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Studies of Diltiazem Hydrochloride Sustained Release Matrices Profile in Multimedia Dissolution Conditions

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ABSTRACT

The present study was focused on the effect of multimedia dissolution profile on the drug release of Diltiazem hydrochloride sustained release matrix tablets. Diltiazem is a calcium channel blocker widely used for its peripheral and vasodilator properties. It is given as oral dosage form in the treatment of angina pectoris and the management of hypertension. Diltiazem matrices were prepared from combination of polymers HPMCK4M and HPMCK15M to sustain the release of the drug.Multimedia dissolution studies were performed to mimic the in-vivo condition by doing in-vitro test and pH/buffer selection is based on the exposure of drug from stomach to intestine/colon and to ensure the impact of pH changes on dissolution and release of drug substance for absorption. The study ensures the impact of pH changes on dissolution and release of drug substance for absorption.

Keywords: Diltiazem hydrochloride, multimedia, Ph

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INTRODUCTION

Diltiazem hydrochloride which is a calcium channel blocker widely used for its peripheral and vasodilator properties. It is also used for lowering blood pressure and has some effect on cardiac induction. It is given as oral dosage form in the treatment of angina pectoris and the management of hypertension. Its short biological half life (3-5 h), high aqueous solubility, and frequent administration (usually three to four times a day) make it a potential candidate for sustained release preparations [1-2].

Sustained release drug delivery system is designed to achieve a prolonged therapeutic effect by continuously releasing medication over an extended period of time after administration of a single dose.

Many known polymer are available for sustained release preparation. Hydroxypropyl methylcellulose (HPMC) is cellulose ether which may be used as the basis for hydrophilic matrices for controlled release oral delivery. Diltiazem matrices were prepared from combination of polymers HPMCK4M and HPMCK15M to sustain the release of the drug [3-5]. Multimedia dissolution is to mimic the in-vivo condition by doing in-vitro test and pH/buffer selection is based on the exposure of drug from stomach to intestine/colon and to ensure the impact of pH changes on dissolution and release of drug substance for absorption [6-10].

MATERIALS AND METHODS

Diltiazem hydrochloride was obtained as a gift sample and tablets were prepared by direct compression using HPMCK_4M and HPMCK_{15}M polymer combinations. Other excipients used were Magnesium stearate, Talc, MCC and dibasic calcium phosphate. The tablet weight was taken 290mg and kept constant. The drug was analyzed spectrophotometrically (UV 1601 Shimadzu, Japan) and absorbance was measured at 237 nm.

Physical Characterization

The tablets were subjected to their physical characterization. Hardness, friability and weight variation and found within the probable limits, Table [1].

Experimental

Three tablets of Diltiazem hydrochloride were taken into three different pH of phosphate buffer (pH2.4, pH 6.8 and pH 7.4).The USP dissolution apparatus was set at rotation 50 rpm and temperature of the assembly was set at 37^0 C. The tablets were placed in above prepared three different media of different pH. Absorbance was measured at 237 nm by collecting sample at different time interval as follows 0.5,1,2,3,4,6,8 hrs. Five milliliters aliquots were withdrawn at predefined intervals, and the volume of the dissolution medium was maintained by adding the same volume of dissolution medium. The percentage drug release

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was calculated at different time intervals at different pH. The graph was plotted between percent drug release and time for different dissolution media.

RESULTS AND DISCUSSION

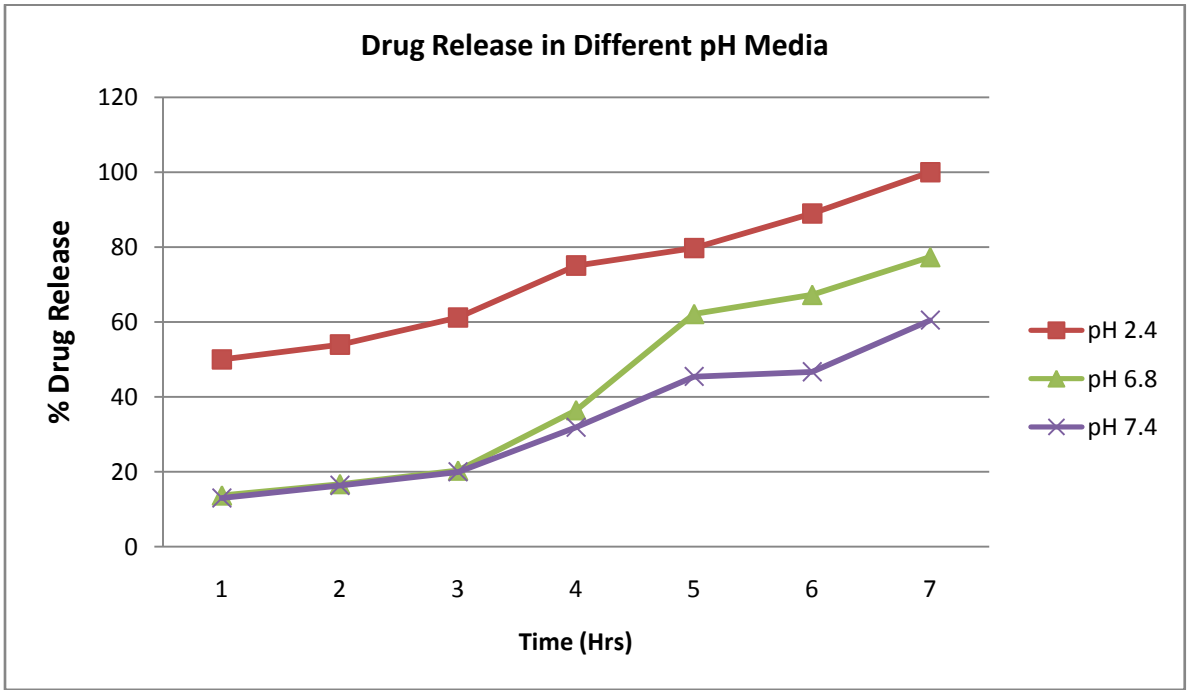
Table [1]

FORMULATION					
HPMC K4M mg	HPMC K15M mg	Weight mg Mean ± SD	Hardness Kg Mean ± SD	Friability (%)	Assay (%)
60	30	290 ± 1.54	5.5O ± 0.14	0.50-0.08	95.83

Table [2]

Sr. No.	Time(hr)	Absorbance at different pH			% Drug Released in Different pH		
		2.4	6.8	7.4	2.4	6.8	7.4
1.	0.5	0.487	0.186	0.180	49.97	13.70	13.02
2.	1	0.521	0.202	0.209	53.94	16.73	16.39
3.	2	0.583	0.242	0.239	61.17	20.33	19.98
4.	3	0.702	0.381	0.349	75.05	36.45	31.88
5.	4	0.752	0.601	0.458	79.71	62.12	45.44
6.	6	0.821	0.632	0.467	88.93	67.22	46.67
7.	8	0.926	0.679	0.579	99.98	77.30	60.44

Fig [1]



Multimedia dissolution is to mimic the in-vivo condition by doing in-vitro test and pH/buffer selection is based on the exposure of drug from stomach to intestine/colon and to ensure the impact of pH changes on dissolution and release of drug substance for absorption, [Table.2]. The graph shows the percent drug release pattern at different time intervals for different dissolution media at different pH [Fig.1].

CONCLUSION

The release profile of Diltiazem hydrochloride from the matrices increased continuously with time, and the amount of drug release best seen in acidic media (pH=2.4). The cumulative amount of drug release is higher at pH 2.4 than that of pH 6.8 by 22.68 % and then that of pH 7.5 by 39.54 %. This increase in drug release at lower pH can be attributed to pH dependent solubility of of Diltiazem hydrochloride. As the pH decrease, the solubility of Diltiazem hydrochloride increases which might increase drug release from matrices.

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