

# Twice Daily Propranolol Hydrochloride Sustained Release Tablets: Formulation Design and in-vitro Evaluation

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## Abstract

The purpose of this study was to develop and optimize the propranolol hydrochloride twice daily sustained release formulations containing hydroxypropylmethylcellulose K100M and microcrystalline cellulose. The effects of various concentration of hydrophilic polymer on in-vitro drug release profile were investigated. Matrix tablets were prepared by wet granulation method. Prepared formulations were evaluated for various parameters like weight variation, hardness, friability, thickness, and assay and water uptake study. In-Vitro drug release was done in 0.1 N HCl (pH 1.2) for first 2 hours followed by phosphate buffer (pH 6.8) for remaining hours. Water uptake indicated the swelling property of tablet when come in contact with the dissolution medium, forming a gel layer around the matrix and simultaneously diffusion. Compatibility study between drug and polymers was done by FTIR revealing no interaction. So the combination of hydrophilic hydroxypropylmethylcellulose K100M, microcrystalline cellulose at different concentrations was successfully used for formulating the sustained release matrix tablets of propranolol hydrochloride.

**Key Words:** Hydroxypropylmethylcellulose, Microcrystalline cellulose, Propranolol hydrochloride, sustained release

## INTRODUCTION

The advantage of designing sustained release dosage form is mainly reducing dosing frequency, maintaining therapeutic concentration of the drug for prolonged period of time with minimized local or systemic adverse effects. The hydrophilic gel-forming matrix tablets are extensively used for oral sustained release dosage forms due to their simple design, economic value and reducing the chances of dose dumping. Moreover intra- and inter-subject variations are not limiting parameters for sustained release formulations showing pH-independent drug release. Hydroxypropylmethylcellulose K100M (HPMC) is a pH-independent polymer used as a release retardant and the drug release rates from HPMC matrix tablets are independent of processing variables. Microcrystalline cellulose (MCC) is often regarded as one of the best excipient for formulations showing increase in dissolution rate and enhancing the compressibility characteristic of tablets prepared by high shear granulation. Propranolol hydrochloride is a nonselective beta-adrenergic blocking agent widely used for treatment of hypertension, angina pectoris and cardiac arrhythmia. Propranolol hydrochloride has half-life of 3 to 5 hours so the frequent dosing reduces patient's compliance. However, the drug show extensive first pass metabolism after oral administration limiting its bioavailability up to 30%. This provides the suitable reason to take Propranolol hydrochloride as the model drug for sustained release dosage form. The objective of the present study was to develop a sustained release matrix formulation of propranolol hydrochloride and to examine the effect of concentration of gel forming hydrophilic polymer HPMC K100M on in-vitro drug release.

## MATERIALS AND METHODS

### Material

Propranolol Hydrochloride was a gift sample from Cipla Lab. Ltd., Mumbai. HPMC K100M, Microcrystalline cellulose (MCC) and starch was procured from Novel pharmaceuticals, India. Other materials and solvents used were of analytical grade.

### Preparation of tablets

The sustained release matrix tablets of propranolol hydrochloride were prepared by wet granulation method. The drug and the total amount of the varying ingredients (HPMC K100M, MCC) was maintained at 300 mg. The drug and excipients were weighed and mixed well. The composition of formulations was given in Table 1. The powder mixtures were passed through sieve no.60 prior to granulation. Water was taken as solvent to make a wet mass. Then the wet mass was passed through sieve no. 14. The granules were dried in an oven for 2 h at 50 °C. Then the dried mass was blended with 0.5% of magnesium stearate. Tablets containing 80 mg of propranolol were compressed using 6 mm flat faced punch at 1.5 ton compaction pressure.

### Evaluation of matrix tablets

The evaluation tests for the matrix tablets, such as hardness, friability, weight variation and drug content etc. were determined using standard procedure. The data's were given in Table 2.

### Water uptake Test

Water uptake study was done to evaluate the swelling characteristic of the polymer. Weighed tablets ( $M_0$ ) were taken on previously weighed watch glass and placed at bottom of dissolution vessel, containing phosphate buffer (pH 6.8) at 37 °C at a stirring speed of 100 rpm. At one hour interval (1-12 hours) tablets were withdrawn and excess amount of water was removed from the tablet by using blotting paper and weighed ( $M_t$ ). The swelling index was calculated using the formula (Table 1).

$$S.I = \{(M_t - M_0) / M_0\} \times 100$$

Where, S.I = swelling index,

$M_t$  = weight of tablet at time 't'

$M_0$  = Initial weight of tablet

### In-vitro drug release Study

The USP basket method was used for the in vitro dissolution studies to estimate the release profile of Propranolol hydrochloride. The stirring speed was maintained at 100 rpm. The dissolution rate was studied using 900 ml of 0.1 N hydrochloric acid (pH 1.2) for first 2 hr followed by phosphate buffer (pH 6.8) up to 12 hours. Samples were withdrawn and analyzed in UV/Visible spectrophotometer at 289.3 nm. The release studies were conducted in triplicate. (Fig.3).

### Compatibility Study

The identification of pure drug and drug excipient compatibility study was done by KBr pellet technique using Jasco FT/IR-4100. The standard spectrum was correlated with the reference IR spectra.

### RESULTS AND DISCUSSION

The data's for physical characterization of the tablets were given in Table 2. All the physical parameters such as weight variation, thickness, hardness, friability were found within the range. The values of hardness test and percent friability indicates good handling property of prepared tablets. The drug content of the tablets was within the range of 99-100 %. Visual observation (Fig. 1) showed the swelling nature of hydrophilic polymer. It is clear that the matrix undergoes swelling due to gelling property of HPMCK100M. Constant release occurred due to increase in diffusion path length owing to swelling. FTIR study (Fig.2) suggested that there was no interaction between the pure drug and the polymer. The drug release rate (Fig.3) decreased with the increase in the tablet content of HPMCK100M. The increased release rate of MCC might result due to its water soluble nature which stimulate the water penetration into the matrix, thus resulting increased drug release rate. From the in vitro evaluation it was found that formulation F5 showing the best result as required.

**Table 1:** Composition of matrix tablets

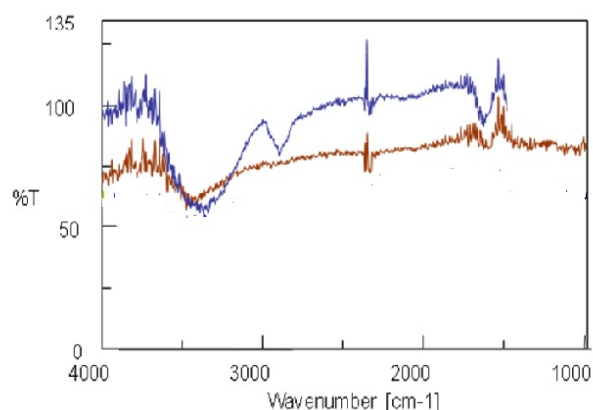
Formulations	Ingredients(mg)				
	Drug	HPMCK100M	MCC	Starch	Talc
F1	80	30	150	37	3
F2	80	60	120	37	3
F3	80	90	90	37	3
F4	80	120	60	37	3
F5	80	150	30	37	3
F6	80	180	----	37	3

**Table 2:** Physical properties of matrix tablet

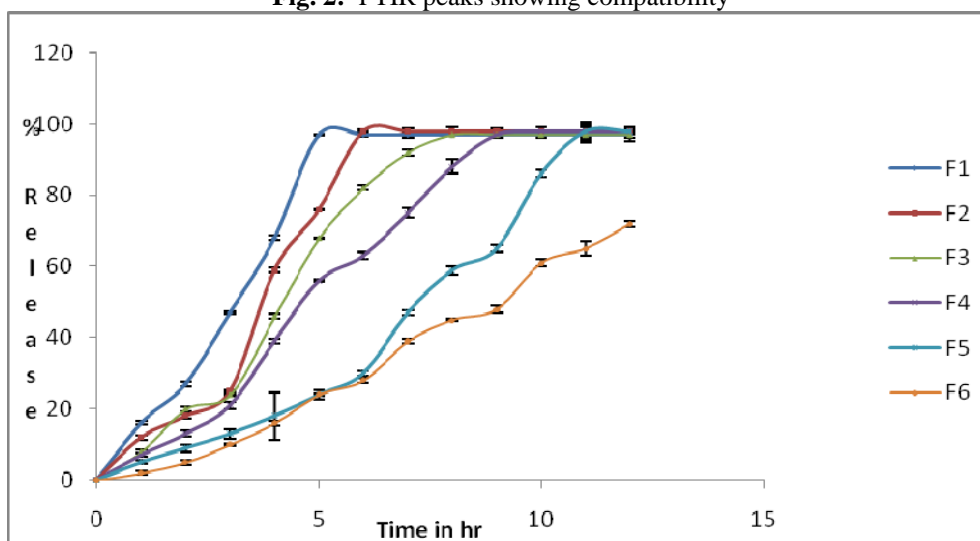
Parameters	Formulations					
	F1	F2	F3	F4	F5	F6
Weight variation test(mg)	300±0.24	300±0.61	300±0.87	300±0.52	300±0.26	300±0.9
% Friability	0.27±0.04	0.34±0.05	0.29±0.02	0.27±0.03	0.3±0.04	0.35±0.02
% Swelling	105±2.34	123±0.45	137±1.34	155±1.59	178±0.98	137±2.12
% Assay	99.2±.98	99.6±1.2	99.4±1.31	99±0.8	100.1±0.9	100±0.87



**Fig.1:** Water uptake study showing Swelling property of HPMC



**Fig. 2:** FTIR peaks showing compatibility



**Fig.3:** In-vitro release profile

### CONCLUSION

From the results of the present research work it can be concluded that the combination of hydrophilic HPMC K100M and MCC can be successfully employed for formulating the sustained release matrix tablets of Propranolol hydrochloride.

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