pH measurement, swelling index, volatile acidity and rheological analysis.

2.2.2 Organoleptic evaluation and solubility behavior[8]

Organoleptic properties, including color and odour, were assessed, and adulteration was evaluated through solubility studies in water, methanol, ethanol, acetone, and ether.

2.2.3 Determination of purity and identification tests for gums

Identification of the obtained gums was performed using RGI and RGII reagents, RGI was prepared by dissolving 3 g of iodine in 100 ml of alcohol, while RGII was formulated by dissolving 8 g of ruthenium red in 10 ml of lead acetate solution. One gram of gum was treated with 5 ml of each reagent. In accordance with FAO specifications (1991), the gums were also evaluated for swelling in ethanol and subjected to color reactions with concentrated HCl, 5N NaOH, aqueous methylene blue, and concentrated sulphuric acid.

2.3 Determination of powder properties[9-10]

- **Bulk density**

Bulk density refers to the ratio of the mass of an uncompressed powder to its bulk volume. A specific weight of dry powder (W) was accurately measured and gently poured into a 100 ml graduated cylinder without tapping.

$$\text{Bulk density } (\rho_b) = \frac{\text{Weight of powder (W)}}{\text{Bulk volume } (V_b)}$$

- **Tapped density**

An accurately weighed quantity of powder was transferred into a graduated measuring cylinder, and the initial volume was recorded. The cylinder was then tapped at a rate of approximately 100 taps per minute from a height of 3 mm. Volume readings were taken after every 100 taps.

$$\text{Tapped density } (\rho_t) = \frac{\text{Weight of powder (W)}}{\text{Tapped volume } (V_t)}$$

- **Bulkiness**

Reciprocal of bulk density gives the bulkiness. Bulkiness was calculated by the following Equation.

$$\text{Bulkiness} = \frac{1}{\text{Bulk density } (\rho_b)}$$

- **Compressibility index (I) and Hausner ratio**

Compressibility index or Carr's index and Hausner ratio are used as indicators for flowability and compressibility of the powder. They were calculated by the following Equations.

$$\text{Compressibility index}(I) = \frac{\rho_t - \rho_b}{\rho_t} \times 100$$

$$\text{Hausner ratio (H)} = \frac{\text{Tapped density}}{\text{Bulk density}}$$

◆ **Angle of Repose**

In the fixed funnel technique, the angle of repose (θ) was calculated by using Equation

$$\theta = \text{Tan}^{-1}\left(\frac{h}{r}\right)$$

- **Determination of Moisture content**

Moisture content was determined using a Karl-Fischer auto titrator. About 1 g of gum powder was placed in a pre-dried titration flask, dispersed in anhydrous methanol, and stirred to release moisture. Titration with pyridine-free Karl-Fischer reagent continued until the solution changed from dark brown to colorless. A blank titration (without sample) was also performed, and the moisture content was calculated using the given equation.

$$\%\text{Moisture content} = \frac{\text{Volume of the KF reagent} \times \text{Water equivalent}}{\text{Sample weight (mg)}} \times 100$$

- **Determination of pH value**

The pH of 1% w/v aqueous solution of gums was determined by using pH meter.

- **Determination of swelling index and water retention capacity**

The swelling index was determined by adding 1 g of gum powder to a measuring cylinder, recording the initial volume (X_o), and filling with water to 100 ml at room temperature. The sealed cylinder was gently shaken and left for 24 hours. The final volume (X_t) was then measured, and the swelling index calculated using the specified equation.

$$\text{Swelling index (SI)} = \frac{X_t - X_o}{X_o} \times 100$$

- **Stability studies (ICH, 2003)**

Stability studies were conducted as per ICH guidelines under long-term (30 ± 2°C/65 ± 5% RH) and accelerated (40 ± 2°C/75 ± 5% RH) conditions. Samples (15 g) were sealed in HDPE bottles and stored in a stability chamber. Assessments at 0, 1, 2, 3, and 6 months included physical appearance, pH, moisture content, and volatile acidity, with microbial analysis performed at 6 months.

2.4 Preformulation Studies[11-13]

2.4.1 Authentication of drugs

It was accomplished through melting point determination, UV spectroscopic analysis, Fourier-transform infrared (FTIR) spectroscopy, and differential scanning calorimetry (DSC).

2.4.2 Melting Point Method

The melting point of the drug was determined using the capillary tube method.

2.4.3 Determination of Solubility: The solubility of RTV and NFM were evaluated in distilled water and buffer solutions of pH 1.2, pH 6.8, and pH 7.4 at 37 °C. An excess amount of each drug was accurately weighed and transferred into separate glass vials, each containing 10 ml of the respective solvent. The vials were placed in a shaker incubator maintained at 37 ± 0.5 °C for 24 h. After shaking, they were kept in an incubator at the same temperature for a 12 h equilibrium period. The resulting solutions were filtered through a 0.45 µm Millipore membrane filter, and the filtrates were

analyzed at the respective λ_{max} of each drug using a UV–Visible spectrophotometer.

2.4.4 Determination of wavelength: A 100 ppm standard solution of NFM was prepared by precisely weighing 10 mg of each drug, dissolving it in 100 ml of methanol, and scanning the solution with a UV–Visible spectrophotometer across the wavelength range of 400–200 nm. The λ_{max} for each drug was determined and confirmed by comparison with literature-reported values.

2.4.5 Preparation of Calibration Curves for Nelfinavir: For NFR, a standard stock solution was prepared by dissolving 50 mg of the drug in 50 ml of methanol to yield a concentration of 1 mg/ml. One ml of this solution was diluted tenfold with 0.1 N HCl to obtain a 100 µg/ml stock solution. Aliquots were further diluted with 0.1 N HCl to prepare concentrations of 2, 4, 6, 8, and 10 µg/ml. The absorbance of NFR solutions at 255 nm using a UV–Visible spectrophotometer, with 0.1 N HCl as the blank in both cases.

2.5 Preparation of floating tablets using synthetic and natural polymers:

Tablets containing HPMC of different viscosity grades (K4M, K15M, and K100M) and natural polymers (Gum Bhara, Albizia gum, and Mesquite gum) were prepared by wet granulation at various drug-to-polymer ratios as per the composition tables 1, 2 for NFR Microcrystalline cellulose was used as diluent and sodium bicarbonate as gas-generating agent. The wet mass was formed, passed through a #20 sieve, dried at 60 °C for 1 h, sifted through #22 sieve, and lubricated with magnesium stearate and talc (#80 mesh). Granules were compressed using a Karnavati R&D tablet press with B-type tooling.

Table 1: Formulation of Nelfinavir floating tablets using synthetic polymers

Ingredients (mg)	**NFS1**	**NFS2**	**NFS3**	**NFS4**	**NFS5**	**NFS6**	**NFS7**	**NFS8**	**NFS9**	**NFS10**	**NFS11**	**NFS12**
Nelfinavir	825	825	825	825	825	825	825	825	825	825	825	825
HPMC K4M	37.5	75	112.5	125	-	-	-	-	-	-	-	-
HPMC K15M	-	-	-	-	37.5	75	112.5	125	-	-	-	-
HPMC K100M	-	-	-	-	-	-	-	-	37.5	75	112.5	125
Microcrystalline cellulose	112.5	75	37.5	25	112.5	75	37.5	35	112.5	75	37.5	35
Sodium Bicarbonate	40	40	40	40	40	40	40	40	40	40	40	40

PVP K30	10	10	10	10	10	10	10	10	10	10	10	10
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Magnesium stearate	5	5	5	5	5	5	5	5	5	5	5	5
Total weight	1032	1032	1032	1032	1032	1032	1032	1032	1032	1032	1032	1032

Table 2: Formulation of Nelfinavir floating tablets using natural polymers

Ingredients (mg)	**NFB1**	**NFB2**	**NFB3**	**NFB4**	**NFA1**	**NFA2**	**NFA3**	**NFA4**	**NFM1**	**NFM2**	**NFM3**	**NFM4**
Nelfinavir	825	825	825	825	825	825	825	825	825	825	825	825
Bhara gum	37.5	75	112.5	125	-	-	-	-	-	-	-	-
Albizia gum	-	-	-	-	37.5	75	112.5	125	-	-	-	-
Mesquite gum	-	-	-	-	-	-	-	-	37.5	75	112.5	125
Microcrystalline cellulose	112.5	75	37.5	25	112.5	75	37.5	35	112.5	75	37.5	35
Sodium Bicarbonate	40	40	40	40	40	40	40	40	40	40	40	40
PVP K30	10	10	10	10	10	10	10	10	10	10	10	10
Talc	2	2	2	2	2	2	2	2	2	2	2	2
Magnesium stearate	5	5	5	5	5	5	5	5	5	5	5	5
Total weight	1032	1032	1032	1032	1032	1032	1032	1032	1032	1032	1032	1032

2.6 Post-compression evaluation of Nelfinavir floating tablets:

Weight variation: The formulated tablets underwent weight uniformity testing, where twenty tablets were weighed both together and separately.

$$\% \text{ Weight Variation} = \frac{\text{Average Weight - Individual Weight}}{\text{Average Weight}} X100$$

Hardness: Tablet hardness was determined using a Monsanto hardness tester. Initially, the lower plunger was positioned against the tablet.

Friability: Friability of the tablets was assessed using a Roche friabilator.

$$\text{Friability} = \frac{\text{Initial Weight - Final Weight}}{\text{Initial Weight}} X100$$

Drug content uniformity: Ten tablets were weighed and powdered. The powder weight equivalent to 825 m g o f Nelfinavir was dissolved in 100 ml of 0.1N HCl separately and filtered using 0.45 µm membrane filter paper.

In vitro buoyancy studies: Floating lag time (FLT) is the interval required for a tablet to rise to the surface of the medium, while total floating time (TFT) is the duration it remains afloat. In vitro buoyancy was evaluated by placing tablets in 100 mL of 0.1 N HCl at 37 °C; FLT was recorded as the time to float, and TFT as the continuous floating duration.

Swelling studies: Each formulated tablet was individually weighed (W_o) and placed in a Petri dish containing 50 ml of 0.1 N HCl. The dishes were incubated at 37 ± 0.5°C. At predetermined time intervals, tablets were removed, reweighed (W_t), and the swelling index (%) was calculated as:

$$\% W_U = (W_t - W_o / W_o) \times 100$$

Where, W_U – Water uptake,
W_t – Weight of tablet at time t,
W_o – Weight of tablet before immersion.

2.7 In vitro dissolution studies: The release of drugs from the prepared floating tablets 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 temperature at 100 rpm. 5 ml of samples were withdrawn at regular time intervals up to 12 h. The samples were replaced by equivalent volume of dissolution medium and were filtered through 0.45 µm Whatman filter paper. The samples were suitably diluted and analyzed by UV spectrophotometer.

2.8 Kinetic modelling studies: To investigate the drug release mechanism and kinetics, the dissolution data were analyzed using Zero-order, First-order, Higuchi, and Korsmeyer–Peppas models. The model showing the highest coefficient of determination (R^2) was considered the best fit.

Drug release kinetic study: To determine the release mechanism, the dissolution data were evaluated using various kinetic models, including Zero-order and First-order equations. The Zero-order drug release equation is expressed as follows:

$Q_t = Q_0 + K_0 t$

where $\mathbf{Q_t}$ represents the amount of drug released at time t, $\mathbf{K_o}$ is the apparent dissolution rate constant (Zero-order release constant), and $\mathbf{Q_o}$ denotes the initial drug concentration in the solution, which may result from a burst release effect.

3.0 Results and discussion:

3.1 Organoleptic evaluation and solubility behavior of gums:

Organoleptic evaluation is a crucial step in developing oral dosage forms, as it directly impacts patient compliance. Sensory analysis was conducted to assess the colour and odour of the gum powders. These characteristics, along with solubility behavior were shown in table 3.

Table 3: Organoleptic evaluation and solubility behavior of gums

Parameter	Observation		
	Bhara gum	**Albizia gum**	**Mesquite Gum**
Colour	Yellow to dark brown	Pale yellow to light	Amber to brownish

		brown	yellow
Odour	Odorless	Odorless	Odorless
Solubility in water	Soluble, forming colorless mucilage	Swells significantly when added to water	Soluble, forming mucilage
Solubility in solvents (chloroform and methanol)	In soluble	In soluble	In soluble

3.2 Determination of purity and identification tests for gums

The assessment of identity and purity of food additives, following AOAC and FAO guidelines, plays a critical role in validating product safety. To characterize the natural gum, specific chemical tests were carried out by adding around 5 ml of reagent to 1 g of the gum powder and shown in table 4.

Table 4: Identification test for gums as per FAO, 1991

Test	**Observation**		
	Bhara gum	**Albizia gum**	**Mesquite gum**
Swelling by ethanol solution	Swelling is observed	80% of swelling	60% of Swelling
Color reaction with Conc. HCl	Brownish yellow color is observed	darker yellow to amber or light brown	light reddish-brown
Color reaction with 5N NaOH	Light yellow to yellowish-brown coloration	yellow or brown coloration is observed	Pale yellow to brownish-yellow is observed
Aqueous methylene blue stain	Deep blue or bluish-purple	Deep blue	Moderate blue
Conc. sulphuric acid	brown to black is observed	Reddish-brown to black	Moderate charring

Table 5: Physico-chemical properties of gums

Property	**Bhara gum**	**Albizia gum**	**Mesquite gum**
Bulk density (gm/cc)	0.612±0.01	0.535±0.33	0.608±0.41
Tapped density (gm/cc)	0.655±0.01	0.675±0.13	0.652±0.15
Bulkiness	1.43±0.04	1.55±0.13	1.57±0.36
Compressibility index (%)	9.82±1.34	8.76±0.68	10.01±0.6
Hausner's ratio	1.02±0.054	1.10±0.21	1.00±0.62
Angle of repose (º)	28.20±1.28	25.12±0.36	26.60±0.45
Moisture content	15.2±1.12	10.11±0.12	11.22±0.32
pH	4.8	4.0	4.2

Swelling index (%)	115±10.00	120±8	113±6
Water retention capacity (ml)	14±1.67	17±0.12	13±0.36

Melting point method

Table 6: Melting point of drugs

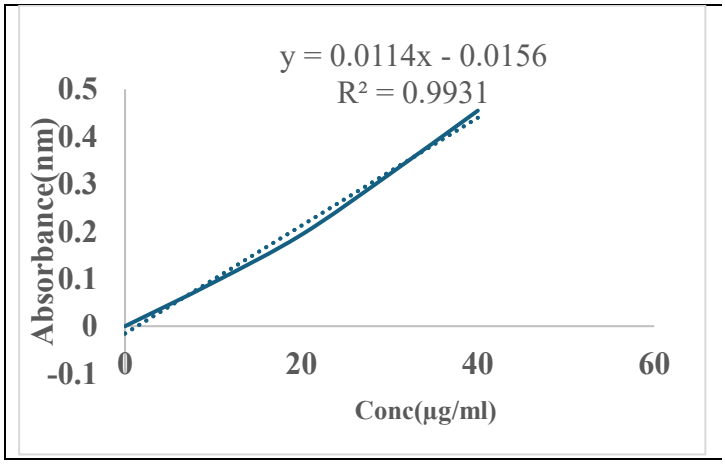
Drug	Melting point(^{0}c)
Nelfinavir	161

3.3 Construction of standard curve for Nelfinavir

Calibration curve using solvent 0.1N HCl:

Standard plot was constructed using 0.1N HCl as solvent. Concentrations ranging from 2 µg to 10 µg was prepared.

Table 7: **Standard curve using solvent 0.1N HCl**



Concentration (µg/ml)	Absorbance (nm)
0	0
2	0.092±0.002
4	0.193±0.001
6	0.321±0.015
8	0.455±0.022
10	0.523±0.019

3.4 Post-compression physicochemical evaluation of floating tablets

The formulated floating tablets were subjected for post compressional evaluation such as hardness, weight variation, friability, uniformity of drug content, in vitro buoyancy, swelling, in vitro dissolution and stability. The results are summarized in Tables 8, 9.

Formulation	Hardness (kg/cm^2)*	Weight variation (mg)	Friability (%)	Drug content (%)	Floating Lag time (min)	Total floating time(h)
NFB1	5.4±0.001	1032.18±3.2	0.51±0.02	99.17±0.14	2.33	12
NFB2	5.5±0.014	1031.23±2.5	0.42±0.01	99.15±0.07	2.20	18
NFB3	5.6±0.011	1030.34±3.3	0.37±0.02	98.14±0.55	1.33	22
NFB4	5.8 ±0.06	1032.12±5.4	0.56±0.34	98.67±0.65	1.47	26
NFA1	5.5±0.024	1032.14±6.1	0.43±0.33	98.15±0.47	2.22	6
NFA2	5.6±0.019	1032.35±5.4	0.26±0.19	98.87±0.65	1.60	10
NFA3	5.7±0.012	1031.13±3.5	0.62±0.12	97.31±0.11	1.45	12

NFA4	5.8±0.009	1030.16±4.7	0.44±0.07	98.11±0.41	1.40	16
NFM1	5.5±0.011	1029.11±5.2	0.41±0.12	98.15±0.63	1.90	12
NFM2	5.6±0.015	1026.01±2.7	0.52±0.19	98.11±0.37	1.80	14
NFM3	5.7±0.011	1029.15±3.3	0.54±0.04	98.93±0.14	1.50	16
NFM4	5.8±0.013	1025.93±5.2	0.49±0.05	99.11±0.06	1.40	18

Table 8: Post compression parameters of Nelfinavir floating tablets by using natural polymers
Table 9: Post compression parameters of Nelfinavir floating tablets by using synthetic polymers
*Data is expressed as mean ±SD (n=10)

The Nelfinavir tablets formulated with synthetic and natural polymers exhibited good mechanical strength and adequate hardness. The measured hardness ranged from 5.0 to 6.3 kg/cm², and it was observed that hardness increased as the polymer concentration increased.

The weight variation of the prepared NFR tablets, it ranged from 1025.93 ± 5.2 to 1032.14±6.1 mg. All tablet batches complied with the weight variation test requirements.

The friability loss of the prepared tablets, determined using a Roche friabilator, ranged from 0.21% to 0.62%. All batches met the requirement of less than 1%, indicating good mechanical stability.

The drug content uniformity of the prepared tablets, evaluated according to I.P. specifications, was found to be compliant. The formulations showed drug content ranging from 97.31 ± 0.11% to 101.33 ± 0.25%, confirming uniform drug distribution. All individual values were within the I.P. acceptance range of 90% to 110% of the average content.

3.5 In vitro buoyancy

Formulation	Hardness (kg/cm^2)*	Weight variation (mg)*	Friability (%)*	Drug content (%)*	Floating Lag time (min)*	Total floating time(h)*
NFS1	5.8±0.11	1030.1±5.9	0.33±0.05	99.14±0.5	1.02	8
NFS2	5.9±0.33	1025.2±6.9	0.61±0.04	99.78±1.2	1.5	14
NFS3	6.0±0.05	1029.5±5.5	0.42±0.05	99.3±1.5	1.0	18
NFS4	6.1±0.033	1028.3±5.7	0.39±0.02	99.12±0.25	1.0	22
NFS5	6.0±0.01	1029.1±7.2	0.28±0.12	99.17±0.33	1.12	18
NFS6	6.1±0.19	1025.6±5.5	0.35±0.11	99.41±0.54	1.10	24
NFS7	6.1±0.03	1028.3±5.6	0.37±0.04	99.15±0.27	1.06	26
NFS8	5.9 ±0.03	1029.7±7.2	0.30±0.19	101.33±0.25	1.14	28
NFS9	5.8±0.15	1027.1±6.4	0.42±0.02	98.96±0.44	1.29	20
NFS10	5.9±0.22	1028.1±6.9	0.38±0.01	99.22±0.15	1.44	26
NFS11	5.8±0.16	1026.6±4.4	0.33±0.03	99.17±0.27	1.8	28
NFS12	6.1±0.19	1025.3±6.5	0.34±0.019	100.16±0.54	1.9	30

Floating tablets were formulated with sodium bicarbonate as the gas generator to achieve minimal floating lag time and 24 h buoyancy. In 0.1 N HCl, CO_2 release caused effervescence, pore formation, and rapid polymer hydration, lowering density (<1 g/ml) for floatation. Low-viscosity HPMC K4M showed the fastest lag time (1–1.7 min), while higher-viscosity grades (K15M, K100M) increased lag

but extended floating duration. Polymer type, viscosity, and concentration influenced buoyancy and drug release, with NFS4 optimized for 24 h float and complete release.

Among natural polymers, Bhara gum performed best, giving shortest lag time with NFB3 (1.33 min). All natural polymer formulations (Bhara, Albizia, Mesquite gums) contained sodium bicarbonate, and higher polymer content prolonged float time.

Fig 1: A) Photograph taken immediately after placing the tablet into the beaker
B) Photograph taken during the intermediate stage of tablet floating
C) Photograph taken immediately after the tablet floated onto the surface indicating the floating lag time

3.6 Swelling Index

Table 10: Swelling studies of Nelfinavir floating tablets formulated with different grades of HPMC

Formulation	Swelling index		
	After 1 h	After 2 h	After 8 h
NFS1	88.9	132.49	185.19
NFS2	95.69	141.89	202.95
NFS3	103.73	149	225.18
NFS4	105.7	157.7	240.54
NFS5	89.99	128.42	190.96
NFS6	92.76	141.8	197.4
NFS7	100.26	144.29	206.86
NFS8	105.66	151.97	213.9
NFS9	85.16	125.59	181.89
NFS10	91.76	134.88	190.79
NFS11	94.56	137.75	194.8
NFS12	99.68	146.23	198.57

Table 11: Swelling studies of Nelfinavir floating tablets formulated with different natural polymers

Formulation	Swelling index		
	After 1 h	After 2 h	After 8 h
NFB1	34.75	46.32	87.7
NFB2	38.02	61.94	102.18

NFB3	41.97	69.63	119.99
NFB4	42.63	72.74	114.81
NFA1	34.75	46.32	87.7
NFA2	38.02	61.94	102.18
NFA3	39.63	66.82	109.97
NFA4	41.52	72.21	116
NFM1	26.76	37.62	77.86
NFM2	30.54	51.67	92.24
NFM3	32.67	60.66	100.13
NFM4	37.8	67.71	107.85

3.7 In vitro dissolution studies of synthetic polymers

The in vitro dissolution behavior of Nelfinavir floating tablets were investigated in 0.1 N HCl over a period of 24 hours. Comparative evaluation was performed for formulations containing three viscosity grades of hydroxypropyl methylcellulose (HPMC K4M, K15M and K100M). The dissolution profiles of formulations NFS1–NFS12 are presented in tables 12-14, while the cumulative drug release versus time plots are depicted in the corresponding figures 2-4.

A clear inverse relationship between polymer concentration and drug release was observed. Formulations incorporating the low-viscosity grade HPMC K4M exhibited the highest drug release, with NFS4 (99.22±0.36%) achieving nearly complete release at 24 hours. At higher concentrations, the increased density of the polymer matrix led to a greater diffusional path length, consequently retarding drug release. In contrast, formulations containing HPMC K15M and K100M demonstrated prolonged release up to 15 hours, which can be attributed to the formation of a more robust gel barrier that effectively delayed drug diffusion from the matrix.

Table 12: Drug release profiles of Nelfinavir formulations NFS1-NFS4 using HPMCK4M

Time (hrs)	Cumulative % drug released ±S.D * (n=6)			
	NFS1	NFS2	NFS3	NFS4
	HPMC K4M			
1	13.23±0.41	11.19±0.47	10.2±0.51	8.19±0.54
2	25.91±0.67	23.28±0.19	17.19±0.52	19.67±0.59
4	44.57±0.24	36.33±0.44	25.36±0.47	29.31±0.47
6	60.44±0.53	50.39±0.63	29.49±0.39	35.61±0.58
8	84.04±0.48	63.20±0.19	35.61±0.22	38.21±0.51
10	99.52±0.23	70.53±0.44	42.33±0.44	47.39±0.65
12	--	76.22±0.49	53.16±0.75	56.51±.0.47
14	--	89.25±0.59	65.21±0.28	62.33±0.14
16	--	99.33±0.17	79.33±0.71	66.20±0.26
18	--	--	86.38±0.43	76.19±0.16
20	--	--	99.31±0.66	82.17±0.45
22	--	--	--	91.33±0.19

24	--	--	--	99.22±0.36

Table 13: Drug release profiles of Nelfinavir formulations NFS5-NFS8 using HPMCK15M

Time (hrs)	Cumulative % drug released ±S.D * (n=6)			
	NFS5	NFS6	NFS7	NFS8
	HPMC K15M			
1	11.54±0.61	10.37±0.44	9.23±0.28	8.41±0.33
2	20.33±0.51	18.33±0.21	14.66±0.19	12.99±0.17
4	28.27±0.05	27.31±0.44	25.55±0.62	20.53±0.63
6	36.33±0.19	35.16±0.49	30.37±0.17	26.78±0.37
8	42.33±0.35	43.44±0.55	37.18±0.62	33.54±0.25
10	50.57±0.63	51.33±0.42	44.32±0.57	40.33±0.29
12	59.19±.0.33	56.60±.0.11	53.57±.0.62	46.19±.0.28
14	69.33±0.54	67.19±0.43	61.22±0.55	52.23±0.49
16	81.49±0.61	76.03±0.57	69.35±0.47	59.61±0.18
18	89.54±0.15	82.33±0.12	73.12±0.39	68.20±0.15
20	99.33±0.67	88.16±0.15	79.23±0.44	75.21±0.43
22	--	93.40±0.47	84.45±0.28	81.33±0.61
24	--	97.33±0.21	88.29±0.33	86.57±0.47

Table 14: Drug release profiles of Nelfinavir formulations NFS9-NFS12 using HPMCK100M

Time (hrs)	Cumulative % drug released ±S.D * (n=6)			
	NFS9	NFS10	NFS11	NFS12
	HPMC K100M			
1	7.21±0.67	6.42±0.49	5.33±0.12	5.22±0.61
2	13.32±0.52	13.22±0.54	11.23±0.19	10.33±0.94
4	22.53±0.69	21.36±0.59	19.33±0.28	18.25±0.67
6	28.42±0.52	28.33±0.68	27.33±0.21	28.33±0.34
8	36.21±0.18	34.18±0.61	33.45±0.14	34.26±0.72
10	43.22±0.34	41.22±0.63	40.52±0.19	41.40±0.29
12	52.84±.0.73	48.19±.0.12	49.23±.0.25	48.26±.0.54
14	60.22±0.63	59.23±0.47	58.51±0.41	57.23±0.31
16	70.19±0.33	64.19±0.83	65.31±0.39	61.29±0.44
18	80.45±0.37	71.44±0.59	69.41±0.81	68.44±0.51
20	92.31±0.67	77.33±0.47	78.33±0.47	79.33±0.40
22	99.26±0.44	81.46±0.51	82.18±0.33	81.63±0.19
24	--	85.17±0.62	87.55±0.63	89.37±0.25

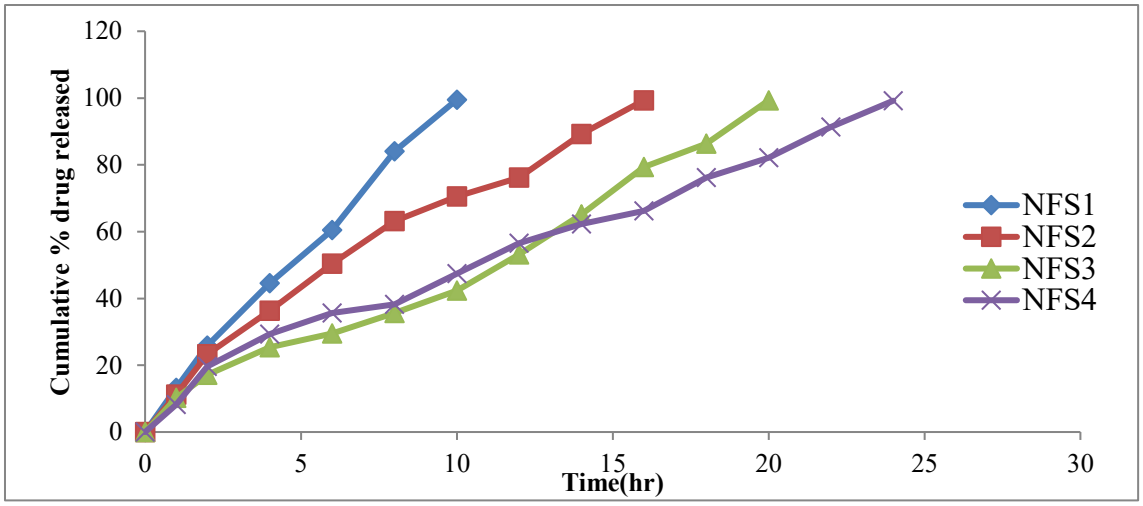


Fig 2: Comparison of cumulative % drug released from NFS1-NFS4

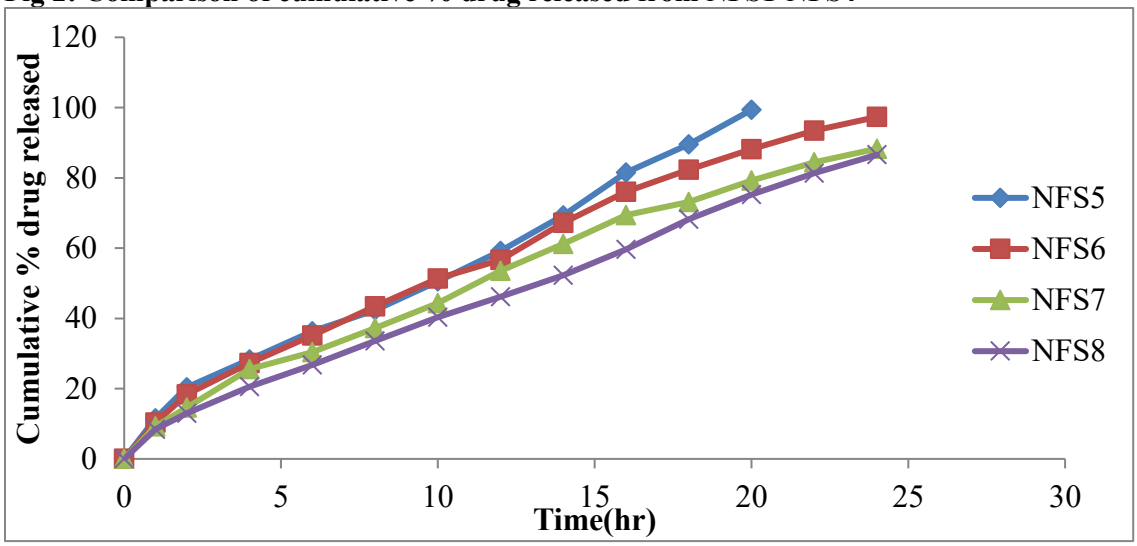


Fig 3: Comparison of cumulative % drug released from NFS5-NFS8

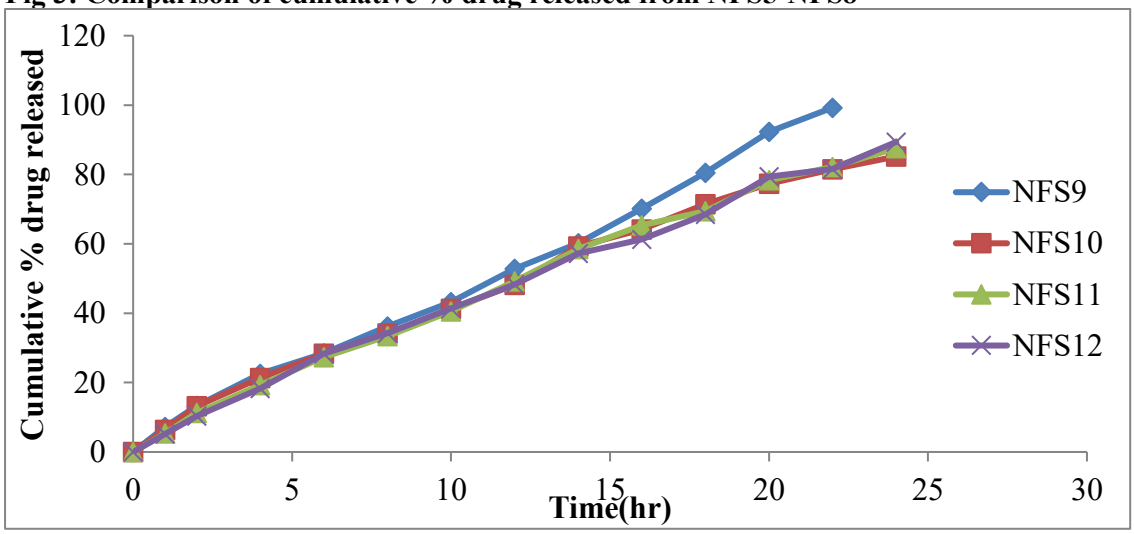


Fig 4: Comparison of cumulative % drug released from NFS9-NFS12

3.8 In vitro dissolution studies of natural polymers were carried out in 0.1 N HCl for 24 h. Drug release from formulations containing three natural polymers—Bhara gum, Albizia gum and Mesquite gum—were compared. The release profiles of NFB1–NFB4, NFA1–NFA4, and NFM1–NFM4 were tabulated and plotted as cumulative release vs. time curves.

Overall, **Bhara gum proved most effective** in extending drug release with comparatively lower polymer concentration.

Table 15: Drug release profiles of Nelfinavir formulations NFB1-NFB4 using Bhara gum

Time (hrs)	Cumulative % drug released ±S.D * (n=6)			
	NFB1	NFB2	NFB3	NFB4
	Bhara gum			
1	13.29±0.56	11.23±0.69	10.28±0.33	8.33±0.91
2	32.55±0.19	26.33±0.17	15.52±0.14	17.25±0.48
4	48.37±0.63	32.47±0.19	26.94±0.31	23.52±0.45
6	56.48±0.39	40.55±0.41	34.50±0.67	31.33±0.37
8	67.99±0.47	45.39±0.56	40.39±0.19	38.59±0.33
10	80.85±0.62	55.53±0.34	46.52±0.37	45.67±0.91
12	90.18±0.43	66.29±0.67	51.57±0.22	52.33±.0.14
14	99.36±0.29	78.44±0.55	57.41±0.39	56.83±0.21
16	--	87.33±0.42	63.43±0.22	60.20±0.44
18	--	95.56±0.27	70.45±0.39	67.19±0.69
20	--	99.44±0.41	80.45±0.51	78.33±0.18
22	--	--	90.35±0.48	82.47±0.25
24	--	--	99.18±0.67	88.69±0.48

Table 16: Drug release profiles of Nelfinavir formulations NFA1-NFA4 using Albizia gum

Time (hrs)	Cumulative % drug released ± S.D * (n=6)			
	NFA1	NFA2	NFA3	NFA4
	Albizia gum			
1	21.81±0.33	15.33±0.41	10.41±0.29	9.35±0.19
2	42.45±0.75	36.28±0.58	20.47±0.63	19.83±0.45
4	62.71±0.44	51.57±0.64	36.29±0.53	32.57±0.52
6	82.32±0.19	65.80±0.41	49.33±0.56	40.33±0.69
8	99.55±0.52	75.33±0.92	60.85±0.49	50.22±0.52
10	--	86.69±0.43	74.92±0.66	60.14±0.21
12	--	99.89±0.55	88.32±0.41	72.19±.0.25
14	--	--	99.33±0.44	77.42±0.52
16	--	--	--	86.39±0.85
18	--	--	--	99.51±0.36

Table 17: Drug release profiles of Nelfinavir formulations NFM1-NFM4 using Mesquite gum

Time (hrs)	Cumulative % drug released ±S.D * (n=6)			
	NFM1	NFM2	NFM3	NFM4
	Mesquite gum			
1	12.33±0.58	10.32±0.45	9.33±0.33	8.11±0.41
2	29.37±0.15	22.45±0.19	17.61±0.45	19.31±0.29
4	46.23±0.48	37.22±0.81	35.63±0.28	37.78±0.16
6	52.57±0.24	43.57±0.69	42.22±0.69	45.20±0.67
8	63.45±0.22	55.99±0.43	53.35±0.19	55.29±0.41
10	78.44±0.84	67.21±0.49	65.33±0.48	66.74±0.33
12	90.39±0.55	81.33±0.63	76.33±0.45	77.22±.0.59
14	99.41±0.68	90.45±0.25	85.71±0.63	83.41±0.61
16	--	99.74±0.96	91.25±0.47	93.47±0.94
18	--	--	99.33±0.45	95.33±0.19
20	--	--	--	99.18±0.45
22	--	--	--	--
24	--	--	--	--

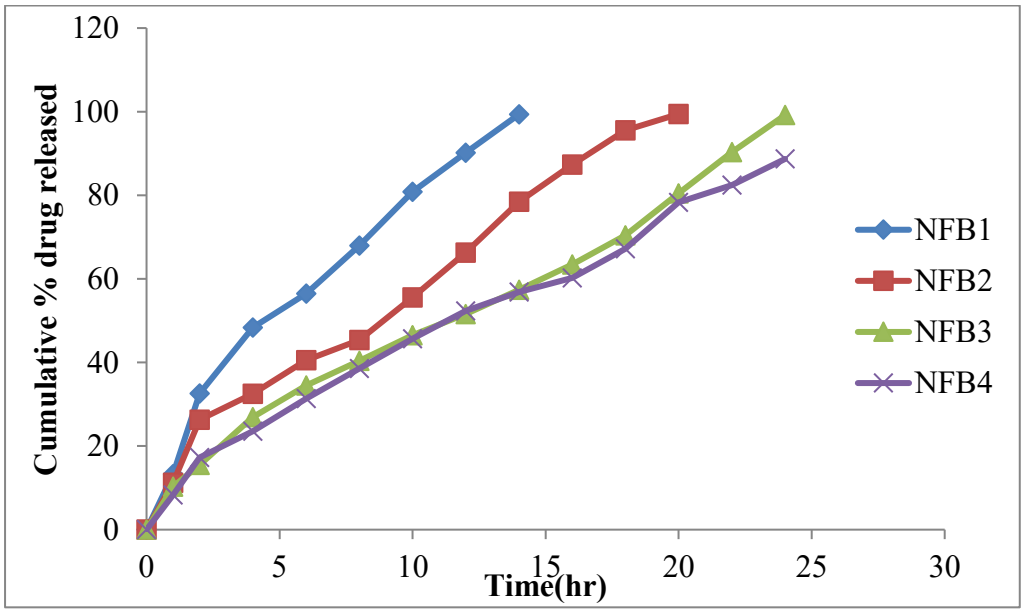


Fig 5: Comparison of cumulative % drug released from NFB1-NFB4

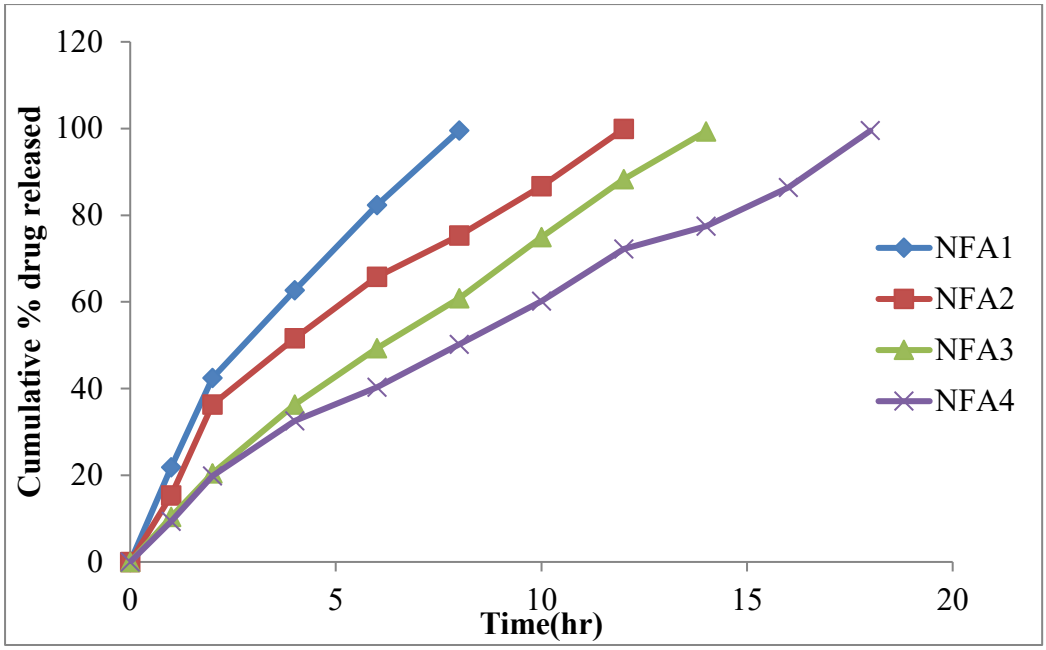


Fig 6: Comparison of cumulative % drug released from NFA1-NFA4

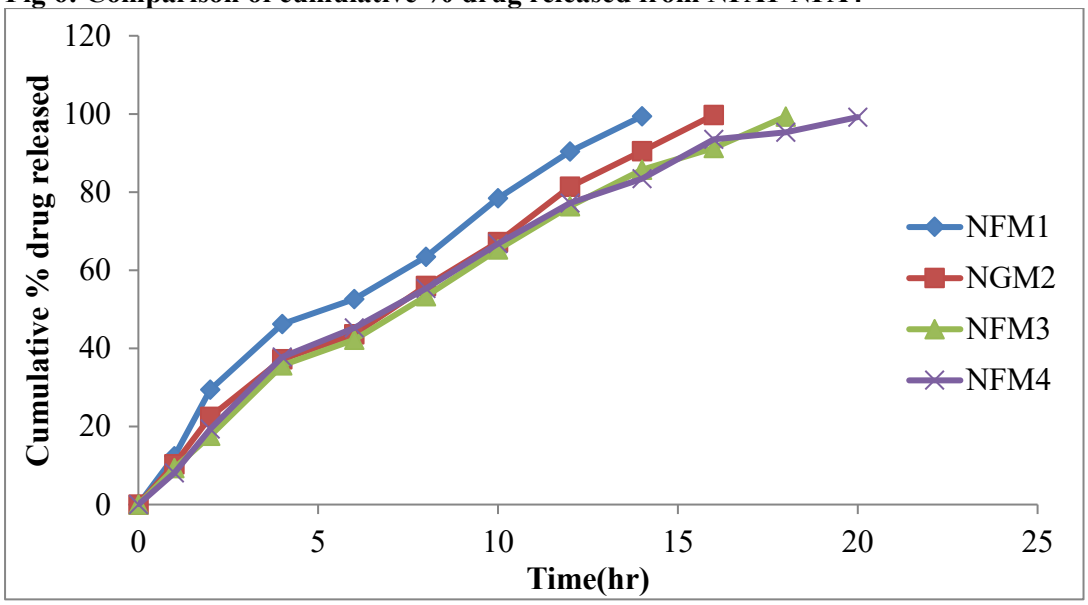


Fig 7: Comparison of cumulative % drug released from NFM1-NFM4

3.9 Drug release kinetics

The drug release mechanism of the prepared formulations was assessed by evaluating the correlation coefficients of different kinetic models, namely zero-order, first-order, Higuchi, and Korsmeyer–Peppas, based on the release data of each formulation as shown on tables 18 19.

Table 18: Correlation Coefficient (r^2) Values of formulations NFS1 – NFS12 as per Various Kinetic Models

Formulation	Correlation Coefficient (r^2) Values				
	Zero order	First order	Higuchi's	Peppas's	n value
NFS1	**0.9740**	0.8704	0.9390	**0.9640**	0.87
NFS2	**0.9552**	0.9411	0.9490	**0.9790**	0.68
NFS3	**0.9630**	0.6306	0.9305	**0.9810**	0.69

NFS4	**0.9340**	0.7097	0.9405	**0.9860**	0.74
NFS5	**0.9938**	0.7997	0.9585	**0.9945**	0.82
NFS6	**0.9687**	0.8926	0.9788	**0.9957**	0.76
NFS7	**0.9878**	0.7936	0.9734	**0.9977**	0.76
NFS8	**0.9950**	0.7394	0.9555	**0.9934**	0.77
NFS9	**0.9925**	0.6997	0.9115	**0.9830**	0.82
NFS10	**0.9956**	0.7840	0.9551	**0.9961**	0.8
NFS11	**0.9924**	0.7890	0.9630	**0.9970**	0.877
NFS12	**0.9905**	0.8330	0.9540	**0.9930**	0.927

Table 19: Correlation Coefficient (r^2) Values of formulations using natural polymers

Formulation	Correlation Coefficient (r^2) Values				
	Zero order	First order	Higuchi's	Peppas's	n value
NFB1	**0.9639**	0.7915	0.7936	**0.8398**	0.86
NFB2	**0.9766**	0.7732	0.8439	**0.9073**	0.77
NFB3	**0.9754**	0.6652	0.9438	**0.9436**	0.80
NFB4	**0.9854**	0.7457	0.9254	**0.9421**	0.83
NFA1	**0.9635**	0.8129	0.9651	**0.9736**	0.68
NFA2	**0.9437**	0.7843	0.9739	**0.9891**	0.61
NFA3	**0.9839**	0.7321	0.9433	**0.9735**	0.78
NFA4	**0.9862**	0.7066	0.9439	**0.9533**	0.76
NFM1	**0.9635**	0.7039	0.9622	**0.9614**	0.75
NFM2	**0.9854**	0.7523	0.9432	**0.9735**	0.80
NFM3	**0.9729**	0.7781	0.9563	**0.9671**	0.72
NFM4	**0.9628**	0.8514	0.9629	**0.9734**	0.86

Based on the studies conducted with synthetic polymers (HPMC K4M, HPMC K15M, HPMC K100M) and natural polymers (Bhara gum, Albizia gum, Mesquite gum) using nelfinavir, the most effective formulations were obtained with HPMC K4M and Bhara gum. These were further studied for stability and in vivo studies were performed.

3.10 Stability studies

In the present study, samples were stored under accelerated conditions (40 ± 2 °C/75% RH) in accordance with ICH guidelines, and withdrawn at predetermined intervals (0, 1, 2, 3, and 6 months).

The optimized formulations (NFS4, and NFB3) were subjected to accelerated stability testing, and the results pertaining to floating behavior and drug release profiles are presented in the respective tables 20-21 and figures.

Table 20: Floating characteristics before and after Storage

Formulations	Floating characteristics			
	Before Storage		After Storage	
	Floating Lag time (min)	Floating time (hr)	Floating Lag time (min)	Floating time (hr)
NFS4	1.0	22	1.0	22
NFB3	1.33	22	1.33	2

Table 21: In vitro dissolution data of optimized Nelfinavir floating tablets (NFS4)tested at 40±2^0 C/75±5% RH for 3 months

Time(h)	Percentage of Nelfinavir Released (X±SD)	
	Before storage	After Storage
0	0	0
1	8.19±0.54	8.23±0.19
2	19.67±0.59	19.33±0.54
4	29.31±0.47	3019±0.33
6	35.61±0.58	37.63±0.29
8	38.21±0.51	41.67±0.49
10	47.39±0.65	49.19±0.25
12	56.51±.0.47	58.19±.0.55
14	62.33±0.14	63.49±0.89
16	66.20±0.26	69.63±0.42
18	76.19±0.16	79.34±0.81
20	82.17±0.45	86.33±0.12
22	91.33±0.19	93.21±0.66
24	99.22±0.36	99.12±0.19

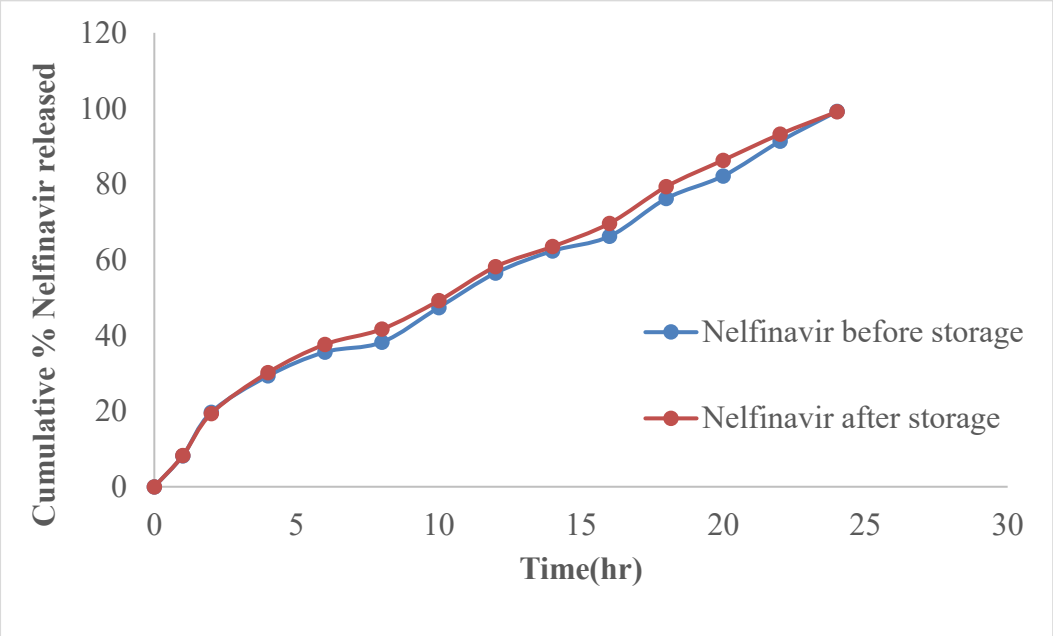


Fig 8: Comparison of cumulative % Nelfinavir released before and after storage

Table 22: In vitro dissolution data of optimized Nelfinavir floating tablets (NFB3)tested at 40±2^0 C/75±5% RH for 3 months

Time (h)	Percentage of Nelfinavir Released (X±SD)	
	Before storage	After Storage
0	0	0
1	10.28±0.33	10.23±0.65
2	15.52±0.14	17.33±0.99
4	26.94±0.31	29.23±0.43
6	34.50±0.67	38.49±0.15
8	40.39±0.19	43.55±0.49
10	46.52±0.37	49.19±0.27
12	51.57±0.22	58.19±.0.04

14	57.41±0.39	66.59±0.23
16	63.43±0.22	69.22±0.18
18	70.45±0.39	76.34±0.46
20	80.45±0.51	81.33±0.67
22	90.35±0.48	93.33±0.19
24	99.18±0.67	99.12±0.48

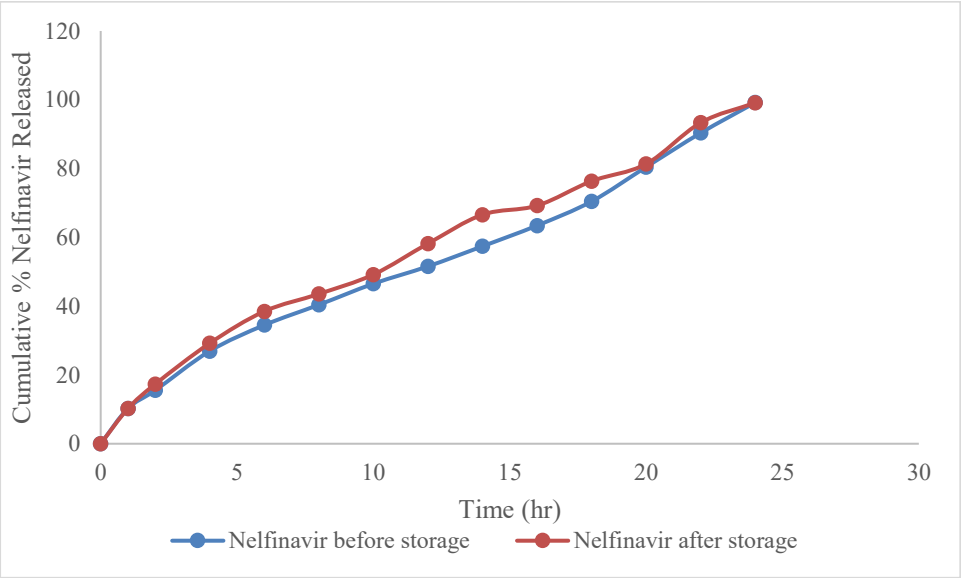


Fig 9: Comparison of cumulative % Nelfinavir released before and after storage

4.0 Conclusion: Manuscript prepared focused on evaluating natural polymers such as Bhara gum, Albizia gum, and Mesquite gum for their properties (viscosity, swelling index, microbial load, etc.) and their applications in designing GRDDS tablets. Comparison was done using natural gums with synthetic polymers like HPMC K4M, K15M, and K100M. The release profiles for NFB1-NFB4, NFA1-NFA4, and NFM1-NFM4 were tabulated and plotted as cumulative release versus time curves. Our findings indicate that floating drug delivery prolonged release and improved bioavailability. Specifically, for Nelfinavir, formulations with Bhara gum (NFB series) showed slower release as polymer concentration increased. The in vitro dissolution behavior of Nelfinavir floating tablets was investigated in 0.1 N HCl over a period of 24 hours. A comparative evaluation was performed for formulations containing three viscosity grades of hydroxypropyl methylcellulose (HPMC K4M, K15M, and K100M). The dissolution profiles of formulations NFS1–NFS12 are presented, showing a clear inverse relationship between polymer concentration and drug release. Formulations incorporating the low-viscosity grade HPMC K4M exhibited the highest drug release, with NFS4 (99.22±0.36%) achieving nearly complete release at 24 hours. At higher concentrations, the increased density of the polymer matrix led to a greater diffusional path length, consequently retarding drug release. In contrast, formulations containing HPMC K15M and K100M demonstrated prolonged release up to 15 hours, which can be attributed to the formation of a more robust gel barrier that effectively delayed drug diffusion from the matrix. Bhara gum-maintained release for 24 hours, whereas Albizia and Mesquite gums required higher concentrations to sustain release beyond 18–20 hours. This clearly indicated that natural polymers exhibited superior performance compared to synthetic ones. For the optimized formulations, the ‘n’ values obtained from the Korsmeyer–Peppas model were within the range of 0.68–0.89, indicating that the release behavior was best explained by non-Fickian (anomalous) diffusion.

Acknowledgement
None.

Conflict of Interest
Authors have no conflict of interest to declare.

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