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Research Article

EFFECT OF HPMC/CARBOPOL ON THE RELEASE OF CHLORPHENIRAMINE MALEATE FROM MATRIX TABLETS

Bipin P. Patel[1*)], Dasharath M. Patel[2], Jayvadan K. Patel[1]

[1]Nootan Pharm. College, S. P. Sahakar Vidyadham, Visnagar-384 315, India
[2]Dept of Pharmaceutics and Pharmaceutical Tech, Shri Sarvajanik Pharmacy College, Mahesan 384001, india

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*Corresponding author
B P Patel
e-mail:
visitbipin111@yahoo.co.in

ABSTRACT

Chlorpheniramine maleate is widely used in treatment for allergic disorder and cold. The controlled release matrix tablets of chlorpheniramine maleate were prepared using HPMC K15M, HPMC K100M and carbopol and studied their effect on drug release. Prepared tablets were evaluated for various physical parameters. In *vitro* drug release study shows that slow release in HPMC K100M than other two polymers. If concentration of polymer increases than the drug release is decreases due to formation of polymeric matrix. Zero order, first order, Higuchi's and Korsmeyer's equations applied to know the mechanism of drug release from prepared tablets. The similarity and dissimilarity factor found to be 77.88 and 4.14, respectively for drug release in stability study which shows there was no significant difference in drug release.

Key words: Chlorpheniramine maleate, matrix tablet, HPMC K15M, HPMC K100M, carbopol and swelling index

INTRODUCTION

An allergy is a hypersensitivity disorder of the immune system. Allergic reactions occur when a person's immune system reacts to normally harmless substances in the environment (Kay, 2001). Chlorpheniramine maleate is first-generation alkyl amine antihistamine drug. It is widely used in symptomatic relief of common cold and allergic diseases. It has also been used in veterinary applications. Chlorpheniramine maleate is well absorbed in the gastrointestinal tract (Sweetman, 2005). So formulating matrix tablet of chlorpheniramine maleate we can control over allergic reaction in the suffering patients.

These formulations are designed to deliver drugs at slow rate over a long time period for allergic condition. One of the most commonly used methods of developing controlled release formulations is to include them in matrix tablets. The matrix tablet prepared by direct compression is easy to manufacture. Using suitable polymer matrix formulation is possible and controlled release of drug is possible.

In these study the effect of various polymers like HPMC K15M, HPMC K100M (Reddy *et al.*, 2003) and carbopol on drug release is studied. All the formulation of matrix tablets was prepared by direct compression method. Drug release kinetics and mechanism was calculated for zero order, first-order, Higuchi's and Korsmeyer's equations (Korsmeyer *et al.,* 1983).

MATERIALS AND METHODS

Chlorpheniramine maleate was received as a gift sample from Kon Text Chemicals Ltd, Kolkata. HPMC K15M and HPMC K100M were gift sample from colorcon India Pvt Ltd. Carbopol and MCC (Avicel PH 102) were gift sample from Signet Chemical Corporation, Mumbai. PVP K30, talc and magnesium stearate were procured from Nice Chemicals (P) Ltd, Cochin. All other reagents were of analytical grade.

Preparation of tablets

All tablet formulations with different drug to polymer ratios were prepared by direct compression technique (Formulations M1-M9, Table I). All powders were weighed accurately in electronic balance then passed separately through 60 # screen sieve. Chlorpheniramine maleate was first mixed with polymer for 5min to a mortar and then adds other excipients and triturated till it was uniform. Rotary eight station punch tablet machine was used to press tablets of 120mg weight (Sakr *et al.*, 2011).

Evaluation of tablets

Thickness: The thickness of the tablets was determined using a vernier caliper. Five tablets from each batch were used and the average values were calculated.

Weight variation: To study weight variation, 20 tablets of each formulation were weighed individually using four digital electronic balance (Sartorius bt 224S).

Drug content: Twenty tablets from each batch were weighed accurately and powdered powder equivalent to 12mg chlorpheniramine maleate was shaken with 100mL of distilled water in 100 ml volumetric flask and dilute up to appropriate volume. Resulting solution was filtered and assayed at 265nm using double beem UV/Vis spectrometer (Shimadzu UV-1800) and content of chlorpheniramine maleate was calculated (Praveen, *et al.*, 2011).

Hardness and friability: For each formulation batches, the hardness and friability of 5 and 20 tablets, respectively, were determined using hardness tester (Monsanto) and the friabilator (Electrolab), respectively (Indian Pharmacopoeia, 2010).

Swelling index: This test was used for guidance to monitor the development of physical changes in the tablets morphology when placed in the dissolution medium (Sriamornsak, *et al.*, 2007). Tablets are placed in the 500 ml distilled water. Weight of tablet was determined at zero time, 1.0, 3.0 and 6.0 h and calculated swelling index for all batches using following equation.

SI= (W2-W1)/W1*100

Where SI is swelling index of tablet, W1 is initial weight of tablet and W2 is reweigh of tablet.

In vitro release studies: The drug-release study was carried out using a USP type-2 apparatus (Electrolab, TDT-06T) at 37±0.5°C and at 50rpm using 900mL of distilled water as a dissolution medium (n=3). A sample (5 ml) of the solution was withdrawn from the dissolution apparatus at half hour interval up to 8 hour and withdrawn volume was replaced with fresh dissolution media. The withdrawn samples filtered through a 0.45-micrometer membrane filter, diluted suitably, and analyzed spectrophotometrically.

In vitro drug release (kinetics and mechanism): To know the mechanism of drug release from these formulations, the data were fitted to zero order (cumulative amount of drug released vs time), first-order (log cumulative percentage of drug remaining vs time), Higuchi's (cumulative percentage of drug released vs square root of time), and Korsmeyer's (log cumulative percentage of drug released vs log time) equations (Korsmeyer *et al.*, 1983).

Zero order equation

$f_t = K_0 t$

Where f_t is the fraction dissolved at time t and K_0 is the apparent dissolution rate constant or zero order rate constant.

First-order equation

$\log Q_t = \log Q_0 - K_1 t/2{:}303$

Where Q_t is the amount released at time t, Q_0 is the initial amount of drug in solution and K_1 is the first order rate constant.

Higuchi's equation

$F_t = K_H - t^{1/2}$

Where F_t is the fraction dissolved at time t and K_H is the Higuchi dissolution constant.

Korsmeyer's equation

$M_t/M_\infty = at^n$

Where M_t is the amount of drug released at time t, M_∞ is the amount of drug released after infinite time (total drug in a dosage form), a is the Korsmeyer's dissolution rate constant and n is the release exponent.

Stability study: stability studies were conducted on optimized formulation (M6) containing HPMC K100M in 41%. Assess their stability with respect to their physical parameters and drug release characteristics after storing them at 40°C with relative humidity (RH) 75% for 6 months.

Similarity factor (f_2) and difference factor (f_1) analysis.

Effect of storage condition on *in vitro* drug release profile of optimized formulation (M6) was performed. The similarity factor (f_2) and difference factor (f_1) was determined using the data obtained from drug release studies (Mukesh, *et al.*, 2005). The data were analyzed by the formula shown in following equations.

$$f_2 = 50 \cdot \log\left\{\left[1 + (1/n)\sum_{t=1}^{n}(R_t - T_t)^2\right]^{-0.5} \cdot 100\right\}$$

Table I. Formulation batches of chlorpheniramine maleate matrix tablet

Ingredients	M1	M2	M3	M4	M5	M6	M7	M8	M9
Chlorpheniramine maleate	12	12	12	12	12	12	12	12	12
HPMC K15M	30	40	50	-	-	-	-	-	-
HPMC K100M	-	-	-	30	40	50	-	-	-
carbbopol	-	-	-	-	-	-	30	40	50
Avicel PH 102	70	60	50	70	60	50	70	60	50
PVP K30	4	4	4	4	4	4	4	4	4
talc	2	2	2	2	2	2	2	2	2
Mg stearate	2	2	2	2	2	2	2	2	2

Table II. Physical properties of the prepared tablets

Batches	Average weight (mg)	Thickness (mm)	Hardness (Kg/cm²)	Friability (%)	Drug content (%)
M1	118.5 ±2	1.93±0.1	2.4 ±0.37	0.52	98.32
M2	120.3 ±3	1.98±0.2	3.7 ±0.40	0.34	99.96
M3	123.1 ±1	2.01±0.1	5.2 ±0.51	0.23	100.40
M4	119.2 ±2	1.88±0.2	2.8 ±0.24	0.43	99.04
M5	118.0 ±2	1.95±0.3	4.1 ±0.86	0.33	101.02
M6	120.6 ±3	1.96±0.1	5.6 ±0.37	0.29	100.04
M7	120.8 ±1	1.97±0.2	2.3 ±0.40	0.50	98.49
M8	121.8 ±1	1.94±0.2	2.9 ±0.66	0.43	99.73
M9	119.9 ±2	1.89±0.3	5.1 ±0.58	0.31	100.24

$$f_1 = 100 \times \left[\frac{\sum_{t=1}^{n} |R_t - T_t|}{\sum_{t=1}^{n} R_t} \right]$$

Where n is the number of data points, R_t is the amount released from the reference at time t, and T_t is the amount released from the test at time t. The similarity of two release profile can observe using the value of f_2 and f_1.

RESULTS AND DISCUSSION

Physical properties of the tablets

The comparison of physical properties of the matrix tablets (Table II). The weight and thickness of the matrix tablets ranged from 118.0 to 123.1mg and 1.88 to 2.01 respectively. All tablets prepared in thisstudy meet the official pharmacopeia requirements for weight variation and uniform thickness.

Drug uniformity results were found to be good among different batches of tablets, and the percentage of drug content was more than 98.32%.

In the present study, the percentage friability for all the formulations was below 1%, indicating that the friability is within the pharmacopeia limits. The hardness of the tablet was found to be 2.4 to 5.6 kg/cm² which show sufficient mechanical strength.

All the tablet formulations showed acceptable pharmacotechnical properties and acceptable according to pharmacopoeial specifications.

The swelling index was calculated with respect to time (Figure 1). As time increases, the swelling index was increased, because weight gain by tablet was increased proportionally with rate of hydration up to 4h. Later on, it decreases gradually due to dissolution of outer most gelled layer of tablet into dissolution medium. From the graph it observed that batch M6 has lower swelling index which contain HPMC K100M in around 41% and batch M7 has higher swelling index and rate of hydration which contain carbopol in 25% concentration.

The in vitro drug release of all batches is show in fig 2, 3 and 4. All the batches shows that around 100% drug release are found at 4.5

hour onward. The almost drug release found in follow zero order (regression coefficient is

Table III. Release kinetics of chlorpheniramine maleate from the prepared formulations

Batch	Zero order (R^2)	First order (R^2)	Higuchi plot (R^2)	Korsmeyer plot	
				(R^2)	Slope (n)
M1	0.994	0.982	0.974	0.986	0.31
M2	0.973	0.987	0.931	0.918	0.26
M3	0.990	0.979	0.970	0.966	0.24
M4	0.969	0.991	0.928	0.947	0.24
M5	0.991	0.985	0.969	0.957	0.26
M6	0.997	0.986	0.974	0.976	0.24
M7	0.996	0.988	0.980	0.983	0.34
M8	0.992	0.996	0.966	0.970	0.31
M9	0.982	0.968	0.956	0.971	0.29

Table IV. Stability study for physical parameter of optimized batch (M6)

Parameter	At 0 month	At 3 month	At 6 month
Drug content	100.04	99.42	98.51
Hardness	5.6	4.9	4.8
Friability	0.29	0.33	0.51

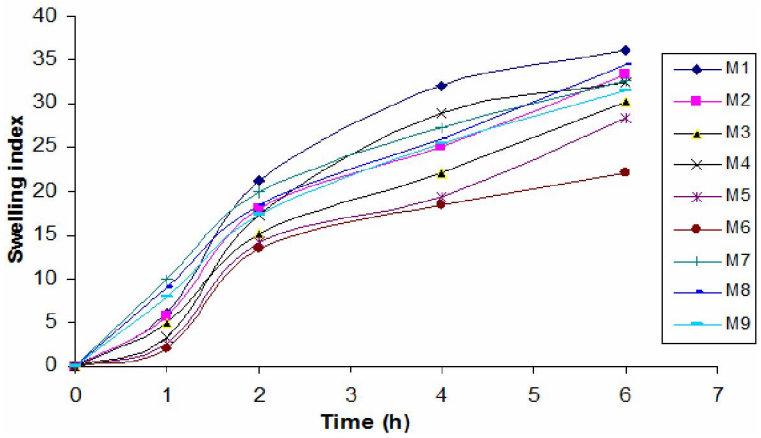

Figure 1. Swelling properties of prepared matrix tablets

batch M1 and M7 are at 4.5 and 5.5hour due to low concentration of polymers that is HPMC K15M and carbopol, respectively. Batch M6 is consider as a best batch from all other batches due to its slow drug release up to 8hour which contains HPMC K100M in 41% concentration.

To know the mechanism of drug release from these tablet formulations, the data were treated according to zero order, first-order, Higuchi's plot and Korsmeyer's plot. As clearly indicated in table III, all the formulations more than 0.982 and near to 0.99) except batch M2 and M4 because the regression coefficient is 0.973, 0.969 respectively. The regression coefficient for batch M2 and M4 is 0.987 and 0.991 respectively, according to first order plot. When the data were plotted according to the Higuchi's equation value is found to be 0.928 to 0.980. Drug release pattern can be finding out by using the slope value of the Korsmeyer's plot. Fickian diffusion was found in all the batches because the slope value is less than 0.45.

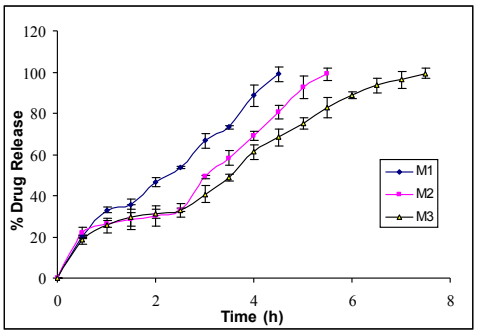

Figure 2. Drug release profile of HPMC K15M containing tablets

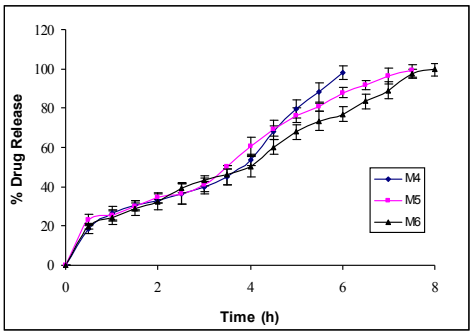

Figure 3. Drug release profile of HPMC K100M containing tablets

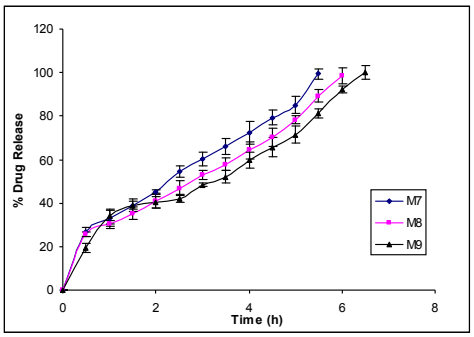

Figure 4. Drug release profile of carbopol containing tablets

The optimized formulation (M6) was further evaluated for stability studies. It was suggested that there was no significant changes in physical parameters such as hardness, weight variation, content uniformity and friability. In-vitro drug release profile of optimized batch (M6) was shown in figure 5. In addition statistically no significant difference was observed in the release rate after 6 month. The value of similarity factor (f_2) was found to be 77.88 which indicate similarity observed after 6 month due to value is near to 100. The value of difference factor (f_1) was found to be 4.14 indicating similarity between both drug release.

CONCLUSION

Matrix tablet of Chlorpheniramine maleate was successfully prepared by using various synthetic polymers such as HPMC K15M, HPMC K100M and carbopol. The

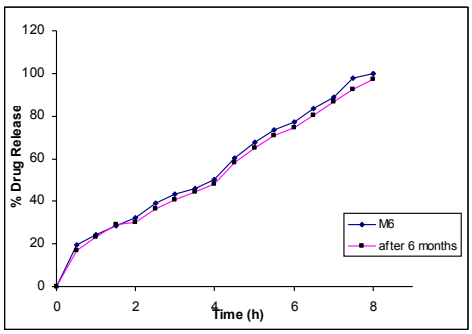

Figure 5. Comparison of dissolution profile of M6 batch before and after stability study

direct compression method is suitable for formulation of matrix tablets. Among these all three polymer HPMC K100M gives slow drug release up to 8 h in 41% concentration. Carbopol gives fast drug release compared to other two polymers. There is no significance change of physical parameter and drug release profile after stability study of matrix tablets.

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