Development and *In-Vitro* Characterization of Tizanidine HCI Floating Tablet using Various Grades of HPMC Polymer

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ABSTRACT:
The goal of the current work was to create and characterise floating tablets of Tizanidine HCl by various grade of HPMC polymer. Total nine formulation were formulated using various concentration of HPMC. The impact of several grades of HPMC (HPMC K4M, HPMC K15M, and HPMC K100M) upon floating lag time as well as drug release is discussed in the current research effort. In pre formulation study the drug and polymers are subjected to FTIR study. Pre-compression as well as post-compression parameters were assessed for each batch, and each batch's findings were found to be within the acceptable range. The total floating time for all formulations exceeded 12 hours and the floating lag time was good. At the end of 8 hours, the optimised batch (F9) displayed 99.53% drug release. Optimized formulation followed by anamolous nonFickian diffusion follow dominantly with zero order release
Keywords: Tizanidine HCl, Floating tablet, HPMC K100M.

INTRODUCTION

Due to its convenience of administration, inexpensive therapy, patient compliance, and versatility in formulation, oral medication delivery is the most favoured method of drug delivery. Design of Systems for delivering oral contraceptives should prioritise achieving more consistent and increased bioavailability[1]. Control release denotes the ability to predictably and repeatedly regulate drug release and drug concentration in the target tissue. andoptimizationofthe therapeutic effect ofdrug bycontrolling its release in the bodywith lower and less frequent dose[2]. Since these dosage forms can stay in the stomach and intestines for extended periods of time, the gastric retentive drug delivery method targets site-specific release of drugs within the upper part of the stomach for local or regional anaesthesia. systemiceffects[3]. Tizanidine isdrugthat isuse as a musclerelaxant. It isa centrallyactingα- 2 adrenergic agonist. It is used to treat spasms of the muscles, cramps, and stiffness brought on by conditions this as multiple sclerosis (MS), spastic deplegia, back pain, or some other spinal or central nervous system injuries4. Tizanidine hydrochloride is a kind of prokinetic drug that can be taken orally and promotes or restores motility across the entire body. gastrointestinaltract. Tizanidine HCl is use as musclerelaxant help relieve muscle spasm, cramping, and stiffness. Drug has a short biological half-life and is best absorbed from the gastrointestinal tract and less taken from the lower section of the GIT. 2.5 hr[5]. It is prefer to take2-3 by creating floating tablets of Tizanidine HCl which enable sustained drug release, the frequency of dose is thereby reduced. andbetterpatient'scompliance[6]

MATERIALS

Formulation	Tizanidine(mg)	HPMC K4M (mg)	HPMC K15M (mg)	HPMC K100M (mg)	Sodium-bicarbonate (mg)	MCC (mg)	Magnesium-Stearate (mg)	Citric acid (mg	Talc (mg)	Total(mg)
F1	13.7	40	----	----	50	78.32	4	10	4	200
F2	13.7	60	----	----	50	78.32	4	10	4	200
F3	13.7	80	----	----	50	78.32	4	10	4	200
F4	13.7	----	40	----	50	78.32	4	10	4	200
F5	13.7	----	60	----	50	78.32	4	10	4	200
F6	13.7	----	80	----	50	78.32	4	10	4	200
F7	13.7	----	----	40	50	78.32	4	10	4	200
F8	13.7	----	----	60	50	78.32	4	10	4	200
F9	13.7	----	----	80	50	78.32	4	10	4	200

Tizanidine HCl was obtained as gift sample from JPN Pharma, Mumbai. HPMC of different gradesobtained asgift sample fromColorconAsia,Sodium bicarbonate,microcrystalline cellulose,citric acid was obtained as gift sample from Finer Chemicals Ltd, Ahmedabad. Magnesium stearate was gifted from Acme Chemicals, Mumbai

METHOD

PreparationofTizanidineHClFloatingTablets

For formulation of floating tablet of Tizanidine Hcl, HPMC K4M, HPMC K15M, HPMC K100M were chosen as matrix forming polymers, Magnesium stearate and talc were used as lubricant[7]. Sodium bicarbonate and citric acid was added gas generating agent. The %of drug Tizanidine Hcl, lubricant (talc and magnesium stearate) and. The % of HPMC K4M, HPMC K15M, HPMC K100M and MCC were varied. Each tablet contained 13.7 mg of drug. The formulas of all the 9 batches have been given in the Table no .1

Table:1FormulationTable of TizanidineHClFloatingTablets

Drug-ExcipientsCompatibilityStudy

Drug excipient play important role in the release of drug from the dosage forms. Fourier transforminfrared spectroscopyhas beenusedtostudythephysicalandchemical interactions between drug and the excipients used. Fourier transform infrared spectra of tizanidine HCl, HPMC K100M and sodium bicarbonate were recorded using KBr mixing method[8].

Evaluation Study for Floating Tablets

WeightVariationTest

The average weight of the 20 tablets was determined after a random selection and weighting. Just a couple of each person's weights should differ over 10 percent from the average weight..

Friability

Foreachformulation,preweighedtabletsample(10tablets)wereplacedintheRochefriabilatorIt is subsequently turned 100 times. The tablets were taken out and weighed again. It is permissible for conventionally compressed tablets to lose between 0.5 and 1% of their weight..

Hardness

HardnessoftabletwasdeterminedusingMonsantohardnesstester.

ContentUniformity

The 20 tablets were broken up, and 10 mg of the medication in powder form was then added to 100 ml of 0.1 N HC1 in a volumetric flask. Following the appropriate dilution, the resultant solution was examined at 320 nm with a dual beam UV-Vis spectrophotometer. A calibration curve was employed to determine the drug's content..

Swelling index study

The swelling of the tablets takes place due to the ability of polymers to hydrate and swell. The swelling characteristics of the tablet was determined by immersing the tablet in a beaker containing 100 ml of 0.1 N HCl and stirred at 37^0C. After the predetermined time intervals, tablet was withdrawn, blotted with tissue paper to remove the excess water and weighed. Swelling index (SI), expressed as percentage, was calculated using following equation

$$\text{Swelling Index\%}=\frac{Weight\ of\ swollen\ Tablet-Initial\ weight\ of\ Tablet}{Initial\ weight\ of\ Tablet}\times 100$$

Invitrobuoyancystudy

The sum of the total floating time (TFT) and drifting lag time (FLT) served as indicators of in vitro buoyancy. (TFT).The testwasperformedusingUSP2typeIIpaddleapparatususing900mlof0.1 NHC1at50rpmat37±0.5°C.Thetimerequiredfortablettoriseto surface of dissolution medium and duration of time the tablet constantly float on dissolution medium were noted as FLT and TFT, respectively.

Invitrodrugreleasestudy

The USP 2 type II paddle equipment was used to carry out an in vitro drug release. in900 mlof 0.1NHC1 at 50 rpm at 37 ± 0.5°C. Thesamples were withdrawnat predetermined time intervals for period of 24 hr and replaced with the fresh medium. The samples were filtered through 0.45 µm membranefilter, suitably diluted and analysed at 319 nm using doublebeamUV-Vis spectrophotometer. The content ofdrug wascalculated using calibrationcurve[9].

Kineticmodelforreleasedata

To determine the drug release, the drug released data collected from all samples were fitted with the selected kinetic model, such as the Higuchi model, the Zero order kinetic model, the First order kinetic model, and the Korsemeyerpeppas model. the medication releases for orders 0 and 1. The drug release depends on whether there is drug concentration or not, as explained by both the zero ordered and the initial order drug releases. The drug release mechanism was characterised by the Korsemeyer-Peppas model and the diffusional drug distribution was described by the Higuchi model.[10].

Zeroorder= $Q_1=Q_0+K_0t$

Firstorder= $Q_t=Q_{0e}^{-K1t}$

Higuchimodel= $m=(100-q)\times t^{1/2}$

HixonCrowellModel= $W_0^{1/3}-W^{1/3}=kt$

Korsemeyerpeppasmodel= $Mt/M\alpha=K\times t^{n}$ t

Where W0 is the beginning quantity of medication in dosage form, Wt is the remaining quantity of drug in dosage form at moment t, Mt/M is the percentage of drug release at time t, n is the diffusion exponent, and Q1 is the quantity of drugs dissolved in time t..K_0,K_1, and k refer to the rate constant.

Results and Discussion

FTIR Study

The FTIR results of pure drug and physical mixture is given in fig:1 and 2,there is no significant shifting of peaks were found in results which refers to higher degree of compatibility between drugs and excipients.

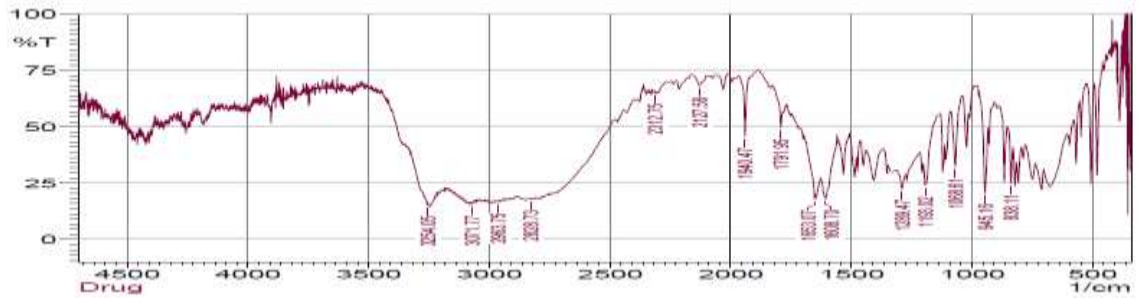

Figure1:FTIRspectrumofPure TizanidineHCl

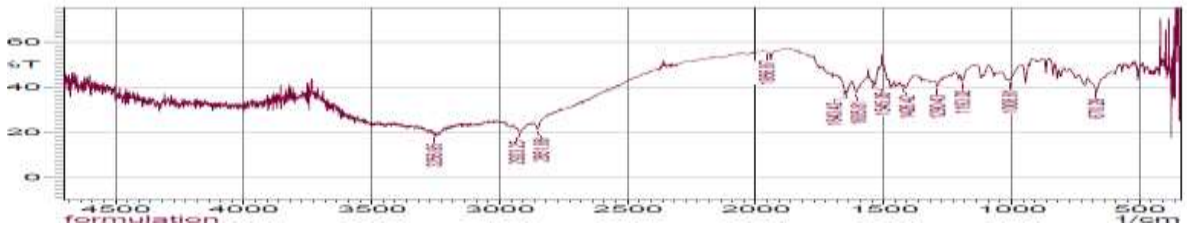

Figure2:FTIRspectrumofTizanidineHClOptimized Formulation

Preparation of Floating Tablet

Low density and gas production are two common processes employed when constructing gastro-retentive drug delivery systems. Utilising the HPMC in polymeric systems for delivery could result in a lower-density drug delivery system. Widespread use of HPMC as a low volume hydro colloid system. Total 9 formulation were formulated using various concentration of different grade of HPMC.The Post compression results for floating tablets are given in table no:2.The weight variation for tablet came in a range between 0.198mg to 0.200mg,Hardeness obtained in range of 4.8kg/cm^2 to 6.4 kg/cm^2 .Friability and content uniformity came in a range 0.176 % to 0.69% and 81.72% to 99.73% respectively

Table2:PostcompressionevaluationparameterofFloating Tablets

Batch code	Weight variation (mg) n=20	Hardness (kg/cm^2) *	Friability (%)	Content uniformity * (%)	Floating lagtime (sec)	Totalfloating time (hr)
F1	0.199	5	0.52264	81.72	20.23	Within 12hr
F2	0.200	6	0.69565	85.76	17.57	>12
F3	0.198	5.5	0.69565	87.12	16.24	>12
F4	0.200	6.2	0.36631	99.72	19.18	Within 12hr
F5	0.198	5	0.18832	99.73	15.94	>12
F6	0.200	6.4	0.17667	89.40	14.81	>12
F7	0.200	4.8	0.52816	91.73	15.48	Within 12hr
F8	0.198	5.3	0.52447	96.42	14.93	>12
F9	0.198	6.1	0.695652	92.32	13.29	>12

Swelling Results

The range of the formulation F1 to F9's absorption of water percentage is 78.11% to 99.42%.A higher proportion of HPMC in the formulation was observed to increase the percentage water uptake.

Table :3 Swelling Index ofFloating Tablets(F1 to F9)

Time(hr)	Formulation								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	25.17	27.68	36.64	27.68	33.55	47.42	40.13	42.37	41.92
1	31.63	38.75	51.02	38.75	39.93	59.10	54.67	55.93	60.13
2	39.45	46.71	63.69	46.71	50	70.44	61.59	65.42	71.82
3	35.37	47.75	64.38	47.75	51.67	84.53	70.58	75.59	78.35
8	78.11	81.22	79.32	86.47	91.03	98.22	89.33	99.42	92.35

Floating Lag Time

Table 2 provided the buoyancy lag time values for various batches. The amount of sodium bicarbonate involved in the production of CO2 determines the buoyancy lag duration for tablets. The optimal matrices or coating materials for a floating system should be extremely permeable to dissolving media to start a quick CO2 generation process and must be permeability for CO2 to support floating. Formulation F1 to F9 showed buoyancy lag time ranges from 13.29sec to 20.23sec Results indicate that FLT was found to be decreased with increase in the concentration of HPMC with in all tablet formulations.

Floating time

It was discovered that the amount of HPMC, the amount of swelling polymer, the degree of gelling, and the strength of the gel all affected the buoyancy of the substance..Floating time of all formulation are reported in table 1

In vitro Release profile of Floating Tablets

All nine formulation showed proper controlled release profile in gastric medium(0.1N HCI).drug release profile is given in table 4 and figure no :3

Table :4 In vitro release study of Floating tablet(F1 to F9)

Time (hr)	%DR								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
0.5	26.72713	23.834	21.58925	23.842	19.685	18.64	21.58925	18.684	15.76488
1	31.33525	29.19738	25.192	29.931	25.451	23.255	27.64875	22.74888	19.21625
2	43.88388	41.24088	38.64875	40.984	38.843	35.738	38.423	35.738	27.43253
4	63.2221	47.669	45.934	60.82725	55.57038	44.107	56.464	47.669	33.33525
6	77.31925	68.121	67.942	73.2975	67.394	58.901	68.2185	62.4353	55.53263
8	90.08413	87.934	82.736	83.284	81.366	80.53263	82.6705	92.4165	99.43538

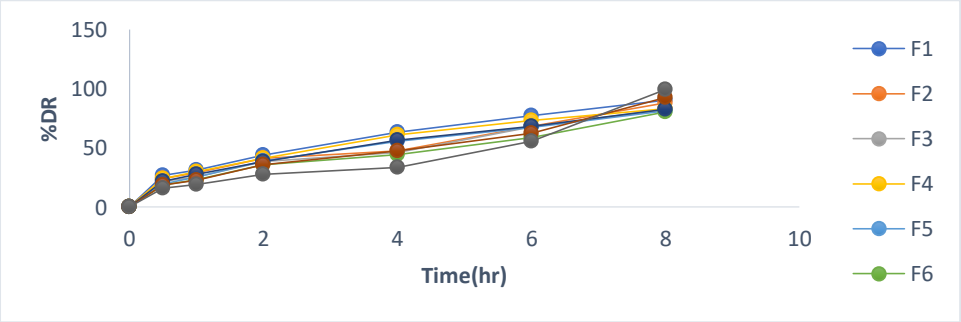

Figure:3 In vitro release study of Floating tablet(F1 to F9)

The drug release reported in the range between 80.53 % to 99.%

Release Kinetics Study

The release kinetics study of all formulation is reported in table :5 the results confirmed that the Optimized F9 formulation showed zero order kinetics

Table :5 R^2 values of all formulation

Formulation	Release kinetics				Release Mechanism
	Zero order kinetics	1st order kinetics	Hixson Crowell kinetics	Higuchi kinetics	Korsemeyerpeppas Kinetics
F1	0.921	0.979	0.997	0.988	0.335
F2	0.930	0.472	0.970	0.968	0.338
F3	0.944	0.497	0.976	0.962	0.364
F4	0.916	0.468	0.998	0.980	0.347
F5	0.938	0.503	0.997	0.984	0.385
F6	0.952	0.517	0.974	0.962	0.387
F7	0.935	0.487	0.997	0.982	0.364
F8	0.951	0.516	0.990	0.981	0.391
F9	0.998	0.544	0.959	0.598	0.404

Conclusions

The HPMC polymers are used in several formulations of the Tizanidine floating tablet formulation to display a sustained dissolution pattern. The tablets are well-formulated, and their swelling indices show that they have good flotational properties. The release kinetics showed followed by optimized F9 formulation was zero order kinetics

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