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Formulation and Evaluation of Gastro Retentive Floating Tablets of Quinapril HCL

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ABSTRACT:

Quinapril HCl is indicated for the treatment of high blood pressure (hypertension) and as adjunctive therapy in the management of heart failure. It may be used for the treatment of hypertension by itself or in combination with thiazide diuretics, and with diuretics and digoxin for heart failure. Quinapril HCl has short half life (2 hrs). To reduce the frequency of administration and to improve patient compliance, gastro retentive floating system formulation is desirable. Thus it is decided to prolong the gastric residence time in terms of making floating gastro retentive drug delivery system to increase drug absorption and hence bioavailability.Totally 12 formulations were formulated by using the above drugs by using two different techniques like Effervescent floating technique and Non Effervescent floating technique. Among them Formulations F1-F12 were formulated by using Quinapril HCL as a drug, whereas the formulations F1-F6 were formulated by Effervescent floating technique and formulations F7-F12 were formulated by Non Effervescent floating technique. All the formulations were evaluated for the pre compression and post compression parameters and all the formulations shows acceptable limits. The *in vitro* drug release profiles of the formulations F1-F12 the maximum drug release was found in the F12 formulation containing Polyox WSR(90mg) as a rate retarding polymer.

Keywords: Quinapril HCL, HPMC K15M, Polyox WSR floating gastro retentive drug delivery system.

INTRODUCTION:

The oral route represents the predominant and most preferable route for drug delivery unlike the majority of parenteral dosage forms it allows ease of administration by the patient and highly convenient way for substances to be introduced in to the human body. Oral drug delivery systems are divided in to immediate release and modified release systems[1]. Modified release systems have been developed to improve the pharmacokinetic profiles of active pharmaceutical ingredients and patient compliance as well as reducing side effects. Oral modified release delivery systems commonly include delayed release, extended release programmed release and site specific or timed release. Oral extended release dosage forms offer the opportunity to provide constant or nearly constant drug plasma levels over an extended period of time following administration. Extended release drug delivery systems offer several advantages compared to conventional drug delivery system including avoiding drug level fluctuations by maintenance of optimum therapeutic plasma and tissue concentrations over prolonged time periods, avoiding sub therapeutic as well as toxic concentrations, thus minimizing the risk of failure of the medical treatment and undesirable side effects, reducing the administered dose and reduced frequency of administered dose while achieving comparable results, Targeting or timing of the drug action.Hence it is highly desirable to develop sustained drug delivery system releasing the drug at predetermined rates to achieve optimal plasma drug levels and/or at the site of action[2,3].

Majority of drugs are preferentially absorbed in the upper part of the small intestine. So, Gastro retentive drug delivery systems are preferred. The retention of oral dosage forms in the upper GIT causes prolonged contact time of drug with GI mucosa leading to higher bioavailability and hence therapeutic efficacy, reduced time intervals for drug administration, potentially reduced dose size and thus improved patient compliance [4-6].

FDDS are preferred as they are economic and has improved patient compliance and they are advantageous for drugs absorbed from the stomach eg: ferrous salts and for drugs meant for local action in the stomach eg :antacids, drugs with narrow absorption window in the small intestine region eg: L-Dopa. When there is a vigorous intestinal movement and a short transit time as might occur in certain type of diarrhoea, poor absorption is expected. Under such

circumstances also it may be advantageous to keep the drug in floating condition in stomach to get a relatively better response [9, 10].

The present work is an attempt to develop FDDS in the form of tablets taking Quinapril HCL as the model drug. Quinapril HCl is indicated for the treatment of high blood pressure (hypertension) and as adjunctive therapy in the management of heart failure. It may be used for the treatment of hypertension by itself or in combination with thiazide diuretics, and with diuretics and digoxin for heart failure. Quinapril HCl has short half life (2 hrs). To reduce the frequency of administration and to improve patient compliance, gastro retentive floating system formulation is desirable. Thus, Quinapril HCl is chosen as a suitable candidate for Gastric floating release drug delivery system to prolong the gastric residence time in terms of making floating gastro retentive drug delivery system to increase drug absorption and hence bioavailability. The tablets prepared by direct compression technique by using different polymer concentrations to enhance gastric retention and to increase its bioavailability and duration of action.

MATERIALS AND METHODS

Materials

Quinapril HCL was procured from Cadila pharmaceuticals Ltd., HPMC K100M, and HPMC K200 M, Polypropylene foam powder, were purchased from S.D. Fine Chemicals (Mumbai, INDIA), sodium bicarbonate and other excipients were procured from spectrum pharma research solutions,Hyderabad.

Preparation of floating tablets By direct compression method:[12]

All ingredients were collected and weighed accurately. Drug with polymers were sifted and passed through sieve #40 and then the remaining excipients were rinsed over, after pre blending all ingredients in mortar for 15minutes Then magnesium stearate and talc were added and blended for 5-6 minutes, lubricated powder was compressed under 8mm punch of tablet punching machine, (Cadmach model DC16 16-Station Tablet Press). The composition of different formulations is shown in the above tables.

EVALUATION OF FORMULATIONS:[13-22]

Pre compressaion parameters:

It includes Angle of repose,Bulk density,Tapped density,Cars index,Hausners ratio.

Pre compressaion parameters:

It includes Weight variation, Hardness, Friability, Thickness and diameter, Drug content, *In-vitro* buoyancy studies, Swelling index and *In-vitro* dissolution studies.

RESULTS AND DISCUSSION

Gastro retentive floating tablets were formulated by Quinapril HCL by Effervescent technique(i.e., from F1-F6) and by Non effervescent technique(i.e.,F10-F12).The formulated tablets have shown the results as given below:

UV Spectra of Quinapril HCL . Wavelength of maximum absorption in 0.1N HCL solution was found to be 259nm, with uv range of Quinapril HCL was found to be 5-30µg/ml with a regression value of 0.999.

Compatability studies by FT-IR:

From the compatability studies it was concluded that the functional groups that were presented in the pure drug were present in the optimized formulation with very minute changes, from this we can concluded that the drug and excipients have no interactions.

In vitro floating buoyancy studies:

All the formulated tablets were evaluated for the buoyancy studies for the determination of Floating Lag Time and Total Floating Time. The formulations having higher polymer concentrations exhibits total floating time for more than 20hours than the other formulations.

Swelling Studies:

From the swelling studies of the folating tablets it was identified that the tablets formulated by effervescent technique have higher swelling index than the Non effervescent floating tablets, among them HPMC K200M having 90mg have higher swelling index.

***IN-VITRO* DRUG RELEASE STUDIES**

***In-vitro* drug release data of Quinapril HCL floating tablets by effervescent technique:**

From the drug release studies of the gastro retentive floating tablets of Quinapril HCL formulated by effervescent technique the maximum amount of drug release was found in F6 formulation containing Polyox wsr 200(90mg) as a rate retarding polymer as it has higher efficiency for retarding the drug relase in the dissolution medium, bit it doesn't maintain the drug release for 24hours.

***In-vitro* drug release data of Quinapril HCL floating tablets by Non-Effervescent technique:**

The in vitro drug release profiles of the formulations F7-F12 shows maximum drug release in F12 formulation containing Polyox wsr in higher concentration i.e.,90mg, formulated by using Non Effervescent floating technique.

While comparing the two different floating techniques better drug release was found in Non Effervescent floating systems as they have slow swelling capacity and can prolong the floating time, due to these reasons the Non Effervescent floating system was better than the Effervescent floating systems.

While comparing the effervescent and Non effervescent floating techniques the maximum drug release was found in the F12 formulation when compared with F6 formulation using same polymers.

The drug release kinetics of the optimized formulation (F12) of the Quinapril HCL follows zero order drug release with Non Fickian diffusion mechanism.

CONCLUSION

Floating drug delivery systems (FDDS) have a bulk density less than gastric fluids and so remain buoyant in the stomach without affecting the gastric emptying rate for a prolonged period of time. While the system is floating on the gastric contents, the drug is released slowly at the desired rate from the system. After release of drug, the residual system is emptied from the stomach. This results in an increased GRT and a better control of the fluctuations in plasma drug concentration.

So for increasing the gastric retention time of the some poorly acidic absorption drugs were selected for increasing the gastric retention time for increasing the bioavailability of the drug.

From the results obtained it was concluded that the the in vitro drug release profiles of the formulations F1-F12 the maximum drug release was found in the F12 formulation containing Polyx WSR(90mg) as a rate retarding polymer formulated by using Non Effervescent floating technique.

COMPOSITION OF QUINAPRIL HCL FLOATING TABLETS

Table1: Composition of Quinapril HCL floating tablets by Effervescent technique:

Ingredients(mg)	F1	F2	F3	F4	F5	F6
Quinapril HCL	20	20	20	20	20	20
HPMC K15M	30	60	90	-	-	-
POLYOX WSR	-	-	-	30	60	90
PVP K30	6	6	6	6	6	6
MCC	82	52	22	82	52	22
NAHCO3	50	50	50	50	50	50
Citric acid	5	5	5	5	5	5
Mg -stearate	3	3	3	3	3	3
Talc	4	4	4	4	4	4
Total wt (mg)	**200**	**200**	**200**	**200**	**200**	**200**

Table2: Composition of Quinapril HCL floating tablets by Non - Effervescent technique:

Ingredients(mg)	F7	F8	F9	F10	F11	F12
Quinapril HCL	20	20	20	20	20	20
HPMC K15M	30	60	90	-	-	-
POLYOX WSR	-	-	-	30	60	90
PVP K30	6	6	6	6	6	6
Polypropylene foam	50	50	50	50	50	50
MCC	87	57	27	87	57	27
Mg -stearate	3	3	3	3	3	3
Talc	4	4	4	4	4	4
Total wt (mg)	**200**	**200**	**200**	**200**	**200**	**200**

Table3:Precompression parameters & Post compression parameters:

Parameters	Range	Parameters	Range
Angle of repose (θ) ±SD	24.18±0.18 - 28.56±0.54	**Average wt in (mg)±SD**	198.9± 0.02-201.02± 0.24
Bulk density (gm/cm)±SD	0.337±0.22 -0.354±0.54	**Hardness (Kg/cm2)±SD**	5.4± 0.14 - 6.4± 0.11
Tappeddensity (gm/cm) ±SD	0.402±0.12 -0.440±0.01	**Diameter in (mm)±SD**	7.84± 0.22 - 8.12± 0.10
Hausnerratio (HR)±SD	1.18±0.06 -1.24±0.28	**Thicknessin (mm)±SD**	2.36± 0.12 - 3.42± 0.26
Carr index (C.I) ±SD	15.42±0.36 - 19.54±0.28	**Friability (%)±SD**	0.24± 0.20 - 0.68± 0.26
		Drug content (%)±SD	91.56±0.42 - 99.58±0.22

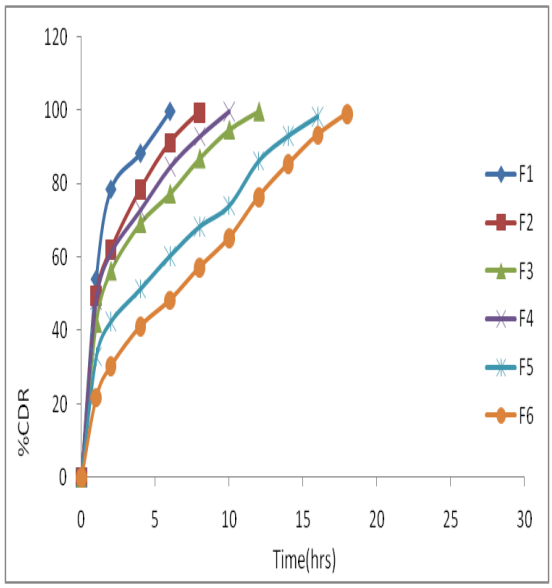

Fig1:%CDR of F1-F6

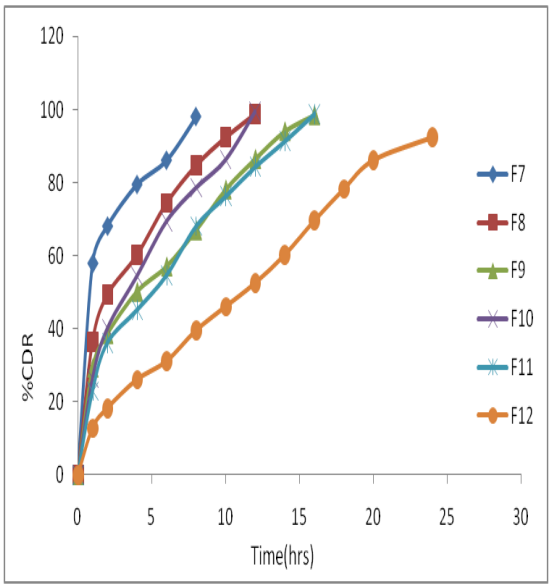

Fig2: %CDR of F7-F12

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