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FORMULATION AND EVALUATION OF EFFERVESCENT FLOATING TABLETS OF TIZANIDINE HYDROCHLORIDE USING COMBINATION OF POLYMERS

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Keywords:

Gastroretension, Tara gum, Tizanidine, HPMC, Floating tablet

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ABSTRACT: The present study was carried out with an objective of formulation and evaluation of effervescent floating tablets of Tizanidine hydrochloride using combination of polymers. The floating tablets were prepared using HPMC and Tara gum as a combination of polymers. The tablet was prepared by direct compression method. The effect of polymer concentration was evaluated for gastroretention and sustained release action. Effervescence was produced by using sodium bicarbonate and citric acid which helps in reduction in floating lag time. The effect of polymer concentration on drug release and gastroretension has also been investigated. The results of *in-vitro* dissolution study shows that the drug formulation containing HPMC K15 M and Tara gum gives sustained action till 15 hr. Tara gum act as a sustained release polymer it sustains the dissolution of formulation by modifying the rheology of matrix. it is inert and non-toxic material. The formulation shows zero order kinetics. The matrix of formulation shows non-fickian diffusion. The present study shows that formulation gives sustained release action with muscle relaxant property till 15 hrs.

INTRODUCTION: The Oral route of administration is most appropriate and commonly acquired route of administration by most of the patient, and also it is easy to administer dosage form by this route. The Oral route of administration has been received more attention in pharmaceutical field. The mechanism of oral controlled drug delivery systems is diffusion, dissolution or combination of both mechanisms, which release the drug in a controlled manner in the Gastrointestinal Tract by understanding of drug profile data, such as dose, absorption properties and the quantity of drug necessary, we can determine the desired drug release rate from controlled release dosage form.

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Some drugs easily get absorbed from our gastrointestinal tract but due to shorter half-life these drugs eliminated from the blood circulation quickly. To overcome this problem the oral sustained release formulations has been manufactured, and these formulations liberate the drug slowly into the gastrointestinal tract which ultimately maintain a constant concentration of the drug in the serum for a longer duration of time. These systems are more advantageous in terms of administration and patient acceptance [1]. An ideal drug delivery system must possess two main properties *viz*. A single dose of medication for the whole duration of treatment, and it should deliver the active drug molecule directly at the site of action.

Controlled Release Drug Administration [2]: The objective of any drug delivery system is to provide a therapeutic amount of drug to the proper site of the body, to maintain the desired therapeutic drug

concentration that bring out the pharmacological action and to reduce the occurrence and the severity of unwanted adverse effects. To achieve this goal, it would be appropriate and more convenient to maintain a dosing frequency to once, or at most, a twice-daily regimen. The oral Controlled release technology had made it possible to release the drugs at a constant rate for longer duration of time. discovery of new polymeric materials which is suitable for prolonging the drug release, and enhancement in therapeutic efficiency and safety achieved by controlled drug delivery systems.

Advantages: Patient Compliance, reduced 'see-saw' fluctuation, reduced total dose, Improved efficiency of treatment.

Gastroretentive System [3]: The most practicable approach for achieving an extended and predictable delivery profile in the GI tract is to control the gastric residence time (GRT). The Dosage form with a prolonged gastric residence *i.e.*, gastro retentive dosage form (GRDFs), which provide us a novel and important therapeutic opportunity. The gastro retentive systems are excellent for drugs which absorbed through the stomach. E.g., Ferrous salts and antacids. Some Acidic substances such as aspirin may cause irritation on the wall of stomach when it comes in contact with it. Hence hydrodynamically balanced formulation may be excellent for the administration of such drugs. The gastroretentive systems are superior for drugs which locally act in stomach.

Factors Affecting the Gastroretentive System: Most of these approaches are influenced by various factors which directly affect bioavailability and efficacy of the gastro retentive system: Density – The gastric retention time is a function of buoyancy of dosage form which depends on the density.

Size: The dosage form with diameter < 7.5 mm is reported to have an increased GRT as compared with those with a diameter of 9.9 mm.

Shape of the Dosage form: The dosage form has tetrahedron and ring-shaped structure with a flexural modulus of 48 and 22.5 kilo pound per sq inch (KSI) are found to have better gastric retention 90% to 100% at 24 hours in comparison with other shapes.

Fed or Fasting State: The migrating myoelectric complex moves out the undigested material from the stomach and, if the administration timing of the dosage form coincides with that of the MMC, then in such case gastric retention time of the dosage unit can be assumed very short.

Nature of Meal: The feeding of polymers which are indigestible or salts of fatty acid can change the pattern of motility of the stomach to a fed state, as a result there is decrease in the gastric emptying rate and drug release become prolonged.

Caloric Content: The retention time can be enhanced by 4 to 10 h with a meal that rich in fats and proteins.

Frequency of Feed: The retention time in gastric cavity can be increased over 400 minutes when successive meals are given instead of single meal due to the low frequency of migrating myoelectric complex.

Gender: Mean fugitive gastric retention time in males (3.4±0.6 hrs.) is less when compared with their age and race, and in females' counterparts (4.6±1.2 hours), regardless of the weight, height and body surface).

Age: Elder people, above the age of 70, have a remarkable longer gastric retention time. Posture – gastric retention time can vary between upright ambulatory and supine states of the patient.

Biological Factors: Certain disease condition like diabetes and Crohn's disease

Floating Drug Delivery Systems [4, 5]: These systems have bulk density lower than the density of gastric fluids and due to this dosage form become buoyant inside the stomach without altering the rate of gastric emptying for a prolonged duration of time.

While the formulation floats upon the gastric contents, the active drug molecule is discharged slowly at the desirable rate from the system, and after the complete release of drug molecule; the remaining material is emptied from the stomach. The floating drug delivery system is divided into two types: Effervescent Systems & Non-effervescent Systems.

Effervescent (Gas-generating) Systems [6]: These floating delivery system employs matrices from swelling polymers and effervescent component like ($NaHCO_3$) sodium bicarbonate, citric acid or tartaric acid. These matrices having chambers of liquid compound that gasify at body temperature.

The matrices are prepared such that when they come in contact with stomach fluid then carbon dioxide is liberated and retained entrupted in hydrocolloid gel, these leads to an upward drift of the formulation and maintained in the floating condition. A single layer tablet can be produced by intimately mixing the CO_2 generating component in tablet matrix. It retains the formulation at the region of absorption and thus increases the bioavailability [7].

Tizanidine: A Muscle Relaxant is a centrally acting alpha-2 adrenergic agonist. Which is responsible for muscle relaxation. Tizanidine, is an a-adrenoceptor agonist with both spinal and supraspinal actions that result in myotonolytic and antinociceptive activity. After oral administration, tizanidine absorbed completely. approximately 30% Tizanidine bound to plasma proteins. Tizanidine drug possess half-life of approximately 2.5 hrs. around 95% amount of an administered dose gets metabolized. The bioavailability of drug tizanidine is predicted to be 21%. The elimination half-life ranges from 2.1 to 4.2 hours in patients with normal renal function. So, due to all this reason a sustained release dosage form is more advantageous than conventional dosage forms[8].

MATERIAL & METHODS:

Materials: Tizanidine HCl were used as active ingredient and obtained as a gift sample from Wilcure Remedies Ahmadabad. Tara gum and HPMC were used as polymer Tara gum were obtained from Pellagic food ingredients Pvt.Ltd. Bangalore. Sodium bicarbonate and Citric acid used as effervescent agent. The other ingredient used are Lactose monohydrate, Talc, Magnesium Stearate [9].

Methods: Preformulation studies were performed on the drug, which included melting point determination, solubility and compatibility studies.

Compatibility Studies: Physical compatibility: The drug and excipient are mixed together and kept for one month to check physical changes in the mixture of drug and excipients.

Compatibility by FTIR: Compatibility with drug and excipients was confirmed by carried out I R studies. In the present studies the potassium bromide disc (pellet) method was employed. Under pressure the potassium bromide melts and seals the sample into the matrix. The resulting KBr pellet is inserted in the instrument [10].

Identification of Tizanidine HCl: Identification test is done by Liquid chromatography. Test solution preparation: 25 mg of the substance (Tizanidine) under examination dissolved in 50.0 ml of the mobile phase. Dilute 10 ml of the sol. to 50.0 ml of the same solution. Reference solution: A 0.01 % w/v solution of Tizanidine hydrochloride RS in the mobile phase. Which indicating purity of the drug sample.

Chromatographic system: A stainless steel column 15 cm × 4.6 mm packed with octyl silane bonded to the porous silica (5µm). Mobile phase: a mixture of 50 volumes of the buffer solution prepared by dissolving 6.8 g of monobasic potassium phosphate in 1000 ml of water adjusting the pH to 7.5 with 5.3M potassium hydroxide and - 50 volumes of acetonitrile. Flow rate: 1 ml per minute. Spectrophotometer set at 230 nm. Injection volume: 10µl [11].

Evaluation of Powder Blend:

Angle of Repose: The angle of repose of powder blend was determined by funnel method. Angle of repose was calculated using following equation.

$$\tan ø = h/r$$

Where, h and r are the height and radius of the powder cone.

Bulk Density & Tapped Density: BD and TD were calculated by using the following equations. BD= Weight of powder blend / Untapped Volume of the packing TD=Weight of the powder blend / Tapped Volume of the packing [12].

Compressibility Index: The Compressibility index of the powder blend was determined by Carr's compressibility index. This test is used to evaluate BD and TD of a powder blend. And also, the rate at

which it packed down. The formula for Carr's Index is as below:

Carr's Index (%) = (Tapped Density-Bulk Density) x 100 / TD

Hausner's Ratio: The hausner's ratio is a value that is corelated with the flowability of a granular material or powder material [13].

Preparation of Gastroretentive Dosage form: Floating tablet containing Tizanidine hydrochloride were manufactured by direct compression method by using variable concentration of polymers with sodium bicarbonate and citric acid.

Different tablets formulations were prepared through direct compression technique. All the powder material were passed through 60 mesh sieves. Required quantity of drug, and polymer were mixed thoroughly.

Talc and stearic acid, lactose was finally added as a glidant and lubricant respectively. The blend was directly compressed (9 mm diameter punches) using tablet compression machine. Each tablet contains 8 mg of Tizanidine HCl, polymers using 23 factorial model and other pharmaceutical ingredients as listed in table 6.5 in each section [14].

TABLE 1: COMPOSITION OF TIZANIDINE HCL GRDDS TABLETS

Ingredients	FT1	FT2	FT3	FT4	FT5	FT6	FT7	FT8
Tizanidine HCl	**8**	**8**	**8**	**8**	**8**	**8**	**8**	**8**
HPMC K15M	60	-	-	120	30	60	30	60
Tara gum	-	60	120	-	60	30	30	60
Sodium bicarbonate	60	60	60	60	60	60	60	60
Citric Acid	30	30	30	30	30	30	30	30
Lactose	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Stearic Acid	3	3	3	3	3	3	3	3
Talc	6	6	6	6	6	6	6	6
Total (mg)	250	250	250	250	250	250	250	250

Weight Variation Test: The test was performed according to the official method given in pharmacopoeia. To study the average wt. 20 tablets were taken from the prepared batch and weighed it is divided by 20 for weight variation test Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation.

Drug Content Determination: 5 tablets were weight individually and then powdered. The tablets were weighed individually and powdered. The powder equivalent to average weight of tablets was taken and drug was extracted in 0.1 N HCl, the drug content was determined measuring the absorbance at 320 nm after suitable dilution using a Shimadzu UV double beam spectrophotometer.

Uniformity of Contents: 30 tablets were selected randomly. 10 of them assayed individually using UV analytical method[15].

Hardness Test: Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. 3 tablets were picked randomly picked; the hardness was determined by Monsanto Hardness tester it is expressed in kg/cm^2.

Thickness: The thickness of the tablets was determined by using vernier calipers. Five tablets were used, and the average values were calculated.

Friability Test: The friability of tablets was determined by the help of Roche Friabilator.

The % friability was then calculated by using formula:

$$\%F = 100\ (1\text{-}W_0/W)$$

% Friability of tablets less than 1% are considered acceptable [16].

Tablet Density: Density of tablet is an important parameter for floating tablets. The tablet floats when its density is less than that of 0.1N HCl (1.004). The density was obtained by using following formula.

$$V = (r2h\ d = m/v)$$

v = Volume of tablet (cc) r = tablet radius (cm) h = thickness of tablet crown (cm) m= Mass of tablet.

***In-vitro* Buoyancy Studies:** The *in-vitro* buoyancy was determined by floating lag time method.

The time required for the tablets to rise from the surface or bottom of the beaker to float is known as floating lag time or the time taken for dosage form to emerge on surface of the medium is called Floating Lag Time (FLT) or Buoyancy lag time (BLT) for measuring FLT, we take 0.1 N HCl in a 250 ml beaker The tablets were placed. The time between introduction of dosage form in the liquid and its buoyancy in 0.1 N HCl and the time up to which the dosage form remain buoyant were measured. The total duration of time by which dosage form remain buoyant is called Total Floating Time (TFT) [17].

***In-vitro* Dissolution Studies:** The rate of release of Tizanidine HCl from floating tablets was calculated using The United States Pharmacopoeia (USP) XXIV dissolution testing apparatus II (paddle method). The test was performed using 900 ml of 0.1 N HCl, at 37º C ± 0.5 and 75 rpm. A sample (5 ml) of the solution was withdrawn from the dissolution apparatus after each hour for 15 hours, and the sample were replaced with fresh dissolution medium. The sample diluted to a suitable concentration with 0.1N HCl. Absorbance of this solution then measured at 320 nm using a Shimadzu UV-1601 UV/V is double beam spectrophotometer. Cumulative percentage drug release was calculated using the equation of standard curve [18].

Swelling Index: The swelling index of tablets was examined using 0.1 N HCl (pH 1.2) at room temperature. The swollen weight of the tablet was calculated at predetermined time intervals. The swelling index was calculated using the formula:

$$\text{Swelling index } WU = (W1 - W0) \times 100\ W0$$

Where, Wt. = Weight of tablet at time t. W0 = Initial weight of tablet [19]

Effect of Hardness on Buoyancy: We have selected Formulation FT8 for study the effect of hardness on buoyancy lag time.

The tablets of batch 10 were compressed at different compression pressures to get the hardness of 5kg/cm^2, 6kg/cm^2, 7kg/cm^2, 8kg/cm^2 and 9kg/cm^2 [20].

Stability Study: Gastro retentive tablets of Tizanidine HCl formulated in our present study were subjected to accelerated stability studies. Stability studies of the prepared formulations were performed at ambient humidity conditions, 30 °C ± 2 °C & 65% ± 5% RH, and 40°C ± 2 °C & 75% ± 5% RH for a period up to 3 months. The samples were withdrawn after periods of 1 month, and 3 month and were analyzed for its appearance, hardness, friability, floating time, drug content and *in-vitro* release [21].

RESULT AND DISCUSSION: Gastroretentive dosage form (Hydrodynamically balanced tablets) of Tizanidine HCl were prepared and evaluated for its local action and bioavailability in the present study 8 batches with variable concentration of polymers were prepared and evaluated for physio-chemical parameters, *in-vitro* release study, in vitro buoyancy studies and stability studies.

Evaluation of Tablet:

Pre-compression Parameters:

Angle of Repose (θ): The angle of repose for the formulated blend was carried out and the results obtained are in the range 18^0.72' to 27^0.61'.

Compressibility Index/Carr's Index: Compressibility index was carried out, it found between 10.50% to 15.96%. indicating the powder blend have the required flow property.

Post-compression Parameters:

Shape of the Tablet: Microscopic examinations of tablets from FT1 to FT8 were found to be circular in shape without cracks.

Hardness Test: The measured hardness of tablets of each batch ranged between 4.3 to 5.6 kg/cm^2.

Friability Test: The % friability was less than 1% in all the formulations ensuring that the tablets were mechanically stable.

Average wt. &Weight Variation Test: All the prepared (FT1 to FT8) tablets passed the weight variation test and the percentage weight variation was obtained within the pharmacopeial limits of ± 5% of the weight. The average weight of all the tablets were found to be uniform with low standard deviation values [22].

Tablet Density: When tablet comes in contact of the test medium, because of swellable polymers

tablet gets expand and because of effervescent agent $NaHCO_3$ there was liberation of CO_2 gas. The density decreased due to this expansion and upward force of CO_2 gas generation. This plays an important role in ensuring the floating capability of the dosage form [23]. To obtain a good floating property in the stomach, the density of the tablets should be less as compare to the density of the gastric contents (1.004g/cm^3). The formulations FT1-FT8 density were found to be less than that of the gastric content.

Drug Content Uniformity: The percentage of drug content for FT1 to FT8 was obtained between 97.01% to 99.81%. The drug content of optimized batch FT8 was also found uniform and complies with the limits of IP [24].

Compatibility Studies: Physical Compatibility: All the physical mixtures showed no colour and odour, hence showed physical compatibility between drug and polymer. In our present study, it has been observed that there is no chemical reaction between Tizanidine HCl and the polymers used. It was observed that there have no changes in these main peaks in IR spectra of mixture of drug and polymers, which show there were no physical interactions between drug and polymers. This indicates that the drug was compatible with the formulation components [25].

TABLE 2: TYPES OF VIBRATION AND PEAK

Types of Vibration	Observed peak of functional groups (cm^{-1})
Secondary amine N-H stretch	3244.73
Secondary amine N-H bending	3079.71
C=C aromatic ring stretch	1643.18 &1403.70
Aromatic C-Cl stretch	1074.71
C-N stretch	1283.22 & 1191.75
C-H of Imidazole ring	2843.18
C-N-C	1191.75
Aromatic N	818.68
Ring bending strong	667.57

TABLE 3: EVALUATION OF PHYSICAL PARAMETERS OF FLOATING TABLETS

Tablets Batch	Weight variation test (%)	Friability (%)	Hardness (kg/cm^2)	Thickness (mm)	Drug content (%)
FT1	± 3.01	0.92	5.6 ±0.47	3.08 ± 0.20	98.12
FT2	±3.52	0.72	4.5 ±0.63	3.16 ± 0.01	97.01
FT3	±1.86	0.86	5.1 ±0.03	3.12 ± 0.06	98.01
FT4	±2.66	0.82	5.6 ±0.83	3.16 ± 0.01	97.04
FT5	±2.11.	0.78	4.3 ±0.83	3.15 ±0 .10	97.11
FT6	±1.89	0.81	5.1 ±1.27	3.10 ± 0.12	99.55
FT7	±2.56	0.96	5.4 ± 0.03	3.11 ±0.06	99.01
FT8	±2.04	0.75	4.4 ±0.83	3.20 ± 0.01	99.81

***In-vitro* Dissolution Study:** All the ten formulations of prepared floating tablets of Tizanidine HCl were subjected to in-vitro release studies these studies were carried out using dissolution apparatus, 0.1N HCl (pH 1.2).

The results obtaining *in-vitro* release studies were plotted in different model of data treatment as follows:

1. Cumulative % drug released vs. time (zero order rate kinetics)
2. Log cumulative percentage drug retained vs. time (First Order rate Kinetics)
3. Log cumulative percentage drug released vs. square root of time (Higuchi's Classical Diffusion Equation)
4. Log of cumulative percentage release Verses log time (Peppa's Exponential Equation) the plot of cumulative percentage drug released as a function of time for different formulations. The *in-vitro* release of all 8 batches of floating tablets showed the release with an initial effect.

The values of *in-vitro* drug release were attempted to fit into various type of mathematical models.Peppas- korsmeyerequation was given as:

$$\% R=kt$$

Where, R= drug release, K=constant, n=slope t=time.

The 'n' values can be used to characterize diffusion release mechanism.

This model is widely used when the release mechanism is not well known or when more than one type of release phenomenon gets involved [26]. The values of regression coefficients for formulation FT8 are given in the **Table 4.**

TABLE 4: VALUES OF REGRESSION COEFFICIENTS

Kinetic Model	Intercept	Slope	R2
Zero-order plot	20.11	5.714	0.978
First-order plot	1.425	0.0514	0.958
Higuchi plot	1.124	0.264	0.977
Peppas-korsmeyer	1.294	0.672	0.943

TABLE 5: EFFECT OF DIFFERENT POLYMERS ON DRUG RELEASE BY PADDLE METHOD

	Cumulative % drug release							
Time (hrs.)	FT1	FT2	FT3	FT4	FT5	FT6	FT7	FT8
0	0	0	0	0	0	0	0	0
1	40.63	34.69	29.44	36.33	20.22	23.09	27.66	19.81
2	51.55	43.63	40.78	51.02	24.09	31.86	40.30	28.74
3	61.44	54.52	45.23	59.98	32.34	39.32	52.96	37.55
4	70.40	64.45	52.45	67.65	40.76	46.06	59.49	42.62
5	81.41	69.40	60.62	73.12	46.06	56.35	66.71	48.17
6	87.01	76.36	70.78	80.08	52.98	61.66	76.34	55.12
7	97.31	82.31	77.23	89.32	63.50	69.28	87.07	64.45
8	-	89.26	83.11	94.01	68.74	78.22	94.18	69.41
9	-	93.21	89.24	99.68	75.22	86.11	98.09	76.36
10	-	97.24	92.11	-	80.19	94.13		82.39
11	-	-	94.36	-	86.18	99.23		86.26
12	-	-	100.18	-	98.78	-		88.81
13	-	-	-	-	-	-		92.61
14	-	-	-	-	-	-		95.29
15	-	-	-	-	-	-		99.81
FLT (sec.)	126	140	151	119	134	106	114	46
TFT (sec.)	7	10	12	9	12	11	9	>15

Swelling Index: Swelling study was performed for all the batches from FT1 to FT8 for 15 hr. The results of swelling index were tabulated in **Table 6.** From the results of swelling index, it is concluded that swelling of tablet increases as the time passes because the polymer absorbs water due to hydrophilicity of polymer. First the outermost hydrophilic polymer gets hydrates and swells and a gel like barrier are formed on the outer surface. As the gelatinous layer dissolves progressively and/or is dispersed, upon hydration, swelling occurs and this process is continuous towards new exposed surfaces, thus maintaining the integrity of the dosage forms [1, 27].

TABLE 6: SWELLING INDEX

Time (hr)	FT1	FT2	FT3	FT4	FT5
1	28	34	26	20	25
3	48	49	34	34	39
6	60	52	59	53	54
9	-	66	67	71	69
12	-	-	76	-	78

***In-vitro* Buoyancy Study:** On immersion in 0.1N HCl solution pH (1.2) at 370°C, the tablets floated, and remained buoyant without disintegration. From the results it is concluded that the batch containing only HPMC polymer showed good floating lag time (FLT). Formulation containing HPMC K15 & Tara gum showed good FLT of 46 sec. This may be due to the nature of polymer and gas generating agent, which were kept constant in the present study. The gas generated cannot be entrapped inside the gelatinous layer, and it escapes leading to variation in FLT and TFT [28].

Effect of Hardness on Buoyancy: -The effect of hardness on floating lag time for batch FT8 was studied. Buoyancy of the tablet were influenced by

both the swelling of the hydrocolloid particle on surface when it comes in contact of the gastric fluid which in turn results in an increase in the bulk volume and porosity. The buoyancy lag time will increase when the hardness increases, at high compression, reduction in porosity of tablets occurs, the compact hydrocolloid particles present on the tablet surface cannot hydrate rapidly [29].

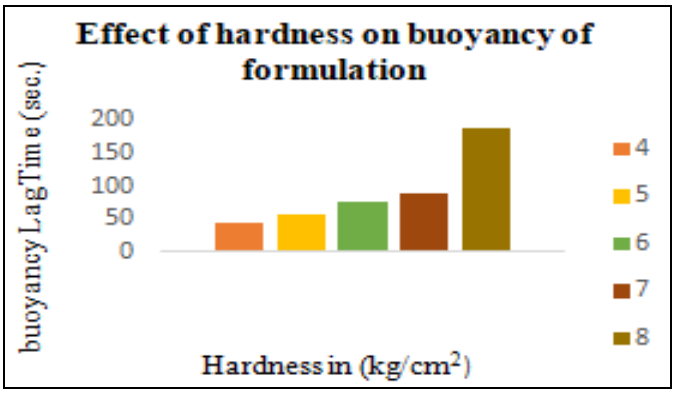

FIG. 1: EFFECT OF HARDNESS ON BUOYANCY

Stability Studies: Gastro retentive tablets of Tizanidine HCl formulated in the present study were subjected to accelerated stability studies. Stability studies of the prepared formulations were performed at ambient humidity conditions, at 30 °C ± 2°C & 65% ± 5% RH, at 40°C ± 2°C & 75% ± 5% RH for a period up to 3 months. The samples were withdrawn after periods of 30 days, and 3 month and were analyzed for its appearance, hardness, friability, floating time, drug content and *in-vitro* release. The results revealed that no significant changes in appearance, floating time, drug content, hardness, friability, and *in-vitro* release for FT8 formulation. When it stored at the different storage condition. However, there was slight variation in *in-vitro* release when it is stored at room temperature, there was no change when it is stored at 0ºC.

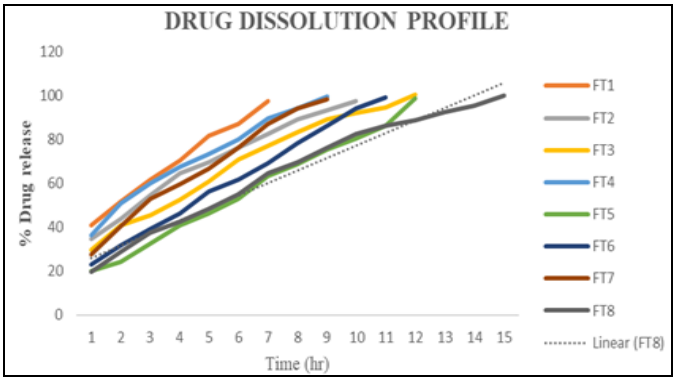

FIG. 2: DRUG DISSOLUTION PROFILE OF BATCH F1-F8

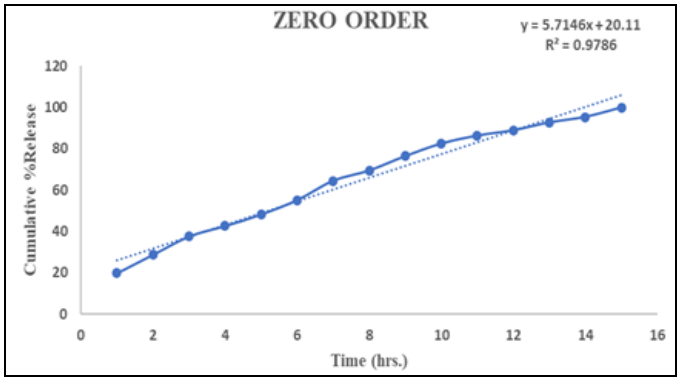

FIG. 3: ZERO ORDER KINETICS OF OPTIMIZED BATCH

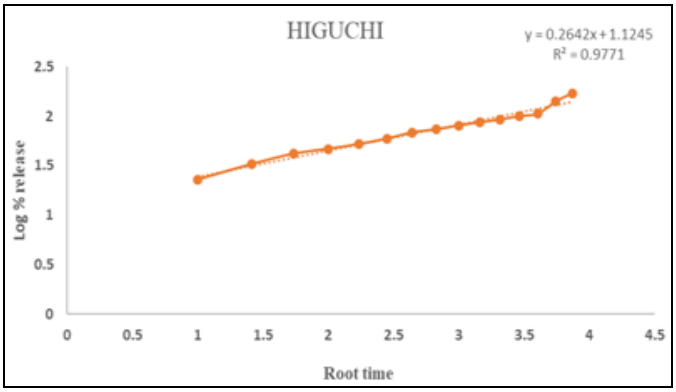

FIG. 4: HIGUCHI CURVE OF OPTIMIZED BATCH

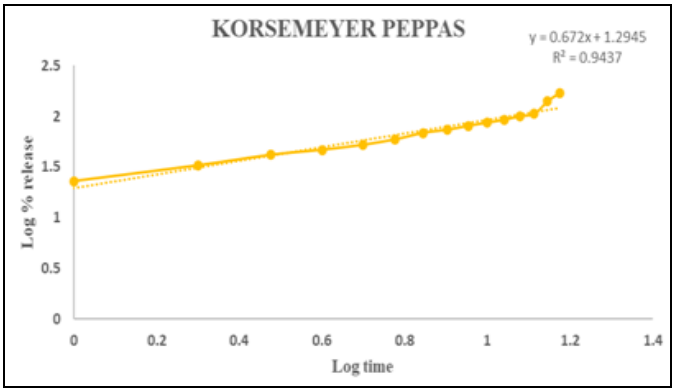

FIG. 5: KORSEMAYER-PEPPAS CURVE OF OPTIMIZED BATCH

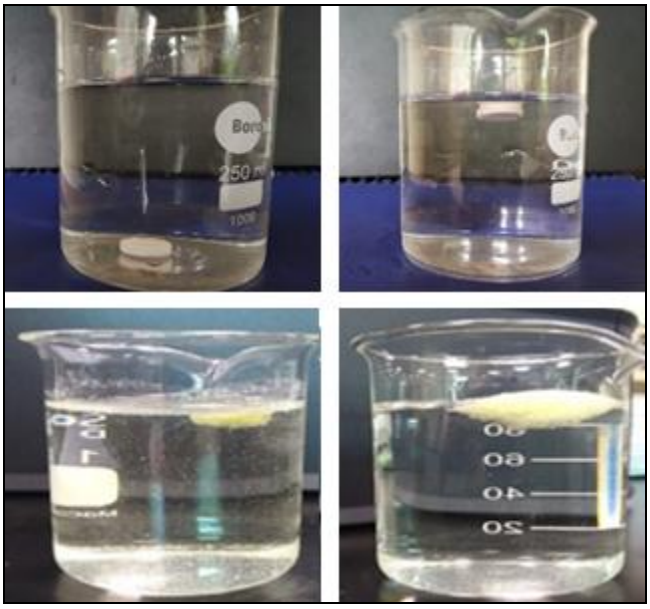

FIG. 6: *IN-VITRO* BUOYANCY STUDY OF OPTIMIZED BATCH

CONCLUSION: The floating tablet of Tizanidine HCl were prepared by direct compression method using different concentration of polymers. By making floating tablet we canprolong gastric retention time and increase efficacy of the dosage form. Different kinds of matrix forming polymers like HPMC K15M, Tara gum, used for the study [30]. The erosion of tablet occurs when it comes in contact of the release medium. The drug diffusion, polymer swelling, and tablet erosion resulting release pattern of drug material from the dosage form Tara gum is used as a natural and edible gum. the gum had stable viscosity over wide range of pH range (3-11). Tara gum to make tablet matrix more viscous which helps in sustained release of drug. The use of Tara gum as a controlled release carrier in the formulation of gastroretentive controlled release tablet due to swelling of gum [31].

If we use Tara gum in combination it increases floating time of formulation thus showing good gastroretentive property. It was also found that the tablet formulations released more than 90 % drug in 15 hours as desired. Gastro retentive (low density) tablets of Tizanidine were prepared using polymer which not only imparted buoyancy to the formulations but also reduced floating lag times to a great extent. The other most important thing that can be concluded from the study was that the formulation and process variables play important role in the release behavior of the tablet matrices [32]. Fast release of the drug from the hydrophilic matrix was mostly due to faster dissolution of the water-soluble drug from the core and its diffusion out of the matrix that fast release of drug retarded by use of Tara gum. Thus, it is summarized and concluded that HPMC K15M, Tara gum can be successfully used in formulation of Tizanidine HCl sustained release gastro retentive floating drug delivery system [33].

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REFERENCES:

1. Jain NK: Progress in Controlled and Novel Drug Delivery System.1st. New Delhi, CBS Publisher 2019; 76.
2. Vyas SP and Khar RK: "Controlled drug delivery: concepts and advances". 2nd ed. Delhi, India: Vallabh Prakashan 2019; 156-157.
3. Bechgaard H: "Design of controlled release product as adopted to gastrointestinal product and transit time". Alfred Benzon Foundation: Copenhagen, Denmark 1981; 67-79.
4. Singh BM and Kim KH: "Floating drug delivery systems: an approach to oral controlled drug delivery *via* gastric retention". J Control Rel 2000; 63: 235-259.
5. Tomar A, Singh A, Gupta A and Singh S: "Floating drug delivery systems. A review Remington's. The Science and Practice of Pharmacy 23rd Edi 20211; 6: 903-913.
6. Tripathi KD: Essentials of medical Pharmacology (8thedition), Jaypee Brothers medical (P) Ltd; New Delhi India 2018.
7. Bramhankar DM and Jaiswal SB: "Biopharmaceutics and Pharmacokinetics A Treatise", (2ndedn) Vallabh Prakashan, Delhi 2005; 335-337.
8. Arora S, Ali J, Abuja A, Char RK and Baboota S: "Floating drug delivery systems: A Review". AAPS Pharm Sci Tech 2005; 06(03): 372-390.

9. Aulton ME and Wells TI: "Pharmaceutics: The Science of Dosage Form Design." London, England, Churchill Livingston 1998; 247.
10. Government of India, Ministry of health & Family welfare; "Indian Pharmacopoeia 2018". 8th edition published by the Indian pharmacopoeia commission, Ghaziabad.
11. Chien YW: Novel Drug delivery system. 2nd Edition Revised and Expanded 2019; 1-2.
12. Martin A: "Micromeritics, In: Martin A", ed. Physical Pharmacy. Baltimores, MD: Lippincott Williams and Wilkins 2001; 423-454.
13. Fell JT: Targeting of drugs and delivery systems to specific sites in the gastrointestinal tract. J Anat 1996; 189: 517-519.
14. Robinson J and Lee R: In Controlled drug delivery. 2nd Edition 1987; 418.
15. Liberman and Lachman L: The Theory and Practice of Industrial Pharmacy", 3rd Edition, Varghese Publication House 171, 293.
16. Roop K. Khar, Alka Ahuja and Javed Ali and Jain NK: Eds., "Controlled and Novel Drug Delivery", (1stedn), CBS publication, Delhi 2011; 353-365.
17. Chien YW: "Novel Drug Delivery system", (2nd ed.), Marcel Dekker 1992; 139-196.
18. Streubel A, Siepmann J and Bodmeier R: "Floating matrix tablets based on low density foam powder: effects of formulation and processing paramete3rs on drug release 2003; (18): 37-45.
19. Arora S, Ali J, Ahuja A and Khar K: "Floating Drug Delivery systems review", Department of Pharmaceutics, Faculty of Pharmacy, Hamdard University, New Delhi, India.
20. ICH Q1A (R2), "Stability Testing Guidelines, Stability testing of a new drug product and new drug substance".
21. Cooper J and Gun C: Powder Flow and Compaction. Inc Carter SJ, Eds. Tutorial Pharmacy. New Delhi, hidix CBS Publishers and Distributors 1986; 211-233.
22. Kishan V and Yambadi S: "Drug Excipient Compatibility, Development and Preliminary Clinical Studies of Tizanidine Hydrochloride Floating Drug Delivery System" https://doi.org/10.37285/ijpsn.2021.14.1.9
23. Loyd V, Allen and Howard C: Ansel; "Pharmaceutical dosage form and drug delivery system"; Wolters Kluwer India pvt.ltd.10th edition; 139-140
24. Khar K, Vyas SP and Ahmad J: "The theory and practice of Industrial Pharmacy "fourth edition CBS publisher 2020; 402.
25. Pramanik S and Thakkar H: "Development of solid self-micro emulsifying system of tizanidine hydrochloride for oral bioavailability enhancement: *in-vitro* and *in-vivo* evaluation". AAPS Pharm Sci Tech 2020; 21: 182. https://doi.org/10.1208/s12249-020-01734-9.
26. Iglesias N, Galbis E, Azogil L and Benito E: "In depth study into polymeric materials in low density gastroretentive formulations. Pharmaceu 2020; 12(7): 636.
27. Sowjanya M, Debnath S and Lavanya P: Thejovathi R. Polymer used in the designing of controlled delivery system. Res J of Pharma & Technology 2017; 10(3): 903.
28. Tiwari R: Controlled release drug formulation in pharmaceuticals: A study on their application and properties. World Journal of Pharmaceutical Research, 2016; 5: 1704-1720.
29. Roche RC, Sheskey PJ and Weller PJ: "Handbook of pharmaceutical excipients", 4th edition, Pharmaceutical Press, London 2003.
30. Choudhary PD and Pawar HA: "Recently Investigated Natural Gums and Mucilages as Pharmaceutical Excipients: An Overview. J Pharm (Cairo). 2014; 2014: 204849. doi: 10.1155/2014/204849. Epub 2014 Apr 7. PMID: 26556189; PMCID: PMC4590793.
31. Wu Y, Ding W, Jia L and He Q: The rheological properties of Tara gum (*Caesalpinia spinosa*). Food Chem. 2015; 168: 366-71.Doi: 10.1016/j.foodchem.2014.07.083. Epub 2014 Jul 23.
32. Tizanidine HCl http/www.wiekipedia.com

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