Research Article

The Study of Differences between MCC and DCP as a Diluent in the Evaluation of Dexchlorpheniramine Maleate Floating Tablet

M. Yaman Alabrazi*, Hind Elzein
Department of Pharmaceutics and Industrial Pharmacy, Damascus College of Pharmacy, Damascus University, Syria.
***Corresponding author's E-mail:** abrazi1985@gmail.com, dr.yaman@live.com

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ABSTRACT

The aim of this study was to formulate and evaluate floating tablet and to investigate the influence of different two diluents microcrystalline cellulose (MCC) and dibasic calcium phosphate (DCP). Dexchlorpheniramine Maleate (DCM) is anti histamine H_1 used to treat symptoms of allergies. It has an absorption window in the stomach and in the upper part of the small intestine. DCM was used with various grades of HPMC and Carbopol 934P as a matrix to formulate the floating tablets which were prepared by direct compression. The prepared tablets were evaluated for uniformity of weight, hardness, friability, drug content, floating behavior and *in vitro* dissolution studies. We used a combination of HPMC, Carbopol 934p and sodium bicarbonate in formulation to increase the gastric residence time of the dosage form to 24 hours. It was found formulation that containing MCC is having floating lag time 8.6 ± 0.608 sec and showed 99.7854 ± 3.254 drug release at the end of 24 hours but when we used DCP it released 99.4037 ± 1.82549 % of drug at the end of 18 hours and having floating lag time 15.63 ± 0.813 second. The dissolution profiles were subjected to various kinetic release investigations and found that drug release from the different polymeric matrix follows Korsmeyer – peppas kinetic in MCC formulation and Higushi kinetic in DCP formulation. The Diluents have appreciable effect on floating drug release rate at high diluent concentration.

Keywords: *floating tablet, Dexchlorpheniramine maleate, floating drug delivery, MCC*

INTRODUCTION

The oral controlled drug delivery system has been developed during the last three decades because of their obvious advantages, especially as ease of administration[1] controlled release of drug at a slower predetermined rate, patient compliance and flexibility in formulation. However, the idea of floating drug delivery system (FDDS) was described in the literature as early as 1968.[2] Floating drug delivery system belongs to oral controlled drug delivery system groups that are competent of floating in the stomach surface because the dosage forms having a density lower than the stomach contents.[3] The bioavailability of drugs that have a narrow absorption window in the gastrointestinal tract (GIT) are candidates for the floating drug delivery system because it absorbed in stomach or the upper part of small intestine and thus improves bioavailability of the drug, especially when it retains in the stomach for a long time.[4] Gastric emptying of dosage forms is an extremely variable process and ability to prolong and control emptying time that is an important asset for floating dosage forms.[5] Several difficulties in designing an oral controlled-release drug delivery system for decreasing dosing frequency, best absorption, best therapeutic effect and enhanced bioavailability. Most important of these difficulties are incomplete release of the drug and a shorter residence time of dosage forms in the upper gastrointestinal tract so that drug absorption from the gastrointestinal tract is a complex procedure and is subject to many variables.[6]

Various gastro retentive techniques were used, including 1) floating system based on the mechanism of buoyancy two distinctly different technologies, which divide for two types effervescent and non – effervescent 2) swelling system 3) high density system or non-floating system 4) bioadhesive or mucoadhesive drug delivery system have been explored to increase the gastro retention of dosage forms, Floating systems is one of the important approaches to remain in the stomach to obtain sufficient drug bioavailability.[7]

DCM is a dextro isomer of chlorpheniramine, and it is twice more potent than the racemic mixture. These drugs find their greatest use in the symptomatic treatment of allergic rhinitis. After 8 h, no significant difference from placebo was found. Dexchlorpheniramine maleate is a propyl amine used in the salt form of maleate. It's used as a drug to improve the bioavailability.[8] It is given by mouth in doses of two mg every four to six hours up to a maximum 12 mg daily). They are useful in the acute rather than the chronic form of urticaria. DCM has a biological half-life (6.0855 ± 1.0 hours).[9-22]

The effects of excipients on the dissolution and release from the hydrophilic polymers were investigated by many authors; they have evaluated the effect of excipient's type on the release from hydroxypropyl methylcellulose (HPMC) matrixes. Similarly Russlo LI and Ghaly (2002) has also investigated and evaluates the effect of the polymer level and diluent type on the release of theophylline from Carbopol 934 matrixes.[10]

The objective of the present study was to formulate and investigate the influence of two diluents polymer concentration in the release of DCM from HPMC and Carbopol 934P in formulating of floating tablet.

MATERIALS AND METHODS

Materials

Dexchlorpheniramine maleate as the model drug was purchased as a gift sample from Schering-plough Corporation (U.S.A), Dexchlorpheniramine maleate as a reference sample was purchased from Sinochem Ningbo LTD, China. Hydroxypropyl methyl cellulose (HPMC K15M, HPMC K100M), Carbopol 934P and PVP-k30 were kindly supplied by Sigma Aldrich (Germany). Sodium Bicarbonate (VWR International, Haasrode Research, Leuven Belgium) was purchased. Other excipients used were of standard pharmaceutical grade or analytical grade.

Methods

Analytical Method Development

The stock solution of the DCM 24 mcg/ml was prepared in 500 ml of 0.1 N HCl pH 1.2. Absorbance was measured at λmax ranging from 200 to 400 nm, using Shimadzu UV-1601 UV/Vis double beam spectrophotometer.

Linearity

Cumulative drug release was calculated using the calibration curve in the linearity range of 0–48 mcg/ml to avoid the erroneous result. This study was performed three times for each formulation.

Preparation of Floating Tablets

Floating tablets of DCM were prepared by direct compression technique employing sodium bicarbonate as a gas-generating agent. HPMC K15M and Carbopol 934P were used as rate controlling polymers. The amounts of the ingredients were optimized based on of trial preparation of the tablets. All the ingredients (Table 1) were weighed accurately then passed through 60 mesh sieve. The drug was mixed with the gas-generating agent and low-density polymers. PVP K30, talc and magnesium stearate were finally added as glidant and lubricant respectively. The powder mix was blended for 10 minutes to have uniform distribution of drug in the formulation. About 300 mg of the powder mix was weighed accurately and fed into the die of single-punch tableting machine (Erweka EK-0; Motor Drive AR 402, Heusenstamm, Germany) and compressed using 10mm flat punches. HPMC K15M offers the advantages of being non-toxic and relatively inexpensive, and also it can be compressed directly into matrices, so it was used in this study.

Table 1: Composition of floating tablets of DCM (all formulations have 10 mg DCM; 40 mg sodium bicarbonate; 1.7% HPMC K100 M 5% PVP k30; 3.3% magnesium stearate; 1.6% talc and 1.6% Aerosil)

	F1	F2	F3	F4	F5	F6
HPMC K15M	50	75	100	50	75	100
Carbopol 934p	30	45	60	30	45	60
DCP	125	85	55	-	-	-
MCC	-	-	-	125	85	55

Evaluation of Powder Blends

The flow properties of powder (before compression) were characterized in terms of angle of repose, Carr index, tapped density, bulk density and Hausner ratio. For determination of the angle of repose, the powder was poured through the walls of a funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blends was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$$\tan\theta = \frac{h}{r}$$

Where, h and r are the height and radius of the powder cone. Hausner ratio and Carr index were calculated according to the two equations given below:

$$\text{Carr's Compressibility Index } (\%) = \frac{(\text{Tapped Density} - \text{Bulk Density})}{\text{Tapped Bulk Density}} \times 100$$

$$\text{Hausner ratio } (\%) = \frac{\text{Tapped Density}}{\text{Bulk Density}}$$

Tapped density it was determined by placing a graduated cylinder, containing a known mass of drug- excipient blends, on mechanical tapping apparatus. The tapped volume was measured by tapping the powder to a constant volume. It is expressed in g/ml and is given by

$$\text{TBD} = \frac{M}{V_t}$$

Where, M is the mass of powder, and Vt is the tapped volume of the powder

bulk density: apparent bulk density was determined by pouring preserved drug excipient blend into a graduated cylinder and measuring the volume and weight “as it is”. It is expressed in g/ml and is given by:

$$\text{BD} = \frac{M}{V_o}$$

Where, M is the mass of powder and V_0 is the Bulk volume of the powder.[11-12]

Evaluation of Tablets

Twenty floating tablets were evaluated for uniformity of weight; all the tablets passed a weight variation test as the % weight variation was within the Pharmacopoeial limits of ± 7.5% of the weight. The weights of all the tablets were found to be uniform with low standard deviation values. Hardness was measured in the hardness examination.

The hardness was measured with a hardness tester using 10 tablets (ERWEKA TBH300 S, GmbH, Germany). The friability of the tablet was determined using ERWEKA TAR20 Twenty previously weighed tablets were rotated at 25 rpm for four minutes. The weight loss of the tablets before and after measurement was calculated.[12]

In vitro Floating Studies

The *in vitro* floating tablet was determined by floating lag time and total floating time. The tablets were placed in dissolution tester; Erweka, Type DT 800, Germany). The dissolution medium was 500 ml of 0.1 N HCl (pH 1.2) and temperature of which was maintained to 37 ± 0.5C throughout the study.

The time required for the tablet to rise to the surface and float were determined as floating lag time (FLT) and duration of time the tablets constantly float on the water surface is called the total floating time (TFT).[13-14]

Drug Content Estimation

The drug content in each formulation was determined by triturating five tablets and powder equivalent to average weight and drug was extracted in 0.1 N HCl. The drug content was determined measuring the absorbance at 269 nm after suitable dilution using a Shimadzu UV-1601 UV/Vis double beam spectrophotometer. The drug content was determined by referring to Analytical method development.[15]

In vitro Dissolution Studies

The release rate of DCM from floating tablets was determined using *the United States Pharmacopeia* (USP) dissolution tester (Erweka, Type DT 800, Germany). The dissolution test was performed using 500 ml of 0.1N HCl (pH 1.2), at 37 ± 0.5°C, Apparatus 2 (paddle method) and 75 rpm. A sample (10 ml) of the solution was withdrawn at 1, 2, 4, 6, 8, 12, 16, 18, 20, 22 and 24 hour and the samples were replaced with fresh dissolution medium.

The samples were filtered through a 0.45µ membrane filter. The percentage drug release was plotted against time to determine the release profile.[16-17]

Stability Study

Gastro retentive tablets of DCM formulated in the present study were subjected to accelerated stability studies.

The optimized formulation F6 was tested for a period of 12 weeks at 40°C with 75% RH, analyzed for its appearance, hardness, friability, floating time, drug content and *in vitro* release.[18-19]

In vitro Drug Release Kinetic Studies

Kinetic model described drug dissolution from dosage form where the release amount of drug is a function of test time. Data of the *in vitro* release were determined by fitting the release data to the various kinetic equations. Drug release data was analyzed according to zero order, first order, Hixon crowel, Higuchi square root, Korsmeyer-Peppas model.

The criteria for selecting the most appropriate model was chosen based on goodness of fit test, to ascertain the kinetic modeling of drug release analysis by using MS EXCEL statistical function, and were found the R^2 (correlation coefficient) values of the release profile corresponding to each model.[20-21]

RESULTS AND DISCUSSION

In this study, HPMC K15M, K100M and Carbopol 934P have been used to formulate floating tablets of DCM, which are commonly used in hydrophilic matrix drug delivery systems. The tablets were developed to increase the gastric residence time (GRT) of the DCM, so that they can be retained in the stomach for a long time and control release of DCM to 24 hours. The tablets were made using low polymers controlling release such as Carbopol 934P and HPMC K15M, with a gas generation agent (sodium bicarbonate) to optimize the drug content, *in vitro* floating and *in vitro* dissolution studies.

Analytical Method Development

The DCM spectrum was obtained with a smooth curve with good resolution. Calibration graphs for DCM (Fig.1) were found two peaks. The first peak is nonspecific at 206 nm and the second peak is specific at 269 nm, so we used as the appropriate wavelength. Good linearity was obtained for DCM (y = 0.018x) with correlation coefficient 0.999 in 0.1 N HCl.

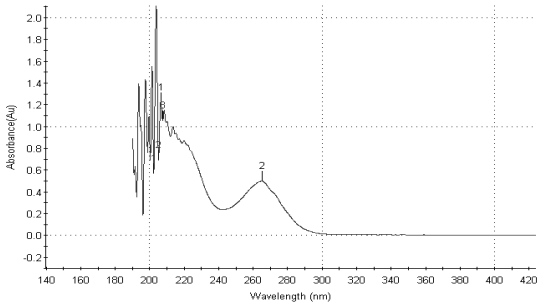

Figure 1: Absorption curve of standard solution with concentration 24 mcg/ml of DCM in 0.1 N HCl

Flow Properties of Powder

The powders prepared for compression of floating tablets were evaluated for their flow properties. Angle of repose was in the range of 18.67 to 20.98 with powder containing MCC and 18.52 to 20.18 with DCP. The obtained values of repose were found indicated good flow properties of the entire formulated powder blend. Bulk density ranged between 0.458 to 0.468 gm/cm3 with powder containing MCC and 0.439 to 0.467 gm/cm3 with DCP. Tapped density ranged between 0.536 to 0.54 gm/cm^3 with powder containing MCC and 0.5 to 0.53 gm/cm3 with DCP. This value of bulk density indicates good packing character. The Carr index (CI) for all the formulations was found to be below 15%, indicating desirable flow properties.

Evaluation of Floating Tablets

Characterization of Tablets

Weight variation was within the Pharmacopoeial limits of ± 7.5 % of the weight indicated no significant difference in the weight of individual tablet from the average value the

hardness of the prepared tablets F1-F6 was observed to be between 6.41-7.352 kg/cm^2 (Table 3), indicating satisfactory mechanical strength. The thickness of six formulations was between 3 and 4.1 mm, Thickness and diameter of tablets, measured by ERWEKA TBH300 S, GmbH, Germany. The friability was in the range of 0.52–0.662 % for all the formulations. The drug content in all the batches of DCM floating tablets was in the range of 95 to 105%, this ensured uniformity of the prepared formulations (Table 3).

Evaluation of Floating of the Tablets

On immersion in Simulated Gastric Fluid pH (1.2) at 37°C, the tablets floated, and remained float without disintegration. From the results, it can be concluded that the formulation containing MCC showed total floating time (TFT) lower than the formulation containing DCP; this may be due to the nature of DCP and density of it, which has 2.389 g/cm3 compared to MCC 1.5 g/cm^3.[23] The results of *in vitro* floating studies are tabulated in Table 2.

Table 2: Tablet Properties of DCM Floating Tablets ± S.D

Batch code	Weight variation (mg)	Thickness (mm)	Diameter (mm)	Hardness (kg/cm^2)	Friability (%)	Drug content %	Floating lag time (sec)	Total floating time (hrs)
F1	299.38 ± 1.32	3.102 ± 0.02	11.32 ± 0.02	6.48 ± 0.36	0.62	100.93 ± 1.38	**46.26 ± 2.46**	20
F2	300.82 ± 2.93	3.093 ± 0.01	11.32 ± 0.005	7.14 ± 0.52	0.53	99.71 ± 0.93	31.48 ± 0.94	20
F3	301.83 ± 1.79	3.096 ± 0.01	11.32 ± 0.002	**7.35 ± 0.21**	0.52	101.28 ± 2.53	15.63 ± 0.81	22
F4	299.42 ± 1.45	4.1 ± 0.01	11.33 ± 0.0057	6.84 ± 0.31	**0.662**	101.106 ± 1.32	22.6 ± 0.26	>24
F5	301.08 ± 2.42	**4.12 ± 0.01**	**11.34 ± 0.02**	6.47 ± 0.089	0.521	99.53 ± 1.51	15.94 ± 0.61	>24
F6	299.78 ± 2.73	4.11 ± 0.02	11.32 ± 0.0016	6.41 ± 0.197	0.641	101.25 ± 0.68	8.51 ± 0.81	>24

Table 3: *In vitro* drug release from DCM floating tablet

	F1	F2	F3	F4	F5	F6
1 hrs	19.8352 ± 0.84373	16.7582 ± 1.08324	14.81125 ± 1.116321	17.52831 ± 0.69324	16.62292 ± 0.399778	13.46525 ± 1.340949
2 hrs	42.2493 ± 2.38424	37.8935 ± 1.72923	27.64083 ± 2.244026	30.36673 ± 1.38294	28.83076 ± 0.932817	21.66682 ± 0.402285
4 hrs	58.5324 ± 0.30945	51.5309 ± 1.42928	41.79767 ± 2.174821	41.9745 ± 0.98342	39.65749 ± 2.132153	29.99087 ± 0.670475
6 hrs	74.8342 ± 1.79432	62.8323 ± 2.09382	59.13883 ± 0.885951	55.02891 ± 2.88539	52.09606 ± 1.051166	34.88724 ± 0.769018
8 hrs	85.7104 ± 2.87532	75.3952 ± 0.72038	67.2725 ± 1.612258	67.26264 ± 2.90284	66.03853 ± 1.051166	49.5766 ± 0.59969
12 hrs	99.9328 ± 0.57413	82.7419 ± 0.98134	81.8532 ± 1.449978	81.37633 ± 1.97283	76.5218 ± 2.547082	65.97972 ± 2.97379
16 hrs		99.9374 ± 2.73584	90.9224 ± 1.305314	98.74239 ± 0.749569	85.39742 ± 1.114044	78.95533 ± 3.352373
18 hrs			99.4037 ± 1.82549		93.79119 ± 1.199336	82.62767 ± 3.0764
20 hrs					99.9416 ± 1.066076	89.97235 ± 0.505704
22 hrs						95.23603 ± 0.875905
24 hrs						99.7854 ± 3.254086

Table 4: Kinetic release data of different model for DCM floating tablet

Best fit Model	Korsmeyer – peppas Model			Higushi Model		Hixson-Crowell Model		First – Order Model		Zero – Order Model		Formula
	r²	n	K	r²	K_H	r²	K_S	r²	K_1	r²	K_0	
Higuchi	0.968	0.6196	3.4538	0.984	3.6294	0.965	0.0196	0.772	0.0209	0.922	0.242	F1
Higuchi	0.95	0.6142	4.3019	0.977	3.1444	0.913	0.0167	0.722	0.0179	0.912	0.1943	F2
Higuchi	0.987	0.633165	2.791326	0.988	2.825558	0.89	0.014361	0.813	0.015417	0.954	0.157027	F3
Korsmeyer – peppas	0.995	0.6338	1.6556	0.994	2.8478	0.952	0.0162	0.844	0.0175	0.974	0.1756	F4
Korsmeyer – peppas	0.991	0.6161	2.3566	0.99	2.7161	0.909	0.0133	0.823	0.0143	0.956	0.1478	F5
Korsmeyer – peppas	0.991	0.63999	1.7216	0.988	2.28399	0.982	0.0106	0.895	0.0115	0.987	0.1088	F6

In vitro Drug Release

All the formulations floating matrix tablets containing an equal amount of gas generating agent (sodium bicarbonate) and were able to efficiently control DCM release over a time period of 12 h. The hydrophilic controlled release agent (HPMC, Carbopol) formed a layer upon hydration. This gel layer was prevention of burst effect and gives the slow release of the drug from this tablet. Studies for all the formulations showed a controlled release of drug for 16 hours, and the optimized formulations (F6) for 24 hours (Table 3). In formulation F4, F5, F6 better drug release was obvious due to two reasons at first the amount of the controlled release agent and second of the DCP tablets which are rapidly and completely penetrated by solvents; this rapid penetration is caused by the hydrophilic nature of DCP and the tablet's porosity. Drug release was from formulations F1 to be 99.9328 ± 0.57413 at 12 h, F2, F3 and F4 were found to be 99.9374 ± 2.73584, 90.9224 ± 1.305314 and 98.74239 ± 0.749569 respectively at 16 h. The release data obtained for formulations F5 and F6 were found over than 20 h of cumulative % drug released. The optimized formulation F6 showed a drug release to be 99.7854 ± 3.254086 (Fig.2).

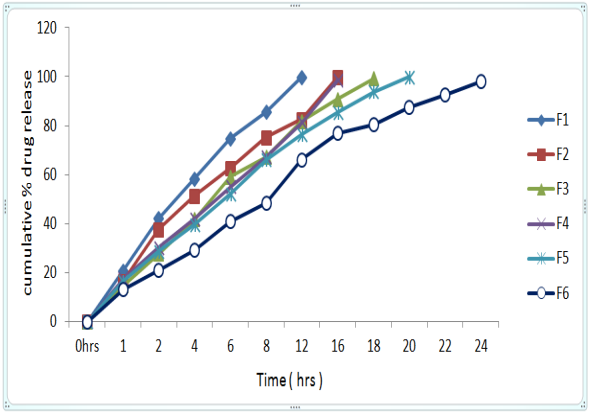

Figure 2: *In vitro* dissolution profile of DCM floating tablet

Drug Release Kinetics

The drug release data were investigated for the type of release mechanism followed. The overall data curve fitting results to various kinetic models such as zero order, first order, Higuchi, Hixson Crowell and Korsmeyer-Peppas.

The best fit with the highest determination R^2 coefficients was shown by both the Higuchi models and Korsmeyer-Peppas. The Higuchi square root kinetic model describes, release drug from the insoluble matrix as the square root of time dependent process. It describes a release of drug from a matrix as a square root of time dependent process based on Fickian diffusion. The values of *n* were in the range of 0.614 to 0.639 (n is more than 0.5) indicating that the release of DCM from floating tablets followed non-Fickian transport mechanism (Table 4) (Fig.3).

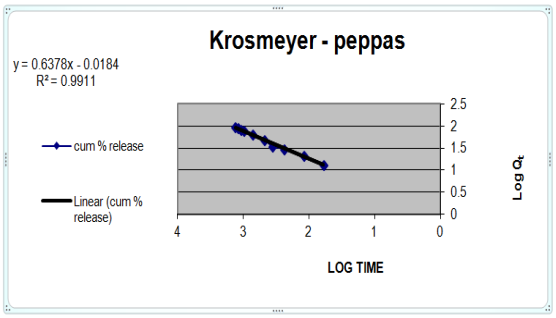

Figure 3: Korsmeyer – peppas release kinetics of optimized formulation F6

Stability Studies

Stability study of optimized floating tablets F6 was selected for stability from the data in the Table 5, the formulation is found to be stable under the accelerated conditions (40°C/75 % RH) and no significant changes in appearance, floating time, drug content, hardness, friability, and *in vitro* release for F6 formulation when it was stored for three months, that indicate that no any change in drug content, floating characteristics, hardness, friability, and *in-vitro* drug release.

Table 5: Stability study of optimized formulation F6

Parameters	First month	Second month	Third month
uniformity of weight (mg)	299.16 ± 2.446	299.03 ± 1.385	298.84 ± 0.926
Hardness (Kg/cm^2)	6.166 ± 0.191	5.92 ± 0.826	5.818 ± 0.529
Friability (%)	0.699	0.638	0.621
Thickness (mm)	4.104 ± 0.02	4.101 ± 0.013	4.093 ± 0.01
Diameter (mm)	11.323 ± 0.00152	11.304 ± 0.002	11.209 ± 0.001
Drug content (%)	102.023 ± 1.80266	101.325	101.632
Floating lag time (second)	8.6 ± 0.608	10.31	12.41
Total floating time (hrs)	>24	>24	>24
Floating behaviour	Float	Float	Float
In vitro release (at 24 h)	99.7854 ± 3.254086	99.1462 ± 1.4629	97.8924 ± 1.8526

Effect of Diluents on Drug Release

The effect of adding directly compressible dibasic calcium phosphate and microcrystalline cellulose fillers to low density matrix tablets containing DCM as a potent drug, carbopol and HPMC K15M on the resulting drug release kinetics is shown in Table 5. The increase in drug release can show in DCP formulations which are rapidly and completely penetrated by solvents due to a fast release of drug from matrix tablets. At the same formulations were evaluated for floating characteristics, which showed floating lag time in the formulation MCC range of 126-223 sec but in DCP formulation total floating time in the range of 12-18 hr and in MCC 20-24hr. Therefore, it is obvious that in floating tablet based on low-density polymer as HPMC K15M the polymer was the key compound for controlling the release rate.

CONCLUSION

The present study shows that the e HPMC K15M, which is a low polymer density, can be used to control the release rates in floating tablets prepared by direct compression. The optimized formulation (F6) shows slow drug release *in vitro* drug release profile for 24 hr. Hence, the study recommended that MCC as a diluent for floating tablet based on HPMC, Carbopol and their derivatives. The floating tablet of DCM was a promising approach to achieve *in vitro* floating.

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REFERENCES

1. Hoffman A, Pharmacodynamic aspects of sustained release preparation, Adv Drug Deliv Rev, 33, 1998, 185-99.
2. Streubel A, Siepmann J, Bodmeier R, Gastroretentive drug delivery system, Expert Opin Drug Delivery, 3(2), 2006, 217-233.
3. Arora S, Javed A, Khar RK, Floating Drug Delivery Systems: A Review, AAPS PharmSciTech, 6(3), Article 47, 2005, 372-390.
4. Garg R, Gupta GD, Progress in controlled gastroretentive delivery systems, Trop. J. Pharm. Res. 7(3), 2008, 1055–1066.
5. Mayavanshi AV, Gajjar SS, Floating drug delivery systems to increase gastric retention of drugs: A Review, Research J. Pharm. and Tech, 1(14), 2008, 345-348.
6. Hirtz J, The git absorption of drugs in man: a review of current concepts and methods of investigation. Br J Clin Pharmacol, 19, 1985, 77-83.
7. Shweta A, Ali J, Ahuja A, Khar RK, Baboota S, Floating drug delivery systems: a review, AAPS PharmSciTech, 6(3), 2005, Article 47.
8. Katzung BG, Basic and clinical pharmacology, Appleton and Lange, Stamford, 7ed, 1992, 363–370.
9. Rajua AJ, Rama G, Sekara R, Siddaiahb MK, Jogheeb NM, Bhojrajc S, Development and Application of a Validated Liquid Chromatography-Mass Spectrometry Method for the Determination of Dexchlorpheniramine Maleate in Human Plasma, Iranian Journal of Pharmaceutical Sciences Summer, 3(3), 2007, 161-170.
10. Russo LI, Ghaly ES. Drug release from Carbopol 934 matrices, P R Health Sci J, 19, 2002, 131-137.
11. Aulton ME, Wells TI. Powder flow. In: Pharmaceutics – the Science of Dosage Form Design, 2nd ed., London, Churchill Livingstone, 2002.
12. Martin A, Micromeretics In: Martin A. Physical Pharmacy, Baltimores, MD: Lippincott Williams and Wilkins, 2001, 423-454.
13. Amit KN, Ruma M, Biswarup D, Gastroretentive drug delivery systems: a review, Asian Journal of Pharmaceutical and Clinical Research, 3(1), 2010, 1-9.
14. Ozdemir N, Ordu S, Ozkan, Studies of floating dosage forms of furosemide: *in vitro* and *in vivo* evaluation of bilayer tablet formulation, Drug Dev Ind Pharm, 26, 2000, 857-866.
15. Viana NS, Moreira-Campos LM, Vianna-Soares CD, Derivative ultraviolet spectrophotometric determination of dexchlorpheniramine maleate in tablets in presence of coloring agents, IL Farmaco, 60, 2005, 900-905.
16. United States Pharmacopeia (USP), USP 30-NF25, 2007 May 1.
17. Desai S, Bolton S, A floating controlled release drug delivery system: *in vitro-in vivo* evaluation. Pharm Res, 10, 1993, 1321-1325.
18. ICH topic 8 Pharmaceutical guidelines, Note for Guidance on Pharmaceutical Developments, (EMEA/CHMP167068/2004).
19. ICH Q1A (R2), Stability Testing Guidelines, Stability testing of a new drug product and new drug substance 2003.
20. Lachman, Liberman and Leon, The Theory and Practice of Industrial Pharmacy, 3rd Edition, Verghese Publication House, 1991, 171-293.
21. Xiaoqiang Xu, Minije S, Feng Z, Yiqiao Hu,Floating matrix dosage form for phenoporlamine hydrochloride based on gas forming agent: *In vitro* and *in vivo* evaluation in healthy volunteers. Int J Pharm, 310, 2006, 139-145.
22. Alabrazi MY, Elzein H, An approach to formulating an oral floating drug delivery system for dexchlorpheniramine maleate using factorial design, Die Pharmazie, 67, 2012, 1–7.
23. Rowe RC, Sheskey PJ, Quinn ME, Handbook of Pharmaceutical Excipients, 6th edition. UK, USA: Pharmaceutical Press; 2009.

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