How to Cite:
Rajmane, A., Trivedi, R., & Nandgude, T. (2022). Formulation and evaluation of raft forming pirenzepinedihydrochloride floating tablets for peptic ulcer. *International Journal of Health Sciences*, *6*(S3), 10558–10574. https://doi.org/10.53730/ijhs.v6nS3.8360

Formulation and evaluation of raft forming pirenzepinedihydrochloride floating tablets for peptic ulcer

Archana Rajmane
Research Scholar, Faculty of Pharmacy, (B. R. Nahata College of Pharmacy), Mandsaur University, Mandsaur -458001 (M.P), India
*Corresponding author email: archurajmae@gmail.com

Rahul Trivedi
Faculty of Pharmacy, (B. R. Nahata College of Pharmacy), Mandsaur University, Mandsaur – 458001 (M.P), India

Tanaji Nandgude
Dr. D. Y. PatilInstitute of Pharmaceutical Science & Research, Pimpri, Pune, 411018, Maharashtra, India

***Abstract*---**Objective: Over past few decades, Peptic ulcer disease remains a common condition despite the lots of novelty in treatment. The objective of this research work was to formulate gastro retentive floating tablet by raft approach using Pirenzepine dihydrochloride (PNZ) as drug candidate. Formulation also contained a raft forming agent (sodium alginate) along with alkalizing agents (Calcium carbonate and Sodium Bicarbonate). Raft strength was only affected by the amount of Raft forming agent, Calcium carbonate and Sodium Bicarbonate. Method: Tablets were prepared by direct compression method and evaluated for raft strength, acid neutralization capacity, weight variation, % drug content, thickness, hardness, friability and In vitro drug release. Experimental work: A Box Behnken design was used in present study for optimization. Amount of gel forming agent, amount of cross-linkingagentsand floating agent were selected as independent variables. Raft strength, Acid neutralization capacity, and drug release were selected as dependent variables. Result: Raft strength, Acid neutralization capacity and In vitro drug release of all the experimental batches were found to be satisfactory. F10 batch was optimized based on maximum raft strength, good acid neutralization capacity and control drug release. Drug-excipients compatibility study showed no interaction between drug and excipients. Conclusion: It was concluded that raft forming floating tablet containing PNZ and alkalizing agents could be efficient in the treatment of peptic ulcer.

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
Manuscript submitted: 18 Feb 2022, Manuscript revised: 27 April 2022, Accepted for publication: 9 June 2022

Keywords---PNZ, direct compression, raft forming, floating drug delivery system.

Introduction

Peptic ulcers occur due to imbalance between dominant factors such as acid secretion (HCL), pepsin, refluxed bile, reactive oxygen species and defensive factors, which include the functions of mucus bicarbonate barrier, prostaglandins, mucosal blood flow, cell renewal and migration, non enzymatic and enzymatic antioxidants and some growth factors.[1]H. Pylori bacterial infection and more use of non-steroidalanti-inflammatory drugs are the main causes fordevelopment of peptic ulcer and duodenal ulcer.[2] The Oral administration is the most convenient and preferred means of any drug delivery to the systematic circulation.[3] Oral controlled release drug delivery have recently been of increasing interest in pharmaceutical field to achieve improved therapeutic advantages, like ease of dose administration, patient compliance and flexibility in formulation. Oral route has high patient acceptability, primarily due to ease of administration.[4] Over the years, oral dosage forms have become increasingly sophisticated with major role being played by control release drug delivery system. The Control release drug delivery system release drug at a predetermined rate, as determined by drug's pharmacokinetics and desired therapeutic concentration.[5] Raft forming system has received much attention for the delivery of antacids and drug delivery for gastrointestinal infections and disorders. The basic mechanism involved in the raft formation includes the formation of viscous cohesive gel in contact with gastric fluids, wherein each portion of the liquid swells forming a continuous layer called raft.[6-9] The raft floats because of the buoyancy created by the formation of co2 and act as barrier to prevent the reflux of gastric content like HCl and enzymes into the esophagus.[10,11] Usually, the system contains a gel forming agent and alkaline bicarbonates or carbonates responsible for the formation of to make the system less dense and float on the gastric fluids.[12] The floating drug delivery system by raft forming method enhances the absorption[13] of drug in stomach and also to increase the bioavailability of drug.[14] Gastric retentive time is increased because of buoyancy studies to avoidance of gastric irritation.

Materials and Methods

Materials

Analytically pure sample of PirenzepineDihydrochloride With purity greater than 99% was obtained as gift sample from clear synth lab,Mumbai, India. Sodium alginate, calcium carbonate, sodium bicarbonate was obtained from. D. Fine Chemicals Ltd., Mumbai, India All Other chemicals and solvents used was of analytical grade.

Methodology Experimental Design

A two-factor, three level (3^2) full factorial designs was employed for the optimization of floating raft drug delivery system using Design Expert® software (Version 7.0.0, Stat-Ease Inc., USA). The effect of three independent variables

namely amount of gel forming polymer (X_1) , amount of cross linking polymer (X_2) and amount floating agent (X_3) on the three dependent variables viz., raft strength (Y_1), Acid Neutralizing capacity(ANC) (Y_2), and percentage cumulative drug release(Y_3) were studied at three levels each i.e., low(-1), medium (0) and high (+1). A total of 17 experimental runs generated with levels as per the Design Expert® software are shown in Table no.2All the prepared formulations as per the design were investigated for raft strength (Y_1), Acid Neutralizing capacity(ANC) (Y_2), and percentage cumulative drug release(Y_3) which were designated as response or dependant variables. The observed responses were simultaneously fitted into various mathematical models (i.e. linear, two factor interaction (2FI), quadratic and cubic). Analysis of variance (ANOVA) was used to determine the statistical significance of the generated model and model terms. The 3D- response surface plots, 2D-contour plots and perturbation graphs generated by the Design Expert® software were used to understand the relationship between the independent and dependent or response variables.[15-20]

Table 1
Translation of coded levels in actual units

Coded levels	Low*	Middle*	High*
	-1	0	1
Factor 1 (X1) (Amount of gel forming polymer)	50	75	100
Factor 2 (X1) (Amount of cross linking polymer)	150	200	250
Factor 3 (X3) (Amount of floating agent)	75	100	125

High, Middle and Low amount (in mg) to be finalized from literature survey.

Table 2
Variables

Sr.No	Independent variables	Dependent variables	Goal for dependent variables
1	Amount of Sodium alginate X1	Raft strength (Y1)	Maximize
2	Amount of Calcium Carbonate X2	ANC (Y2)	Maximize
3	Amount of Sodium Bicarbonate X3	Drug Release (Y3)	Minimize

Preparation of raft forming floating tablet of PNZ

The Floating Raft forming approach tablets of PNZ were prepared through direct compression method. The preparations of PNZ by various steps involved in tablet production are sieving, mixing, lubrication and compression. Sodium alginate use as viscous gel forming, calcium carbonate used as cross-linkingagents' sodium bicarbonate used as gas generating agent. Talc is used as diluents, magnesium stearate used as lubricant. Sodium starch glycolate used as super disintegrantFinally, the powder mixture was compressed into tablets using rotary tablet punching machine at the weight of 500mg each. The below expressed

gastro retentive drug delivery of PNZ tablets performed a different formulation from F1 to F17 batches study with various concentrations of polymer, crosslinking agent and floating agent.[21]

Ingredient	B1	B2	B3	B4	B5	B6	B7	B8	B9	B10	B11	B12	B13	B14	B15	B16	B17
PYZ	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100	100
Sodium alginate	200	250	250	250	250	300	300	250	100	300	200	200	300	200	250	250	200
$Caco_3$	100	150	100	100	150	150	150	150	200	200	150	200	100	200	150	150	150
Na_2co_3	50	50	75	25	50	25	75	50	75	50	25	50	50	25	50	50	75
HPMC	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50	50
Talc	130	20	45	95	20	105	05	20	95	05	95	20	20	45	20	20	45
Magnesium stearate	10	20	20	20	20	20	10	20	20	10	20	20	20	20	20	20	20
Sodium Starch Glycolate	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10	10
Total weight	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650	650

Evaluation and Characterization
Pre-formulation Studies

- Drug Excipients Physical Compatibility Study (FTIR)
- The active drug nature and drug-excipients compatibility study was done prior to the formulation by Fourier transform infra-red (FTIR) by comparing spectral peaks in the spectra of PNZ drug and excipientswith standard reference spectra.[22]
- Differential Scanning Calorimetry (DSC)
- DSC is one of the most used calorimetric techniques, employed to characterize the solubility and physical state of drug in the complex. Thermo grams of PNZ and one formulation of PNZ loaded formulation was recorded using a DSC and were compared. The samples (5 mg) were hermetically sealed in flat bottomed aluminum pans and heated at a temperature of 100-300 °C using alumina as a reference standard.[23]
- P-XRD Studies: This test method is performed by directing an x-ray beam at a 0.2 gm. sample and measuring the scattered intensity as a function of the outgoing direction. Once the beam is separated, the scatter, also called a diffraction pattern, indicates the sample's crystalline structure.

Pre compression evaluation:[24]

Angle of repose: Angle of repose is defined as the maximum angle between the surface of pile of the powder and the horizontal plane 10. Fixed funnel method was used. The angle of repose (ɵ) was then calculated.

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

Where ɵ = Angle of repose,
h =Height of pile,
r = Radius of the base of pile.

Bulk density: Bulk density was determined by using bulk density apparatus, during measurement accurately weighed quantity of the powder were taken in a measuring cylinder and recording the volume and weight of the total powder. Bulk density is expressed in gm/ml and is given by,

BD=W/Vo

Where, BD = Bulk density (gm/ml)
W = weight of powder (gm)
Vo = Initial volume of the powder

Tapped density: Tapped density was determined by using Tapped density apparatus during measurement accurately weighed quantity of the powder were taken in a measuring cylinder and recording the volume of powder after 30 tapping and weight of the total powder.[25]

TD =W/VF

Where, TD= Tapped density (gm/ml)
W = weight of powder (gm)
VF **=** Final volume of powder (ml)

Compressibility index (or) Carr's index[26]**:**Compressibility index is an important measure that can be obtained from the bulk and tap densities. The percentage compressibility of the bulk drug was determined by using the following formula.

Compressibility index = [(T-B)/B]× 100
Where, T = Tapped density of the powder,
B = Bulk density of the powder.

Hausner's ratio: It indicates the flow properties of the powder. The ratio of tapped density to bulk density of the powder is called Hausner's ratio.

Hausner's Ratio=TD/BD
Where, TD = Tapped density of the powder,
BD = Bulk density of the powder.

Interparticle porosity
Post compression evaluation

Hardness: Resistance of the tablet during transportation or breakage under storage conditions and handling before usage depends on its hardness.[27]The hardness of tablets was measured using Monsanto tester.The hardness was measured in terms of kg/cm2. Five tablets were chosen randomly and tested for hardness. The average hardness of five tablets was recorded.

Thickness: Thickness was measured using a calibrated verniercaliper. It was determined for check the thickness of tablet. Five tablets of each formulation were picked randomly and thickness was measured individually.[28]

Friability: The friability of the prepared tablets was determined using Roche friability apparatus. It is expressed in percentage (%). To calculate the percentage friability determines 20 tablets initial weight and transferred into friabilator. The friabilator was operated at 25 rpm for four minutes. After four minutes the tablets were weighed again. Then % friability was then calculated using formula.[29]

% Friability =W1-W2/W1 ×100
w1= Initial weight of tablets.
w2= Final weight of tablets.

Weight variation: The weight of the tablet being made was determined to ensure that a tablet contains the proper amount of drug. 20 tablets were selected at random from each formulation and weighed on electronic weighing balance. The average weight of the tablets was determined. The weight of individual tablets was compared with the average weight variation.[30]

Drug content uniformity: The drug content of prepared tablets was accurately weight and finely powered by pestle in a mortar. Weighed tablet of each powder equivalent to 100mg of PNZ was transferred in to volumetric flask, dissolved in 60ml of 0.1N HCL and content of the flask were sonicated for 15 minutes. Then the volume was made up to100ml. The samples were analyzed UV-Visible spectrophotometer, and concentration of the drug in the sample was calculated.[31]

***In-Vitro* Buoyancy Studies**: The in vitro buoyancy was determined by floating lag time. The time between introduce of dosage form and its buoyancy on the simulated gastric fluid and the time during which the dosage form remain buoyant were measured. The time taken for dosage form to emerge on surface of medium called floating lag time. Method described by the tablets was placed in a 100ml beaker containing 0.1 N HCL. The time required for the tablet to rise to the surface and float was determined as floating lag time.[32]

***In-vitro* dissolution studies:** Dissolution of the tablets was carried out on USP XXXIII dissolution type II apparatus using paddle. The tablet was fixed to the paddle by hydration mechanism 900 ml of 0.1N HCL as dissolution medium was filled in a dissolution vessel and the temperature of the medium was set at 37± 0.5oc. The rotational speed of the paddle was set at 100 rpm. At particular intervals 5 ml of sample was withdrawn at predetermined time intervals of 15 mints, 30 mints, 1hrs, 2hrs, 4hrs, 6hrs, 8hrs, 10hrs,12hrsand same volume of fresh medium was replaced. The withdrawn samples were diluted to 10 ml with 0.1N HCL, filtered and analyzed on UV spectrophotometer at 281 nm 0.1NHCL using buffer as a blank. Percentage cumulative drug release was calculated.[33]

Raft strength measurement by in house method: A tablet powder equivalent to unit dose was transferred to 150 ml of 0.1N HCL and maintained at 37°c in a 250 ml glass beaker. Each raft was allowed to form around an L- shaped wire probe (diameter: 1.2mm) held upright in the beaker throughout the whole period (30 min) of raft development. Raft strength was estimated using the modified balance method. Water was added drop wise to the pan and the weight of water required to break the raft was recorded.[34]

In Vitro acid neutralization Study[35]

Tablet powder equivalent to unit dose was transferred to a 250 ml beaker; 50 ml of water was added to it and was mixed on a magnetic stirrer for 1 min. A 30-ml volume of 0.1 N HCl was added with continuous stirring on the magnetic stirrer for 10 min after addition of the acid. Stirring was discontinued and the gum base was removed using a long needle without delay. The needle was promptly rinsed with 20 ml of water, and the washing was collected in the beaker; stirring was resumed for 5 min. Titration began immediately. Excess HCl was titrated against

0.5N sodium hydroxide to attain a stable pH of 3.5. The number of mEq of acid consumed by the tablet tested was calculated by the following formula-
Total mEq = (30 * N HCl) -(V NaOH * N NaOH)
Where, N HCI=Normality of HCl; V NaOH =Volume of NaOH required; and N NaOH =Normality of NaOH.

Results and Discussion

Pre-formulation studies
Drug-excipients compatibility study

FTIR: The FTIR spectral analysis was employed to ascertain compatibility between the PZN and excipients of raft system. The FTIR spectra of pure PZN, sodium alginate and physical mixture of formulation excipients of raft are shown in fig. 01.FTIR spectra of PZN (Fig.1A) showed alkene stretching =C–H at 3476.77cm^{-1} CH2 vibration at 3015.61 cm^{-1}, alkane stretching (–CH3, – CH2 and –CH) vibration at 2943.58 cm^{-1}, C=O stretch at 1701.74 cm^{-1} due to saturated ketone and C=O–NH stretching at 1659.77 cm^{-1}.A selective stretching vibration at 1588.19 cm^{-1} and 1457.25 cm^{-1} for primary and secondary amine was also observed. For functional groups like S=O stretch and –C–S stretch showed vibrations at 1072.22 cm−1 and 759.00 cm−1 respectively. The FTIR spectra of physical mixture of PZN and formulation excipients of raft are shown in fig. 1B, it showsfunctional groups peaks of alkene stretching =C–H at 3435.95 cm^{-1} CH2 vibration at 3141.77 cm^{-1}, alkane stretching (–CH3, – CH2 and –CH) vibration at 2947.77 cm^{-1}, C=O stretch at 1702.41 cm^{-1} due to saturated ketone and C=O–NH stretching at 1660.26 cm^{-1}. A selective stretching vibration at 1587.81 cm^{-1} and 1457.09 cm^{-1} for primary and secondary amine was also observed. For functional groups like S=O stretch and –C–S stretch showed vibrations at 1069.41 cm−1 and 758.38 cm−1 respectively. The principal peaks of PZN are retained in the FTIR spectra of PZN raft. Thus, obtained results clearly revealed compatibility (no chemical interaction) between PZN and formulation excipients of raft.

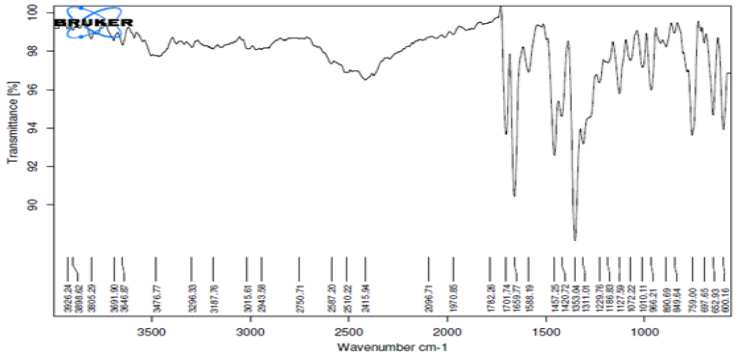

Fig.01 (A) FTIR PNZ

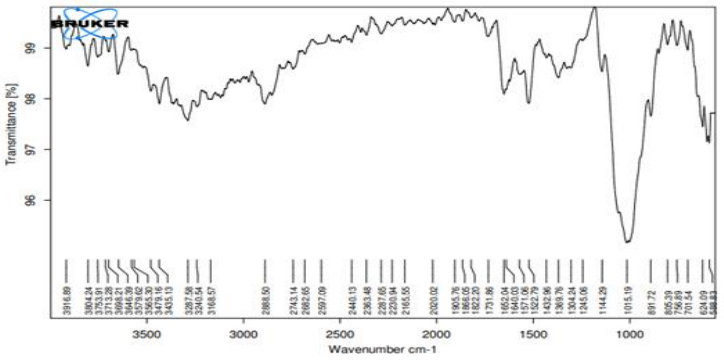

Fig. 01(B) FTIR Sodium alginate

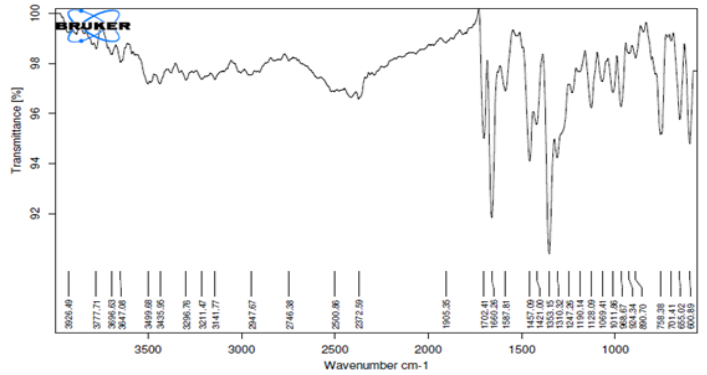

Fig. 01(C) FTIR Physical mixture

DSC Studies: Differential scanning calorimetry is and unique tool utilized to ascertain compatibility between the PZN and formulation excipients of raft. The DSC thermo grams of plain PZN, and physical mixture of PZN and excipients of excipients of raft is shown in Fig. 2. The DSC thermo gram of plain PZN(Fig. 2A), and sodium alginate(Fig. 2B), showed peaks corresponding to PZN at 269.44 °C,sodium alginate showed endothermic peak at 81.57°C and exothermic peak at 258.91°C. On the other hand, DSC thermo gram of physical mixture of PZN and excipients of raft (Fig. 2C) endothermic peak observed at 267.82°C which is analogous to the peak of PZN. Thus, obtained results revealed that integrity of PZN was retained after combining with raft excipients which conforms compatibility of PZNwith formulation excipients.

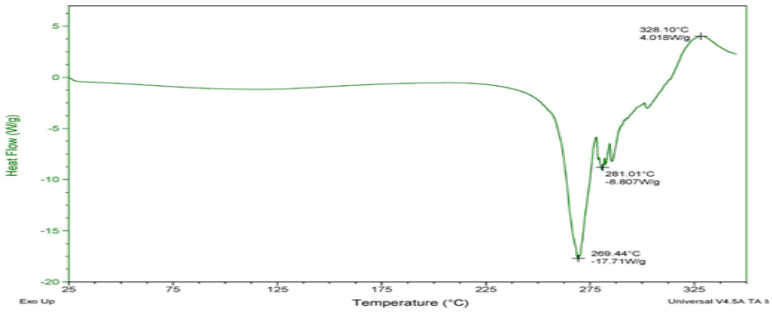

Fig. 02 (A) DSC PNZ

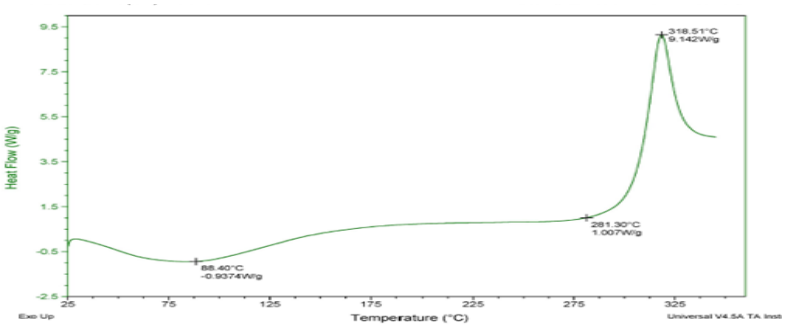

Fig. 02 (B) DSC Sodium alginate

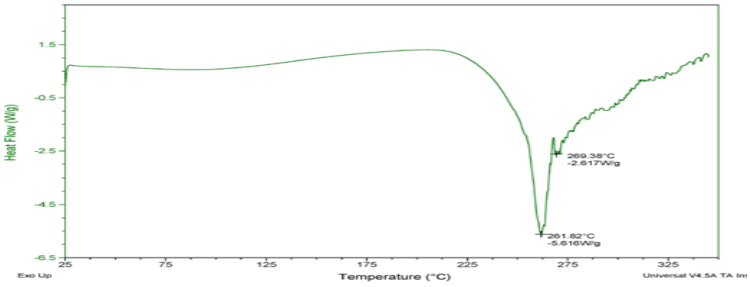

Fig. 02 (C) DSC Physical mixture

XRD Studies: The influence of process parameter's raft preparation on physiochemical nature of PZN was determined by p-XRD. The p-XRD motif of plain PZN and optimized PZN raft formulation is delineated in Fig.3 The p-XRD motif of PZN(Fig.3A) manifested distinctive intensity reflections counts of 5824.3,5984.7,7694.3,8916.7,5908.5 and 3978.7 at diffraction angles of 8.14,16.23,18.46,22.76,25.12 and 34.27 (2θ), respectively, indicating its crystalline nature. However, these distinctive peaks were vanished in optimized PZN raft formulation p-XRD pattern (Fig.3C) which conforms that change crystalline nature of PZN during processing of raft formation.

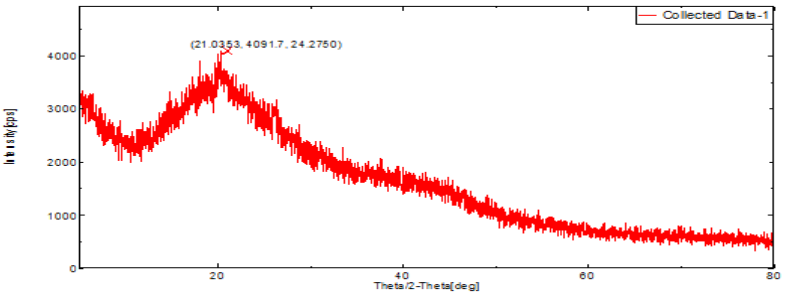

Fig. 03 (A) XRD PNZ

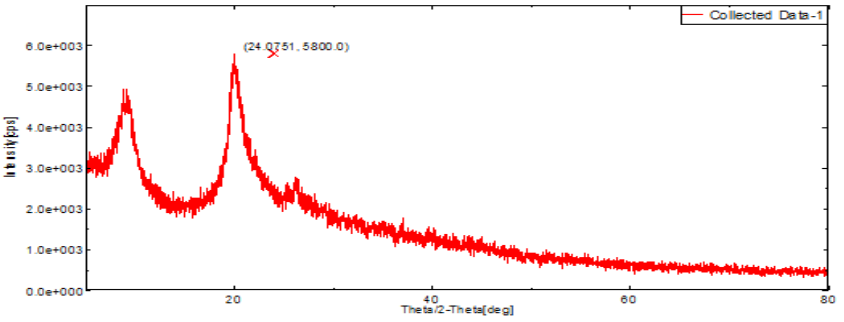

Fig. 03 (B) XRD Sodium alginate

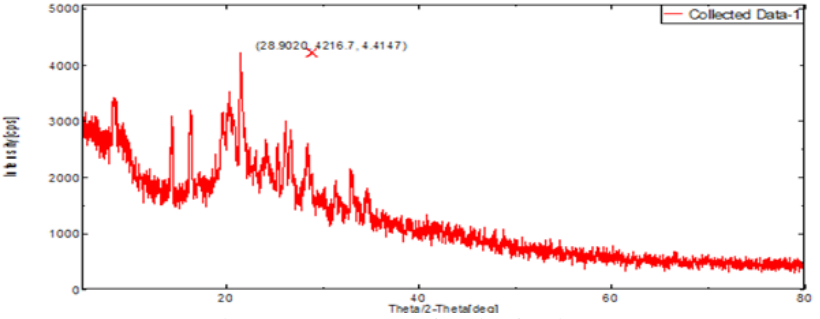

Fig. 03 (C) XRD Physical mixture

Pre-compression parameters

Angle of repose: The results obtained for angle of repose for all the formulations. The values were found to be in the range of 26°.98' to 30°.87'All the formulation showed the angle of repose below 30°, which indicates good flow.

Bulk density & Tapped density: The loose bulk density and tapped bulk density for all the formulations varied from 0.38 gm/cm3 to 0.54 gm/cm3 and 0.39gm/cm3 to 0.57gm/cm3 respectively. The values obtained lies within the acceptable range and no large difference found between loose bulk density and tapped density. These results help in calculating the % compressibility of the powder.

Percentage compressibility (Carr's consolidation index): The percentage compressibility of powder mix was determined by the equation given for Carr's

consolidation index. The percentage compressibility lies within the range of 3.31 to 7.01 which indicates that the flow of the tablet mixture of various formulations is good to excellent.

Hausner's ratio: The Hausner's ratio of powder mix was determined by the data of loose bulk density and tapped bulk density. The Hausner's ratio for all the formulations lies within the range of 1.030 to 1.07, which indicates flow of powder is excellent

Interpartical porosity: The Interpartical porosity ratio for all the formulations lies within the range of 0.69 to 1.10, which indicates flow of powder is excellent.

Table 04
Pre compression evaluation data

Run	Bulk Density	Tapped Density	Carrs Index	Hausner Ratio	Inter Particle Porosity	Angle of Repose
F1	0.3848± 0.034	0.4113± 0.038	6.44±0.23	1.068±0.073	0.82	34.18±0.170
F2	0.3956± 0.026	0.4093± 0.030	3.34±0.16	1.034±0.065	1.06	29.88±0.263
F3	0.3960± 0.039	0.4242± 0.041	6.64±0.27	1.071±0.036	0.75	30.21±0.206
F4	0.3816± 0.031	0.4079± 0.032	6.44±0.18	1.068±0.082	0.85	30.71±0.195
F5	0.3721± 0.042	0.3970± 0.033	6.27±0.32	1.072±0.083	1.05	30.87±0.204
F6	0.3963± 0.030	0.4100± 0.022	3.34±0.15	1.034±0.062	0.81	29.93±0.266
F7	0.3848± 0.021	0.3973± 0.037	3.14±0.26	1.032±0.087	.95	30.19±0.342
F8	0.3940± 0.034	0.4075± 0.039	3.31±0.14	1.034±0.049	1.10	30.66±0.241
F9	0.3832± 0.052	0.3960± 0.034	3.34±0.21	1.033±0.072	0.69	28.96±0.282
F10	0.3963± 0.035	0.4100± 0.026	3.34±0.27	1.034±0.059	0.73	24.65±0.265
F11	0.3963± 0.042	0.4100± 0.033	3.34±0.13	1.034±0.062	0.76	26.76±0.762
F12	0.3956± 0.038	0.4240± 0.047	6.69±0.17	1.071±0.084	0.71	27.76±0.546
F13	0.3970± 0.031	0.4107± 0.035	3.33±0.21	1.034±0.035	0.82	26.98±0.875
F14	0.54±0.0282	0.57±0.020	5.26±0.298	1.05±0.0723	0.78	28.23±0.437
F15	0.53±0.0129	0.57±0.010	7.01±0.282	1.07±0.0803	1.04	30.21±0.125
F16	0.53±0.0282	0.55±0.0282	3.63±0.191	1.03±0.0682	1.07	29.76±0.547
F17	0.54±0.0282	0.57±0.0352	5.26±0.165	1.05±0.0094	0.87	25.64±0.542

Post compression evaluations

Thickness

The thickness of floating tabletswas measured by Vernier caliper of formulation F1 to F17
and were range between 3.09.±0.12to 4.14±0.24mm .

Weight variation

All the formulation tablet F01 to F17 passed the weight variation test as the percent weight
variation was within the pharmacopeia limit of 5% of average weight.

Hardness

The hardness of the floating tablet was measured by the Monsanto tester of forF01 to F17 and were controlled between 3.7 to 4.1 kg/cm2. The standard hardness of the tablet is 4kg/cm2.

Friability

The friability of the floating tablet was measured by The Roche Friabilator of formulation F01 to
F17 and were controlled between 0.51±0.04 % to 0.65±0.01%. The standard friability of the tablet is below 1%

Drug content uniformity

The drug content of prepared tablets was accurately weight and finely powered by pestle in a mortar. Weighed tablet of each powder equivalent to 100mg of PNZ was transferred in to volumetric flask, dissolved in 60ml of 0.1N HCL and content of the flask were sonicated for 15 minutes. Then the volume was made up to100ml. The samples were analyzed UV-Visible spectrophotometer at 281nm, and concentration of the drug in the sample was calculated. The percent drug content of formulation F1 to F17 was found to be 98.30±0.51to 99.65±0.58% of PNZ in which was within the acceptable limit, the standard drug content uniformity 100±10%

Table 05
Result of Post CompressionParameters

Run	Thickness (mm)	Hardness (kg)	Friability (%)	weight variation(gm)	Drug content (%)
F1	4.14±0.12	3.9±0.1	0.65±0.01	650±0.24	98.80±0.48
F2	4.09±0.32	4.1±0.3	0.58±0.04	650±0.33	99.10±0.07
F3	4.14±0.25	3.4±0.3	0.64±0.04	650±0.36	98.87±0.06
F4	4.14±0.12	3.7±0.4	0.58±0.03	650±0.38	98.95±0.58
F5	4.14±0.24	3.6±0.2	0.55±0.04	650±0.32	99.45±0.45
F6	4.14±0.12	3.6±0.3	0.54±0.02	650±0.22	98.88±0.53
F7	3.09.±0.11	4.2±0.1	0.53±0.04	645±0.36	99.54±0.58
F8	4.14±0.12	3.9±0.3	0.59±0.04	620±0.31	99.50±0.62
F9	4.14±0.12	3.9±0.3	0.61±0.02	675±0.18	98.30±0.51
F10	4.14±0.23	3.4±0.4	0.58±0.01	645±0.32	99.65±0.58
F11	4.14±0.12	3.9±0.2	0.65±0.02	650±0.1	98.6±0.55
F12	3.94±0.22	4.1±0.3	0.55±0.01	650±0.22	99.34±0.61
F13	4.12±0.11	3.9±0.1	0.58±0.03	634±0.19	98.89±0.58
F14	3.94±0.12	4.1±0.3	0.58±0.03	670±0.22	99.10±0.58
F15	4.14±0.10	3.7±0.2	0.51±0.04	670±0.32	99.20±0.59
F16	4.14±0.12	3.8±0.3	0.53±0.04	680±0.23	98.87±0.57
F17	3.8±0.12	3.9±0.3	0.58±0.02	665±0.16	98.77±0.68

***In-vitro* buoyancy studies**

On immersion of tablets of different formulations from F01 to F17 in 0.1N HCl solution at 37±5°C, the tablets floated, and remained buoyant without disintegration, the results of the buoyancy lag time (BLT) and total floating time

(TFT) were shown in Table No. 6.F01 toF17 buoyancy lag time (sec.) between 10 to 26 sec. and total floating time (hrs) 10 to 12 hrs.or more

Fig. 04 Buoyancy floating of formulated floating tablets

Table 06
Floating lag time of the gastro retentive PNZ tablets (F1-F17)

Run	Floating lag time (sec)	Buoyancy time (hrs)	Run	Floating lag time (sec)	Buoyancy time (hrs)
F1	19	10	F10	10	12
F2	13	10	F11	15	10
F3	22	11	F12	19	11
F4	26	10	F13	20	11
F5	11	11	F14	18	10
F6	25	10	F15	12	11
F7	25	11	F16	12	10
F8	12	11	F17	18	11
F9	21	11			

***In-vitro* Raft Strength measurement**

Raft Strengthof batches of PNZ floating tablet F01-F17 was measured by inhouse method value is shown in table no.06 among that formulation F10 found higher strength i.e5.42±0.40 gm.

***In-vitro* Acid Neutralizing Capacity**

In-vitro Acid Neutralizing Capacity of batches of PNZ floating tablet F01-F17 was measured. value is shown in table no.06 among that formulation F10 found higher Acid Neutralizing capacity i.e6.56±0.54

***In-vitro* dissolution study**

Drug release profile of batches of PNZ floating tablet F01-F17 was measured. value is shown in table no.06 after 12 hrs. F10 formulation of PNZ floating tablet shows sustain release of drug among the all batches

Table 06
Result of Raft Strength,Acid Neutralizing Capacity&Drug Release

Run	Raft Strength (g) Y_1	Acid Neutralizing Capacity (min) Y_2	Drug Release (%) Y_3
F1	4.89 ±0.58	5.47±0.61	92.54±2.87
F2	4.38 ±0.53	6.43 ±0.64	85.54±1.25
F3	3.85 ±0.62	5.56±0.67	88.14±1.25
F4	3.78 ±0.54	5.39±0.57	87.43±1.25
F5	4.34 ±0.48	6.40 ±0.58	85.92±1.78
F6	5.48±0.44	6.12±0.35	84.14±2.54
F7	5.44 ±0.39	6.47±0.26	86.34±2.54
F8	4.36 ±0.50	6.35±0.43	85.12±1.54
F9	5.22±0.35	5.74 ±0.52	81.87±2.65
F10	5.42 ±0.40	6.56±0.54	80.76±2.12
F11	5.06 ±0.30	5.38±0.45	85.76±2.12
F12	5.18 ±0.38	5.56±0.48	91.22±2.87
F13	4.95 ±0.52	5.21±0.43	82.34±2.87
F14	5.84 ±0.45	5.13±0.37	83.12±3.76
F15	4.35 ±0.45	6.41±0.39	85.85±1.12
F16	4.37 ±0.48	6.42±0.38	85.32±1.87
F17	5.10 ±0.33	5.64 ±0.51	90.23±3.65

Conclusion

From the experimental results, it can be concluded that the sodium bicarbonate and sodium alginate has shown a predominant effect on the buoyancy lag time, while HPMC have the predominant effect on drug release. Sodium bicarbonate has shown a predominant effect on the buoyancy lag time, while calcium carbonate shows effect on raft strength. Floating drug delivery of PNZ tablet has controlled release. In vitro release rate studies showed that the maximum drug release was observed F10 formulation up to 12 hours. From the study it is evident that promising controlled release tablets of PNZ can be developed. Further detailed investigations are required to establish efficacy of these formulations

References

1. Kamsali A, Eranti B, CH M, Manne R, Reddy S. Development and Optimization of Amoxicillin Floating Raft System to effectively treat Helicobacter pylori infection.
2. Verma A, Dubey J, Hegde RR, Rastogi V, Pandit JK. Helicobacter pylori: past, current and future treatment strategies with gastroretentive drug delivery systems. Journal of drug targeting. 2016 Nov 25;24(10):897-915.
3. Soni H, Ghulaxe C, Upadhyay S, Pillai S. Development and in vitro evaluation of an oral floating tablet of metronidazole. Journal of Drug Delivery and Therapeutics. 2018 Mar 14;8(2):83-6.
4. Bunlung S, Nualnoi T, Issarachot O, Wiwattanapatapee R. Development of raft-forming liquid and chewable tablet formulations incorporating quercetin

solid dispersions for treatment of gastric ulcers. Saudi Pharmaceutical Journal. 2021 Oct 1;29(10):1143-54.
5. YADAV S, YADAV S, KUMAR A, MISHRA A. Floating Drug Delivery System an Aid to Enhance Dissolution Profile of Gastric. Journal of Drug Delivery and Therapeutics. 2021 Nov 15;11(6):286-96.
6. Abbas G, Hanif M. Development and pharmacokinetic evaluation of alginate-pectin polymeric rafts forming tablets using box behnken design. Drug Development and Industrial Pharmacy. 2018 Dec 2;44(12):2026-37.
7. Niu J, Song K, Lim CW. On active vibration isolation of floating raft system. Journal of Sound and Vibration. 2005 Jul 6;285(1-2):391-406
8. Jeganath S. Recent Approaches of Gastroretentive Drug Delivery System–A Review. Asian Journal of Pharmaceutics (AJP): Free full text articles from Asian J Pharm. 2022 Mar 15;16(1).
9. Sanghavi RS, Agrawal O, Usman MR. Gastroretentive Drug Delivery System: An Overview. Research Journal of Pharmacy and Technology. 2022 Mar 24;15(3):1343-7.
10. Abou Youssef NA, Kassem AA, Magda AbdElsamea EM, Boraie NA. Development of gastroretentive metronidazole floating raft system for targeting Helicobacter pylori. International journal of pharmaceutics. 2015 May 30;486(1-2):297-305.
11. Kiran CV, Gopinath C. Development and evaluation of interpenetrating polymer network based superporous hydrogel gastroretentive drug delivery systems (SPH IPN-GRDDS). Materials Today: Proceedings. 2021 Jan 1;46:3056-61.
12. Tripathi J, Thapa P, Maharjan R, Jeong SH. Current state and future perspectives on gastroretentive drug delivery systems. Pharmaceutics. 2019 Apr;11(4):193.
13. El Nabarawi MA, Teaima MH, Abd El-Monem RA, El Nabarawy NA, Gaber DA. Formulation, release characteristics, and bioavailability study of gastroretentive floating matrix tablet and floating raft system of MebeverineHCl. Drug design, development and therapy. 2017;11:1081.
14. Panda S, Madhusrota P, Sethi G. Raft Forming System-A Novel Approach for Improving Gastric Retention. Journal of Pharmaceutical Sciences and Research. 2019 Dec 1;11(12):3761-72.
15. Prajapati VD, Jani GK, Khutliwala TA, Zala BS. Raft forming system—An upcoming approach of gastroretentive drug delivery system. Journal of controlled release. 2013 Jun 10;168(2):151-65.
16. Yousaf, Maria, et al. "Raft-forming polysaccharides for the treatment of gastroesophageal reflux disease (GORD): Systematic review." Journal of Applied Polymer Science 136.40 (2019): 48012.
17. Yerikala R, Pudi VP, Saravanakumar K, Vadhireddy S. Formulation and evaluation of floating drug delivery of cefotaxime using raft forming approach. Journal of Drug Delivery and Therapeutics. 2017 Jul 15;7(4):110-9.
18. Darwish MK, Abu El-Enin AS, Mohammed KH. Formulation, optimization, and evaluation of raft-forming formulations containing Nizatidine. Drug Development and Industrial Pharmacy. 2019 Apr 3;45(4):651-63.
19. Bunlung S, Nualnoi T, Issarachot O, Wiwattanapatapee R. Development of raft-forming liquid and chewable tablet formulations incorporating quercetin

solid dispersions for treatment of gastric ulcers. Saudi Pharmaceutical Journal. 2021 Oct 1;29(10):1143-54.
20. Abbas G, Hanif M. Development and pharmacokinetic evaluation of alginate-pectin polymeric rafts forming tablets using box behnken design. Drug Development and Industrial Pharmacy. 2018 Dec 2;44(12):2026-37.
21. Sharma R, Mishra A. Development and Characterization of Gastro Retentive Tablets of Clarithromycin for Antiulcer effect. Current Research in Pharmaceutical Sciences. 2022 Apr 6:40-5.
22. Lawal MV. Modified starches as direct compression excipients–effect of physical and chemical modifications on tablet properties: A review. Starch-Stärke. 2019 Jan;71(1-2):1800040.
23. Gulsun T, Cayli YA, Izat N, Cetin M, Oner L, Sahin S. Development and evaluation of terbutaline sulfate orally disintegrating tablets by direct compression and freeze drying methods. Journal of Drug Delivery Science and Technology. 2018 Aug 1;46:251-8.
24. Moganti M, Shivakumar HN. Oral raft forming in situ gelling system for site specific delivery of calcium. Journal of Drug Delivery Science and Technology. 2021 Feb 1;61:102113.
25. Mandal UK, Chatterjee B, Senjoti FG. Gastro-retentive drug delivery systems and their in vivo success: A recent update. asian journal of pharmaceutical sciences. 2016 Oct 1;11(5):575-84.
26. Raut SS, Shinde HA. In-situ raft forming system: a review. Int J Pharmacognosy. 2018;5(6):337-49.
27. Birajdar AA, Deshmukh MT, Shete RV. A Review on Gastro-Retentive Floating Microspheres. Journal of Drug Delivery and Therapeutics. 2021 Feb 15;11(1-s):131-8.
28. Wannasarit S, Mahattanadul S, Issarachot O, Puttarak P, Wiwattanapatapee R. Raft-forming gastro-retentive formulations based on Centellaasiatica extract-solid dispersions for gastric ulcer treatment. European Journal of Pharmaceutical Sciences. 2020 Feb 15;143:105204.
29. Najm AS, Ali WK. Preparation and in-Vitro Evaluation of Cinnarizine Raft Forming Chewable Tablets. Al-Mustansiriyah Journal of Pharmaceutical Sciences (AJPS). 2019 Aug 1;19(3):42-53

30. Huanbutta K, Sangnim T. Design and development of zero-order drug release gastroretentive floating tablets fabricated by 3D printing technology. Journal of Drug Delivery Science and Technology. 2019 Aug 1;52:831-7.
31. El Nabarawi MA, Teaima MH, Abd El-Monem RA, El Nabarawy NA, Gaber DA. Formulation, release characteristics, and bioavailability study of gastroretentive floating matrix tablet and floating raft system of MebeverineHCl. Drug design, development and therapy. 2017;11:1081.
32. Negi P, Gautam S, Sharma A, Rathore C, Sharma L, Upadhyay N, Tambuwala MM, Chellappan DK, Gupta G, Prasher P, Dua K. Gastric ulcer healing by chebulinic acid solid dispersion-loaded gastroretentive raft systems: preclinical evidence. Therapeutic Delivery. 2022 Feb;13(2):81-93.
33. Opeyemi OT, Adegbenro OO. Development and characterization of direct compressed matrix mini tablets of naproxen sodium. Universal Journal of Pharmaceutical Research. 2018;3(5):7-11.

34. Yeleken G, Kotłowska H, Sznitowska M, Golenia E, Ustenova G. Development of direct compressed loratadineminitablets. Journal of Pharmaceutical Sciences and Research. 2017 Apr 1;9(4):401.
35. Dai S, Xu B, Shi G, Liu J, Zhang Z, Shi X, Qiao Y. SeDeM expert system for directly compressed tablet formulation: A review and new perspectives. Powder Technology. 2019 Jan 15;342:517-27.
36. Arnawa, I.K., Sapanca, P.L.Y., Martini, L.K.B., Udayana, I.G.B., Suryasa, W. (2019). Food security program towards community food consumption. *Journal of Advanced Research in Dynamical and Control Systems, 11*(2), 1198-1210.
37. Gede Budasi, I. & Wayan Suryasa, I. (2021). The cultural view of North Bali community towards Ngidih marriage reflected from its lexicons. *Journal of Language and Linguistic Studies*, *17*(3), 1484–1497