RESEARCH ARTICLE

FORMULATION AND EVALUATION OF BI-LAYERED TABLETS OF PROPANOLOL HCl BY USING GUMS

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Abstract: Bi-layered tablets of propanolol hydrochloride were formulated by xanthan gum, locust bean gum, guar gum with different drug: gum ratios of 1:0.25, 1:0.5 and 1:1 by wet granulation method. Immediate release layer of the tablet was prepared using super disintegrant such as sodium starch glycolate and sustained release layer was prepared by using gums in different drug to gum ratio. The prepared bi-layered tablets were of round shape and convex with diameter of 8 mm. The drug content of the formulations was found with in 98.9-101.7%. The release of propanolol HCl was extended up to 12 h and was dependent upon the concentration of the gum. The release was better sustained with xanthan gum at the concentration of 1:1.

Keywords: Propanolol, xanthan gum, locust bean gum, guar gum, bi-layered tablets.

INTRODUCTION

The main objective of any drug therapy is to achieve desire therapeutic concentration of the dug in blood, tissues. In matrix tablets the bilayered concept is used for sustained the release of drug. Drug release from the fast releasing layer leads to a sudden rise in the blood concentration. However, the blood level is maintained as steady state, as the drug is released from the sustained layer.

Propanolol HCl is a non-selective β-adrenergic blocking agent used in the treatment of hypertension, angina pectoris and many other cardiovascular disorders [1]. Its short biological half-life (3-6hrs) and thus frequent administration (usually 3-4 times a day) makes it a potential candidate for the design of sustained release dosage forms [2]. Propanolol is almost completely absorbed from the gastro intestinal tract, but is subject to considerable hepatic tissue binding and first-pass metabolism [3]. Peak plasma concentration occur about 1 to 2 hours after an oral dose.

In the present study, Propanolol HCl bi-layered tablets were formulated consisting of two layers such as fast releasing layer and sustaining layer. Fast releasing layer was prepared using super disintegrant such as sodium starch glycolate and sustaining release layer was prepared using gums such as xanthan gum, locust bean gum, guar gum with different drug : gum ratios of 1:0.25, 1:0.5 and 1:1 by wet granulation method.

MATERIALS AND METHODS

Propanolol HCl was obtained as a gift sample from Dr. Reddys Laboratories, Hyderabad. xanthan gum (XG), locust bean gum (LBG), guar gum (GG), sodium starch glycolate, magnesium stearate and talc were of analytical grade and procured commercially.

Preparation of bi-layered tablets

Propanolol matrix tablets were prepared by wet granulation technique. The drug, gums and other excipients used were passed through sieve no. 80 before their use in the formulation. The layer with sustaining dose was formulated with various amounts of gums like xanthan gum, locust bean gum, guar gum. The dose in the formulations for fast release was 25 mg. The maintenance dose or sustaining dose of propanolol was 55 mg. The maintenance dose of propanolol hydrochloride was calculated as per the reported method [4, 5].

Formulation of fast released layer

The fast release layer was formulated by mixing the drug uniformly with 15 mg of sodium starch glycolate. Granulation was carried out with a 2% w/v of PVP in alcohol.

Formulation of sustaining layer

Granules for sustaining layer were prepared by mixing maintenance dose of drug with matrix materials (xanthan gum, locust bean gum, guar gum). The powders were mixed with sufficient quantity of 2% w/v of PVP in alcohol until a wet mass formed. The cohesive mass obtained was passed through sieve no. 12 and the granules were dried in an over at 45 °C for half an hour. The dried granules were again sieved by passing through sieve no. 16. The granules were mixed with required quantities of lactose, talc and magnesium stearate. The required amount of granules for sustained release layer was compressed into tablets on a single punch tablet machine (Cadmach, India) using 8 mm round and convex punches. Over this compressed layer, required quantity of fast release layer granules was placed and compressed lightly to form a bi-layered tablet.

Evaluation of propanolol matrix tablets

Propanolol HCl matrix tablets were evaluated. Prepared tablets were evaluated for hardness (Pfizer hardness tester), friability [6] (Roche's friabilator), weight variation, thickness, drug content [7] and *in vitro* release studies [8].

Estimation of propanolol

Ten tablets were weighed individually and powdered. An amount equivalent to 50 mg of drug was extracted with 50 ml of methanol and sonicated for 15 min. The volume was made up to 100 ml with distilled water. The mixture was filtered, diluted suitably and the drug content was measured at 290 nm using ELICO-167 double beam UV spectrophotometer.

In vitro release study

Dissolution rate of propanolol from various bi-layered tablets was studied using USP XXIII six-station dissolution rate test apparatus (DISSO 2000, LABINDIA) with paddle stirrer. The dissolution rate was studied in 900ml of distilled water maintained at 37 ± 0.5 °C with a speed of 50 rpm. Samples of 5 ml were withdrawn different time intervals, filtered (through 0.45μ) and replaced with 5 ml of fresh dissolution medium. The samples were suitably diluted if necessary and estimated spectrophotometrically at 290 nm. The dissolution experiments were conducted in triplicate.

RESULTS AND DISCUSSION

The prepared bi-layered tablets were found to contain the medicament with in 100 ± 2% of labeled claim. Hardness of the tablets in all the batches was found to be in the range of 5-7kg/cm^2. Friability of the tablets was less than 1%. The thickness of the tablets ranged from 2.9-3.2 mm. The values of hardness and friability indicate good handling property of the prepared bi-layered tablets. The physical characteristics of the tablets were given in Table 1. The prepared bi-layered tablets were subjected to *in vitro* drug release studies using distilled water as a dissolution medium for 12 h. From all the formulations over 35% of propanolol was released with in the fist hour of dissolution study. Dissolution profiles of various tablets are shown in Table 2 and in the Figure 1. The remaining drug is released in a sustained manner due to gum used. As concentration of gum in the sustained layer was increased, the drug release was decreased in all the formulations prepared with xanthan gum, locust bean gum, guar gum. It was observed that bi-layered tablets prepared with xanthan gum were retarding the drug release more when compared with the tablets prepared with locust bean gum, guar gum.

Table 1. Evaluation of various parameters of propanolol HCl tablets prepared

Formulations	Composition	Thickness (mm)	Hardness (kg/cm²)	% friability	% Drug content
F1	XG (1:0.25)	3.1±0.02	5.2±0.2	0.53	97.6±0.83
F2	XG (1:0.5)	3.0±0.1	5.4±0.6	0.68	101.25±0.31
F3	XG (1:1)	3.2±0.2	5.9±0.4	0.45	100.2±0.65
F4	LBG (1:0.25)	2.9±0.1	6.2±0.1	0.54	98.6±0.79
F5	LBG (1:0.5)	2.9±0.3	6.4±0.3	0.68	100.7±0.35
F6	LBG (1:1)	3.0±0.1	5.8±0.8	0.54	99.3±0.48
F7	GG (1:0.25)	3.2±0.2	6.4±0.7	0.58	98.9±0.49
F8	GG (1:0.5)	3.0±0.02	6.7±0.3	0.69	99.45±0.55
F9	GG (1:1)	3.2±0.05	5.7±0.4	0.67	101.53±0.12

Table 2. Release parameters of propanolol HCl bi-layered tablets formulated

Formulations	Zero order 'r'	First order 'r'	Higuchi 'r'	Release exponent 'n'	k	$t_{1/2}$ (hr)
F1	0.996	0.964	0.992	0.718	0.210	4.78
F2	0.959	0.939	0.994	0.649	0.160	5.49
F3	0.982	0.969	0.984	0.604	0.128	6.93
F4	0.983	0.968	0.995	0.673	0.187	4.92
F5	0.967	0.945	0.991	0.585	0.115	6.56
F6	0.977	0.963	0.990	0.589	0.110	8.45
F7	0.984	0.969	0.993	0.745	0.260	4.26
F8	0.965	0.964	0.994	0.672	0.118	5.06
F9	0.979	0.952	0.988	0.610	0.139	6.15

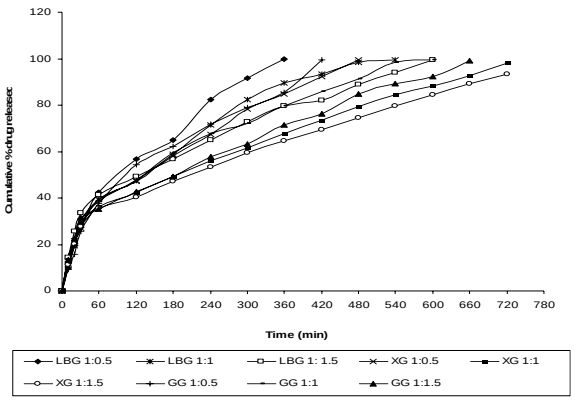

Figure 1. *In vitro* dissolution profile of bi-layered tablets of propanolol HCl prepared with various gums

The propanolol release data of all the tablets formulated were evaluated as per zero order, first order and higuchi kinetics [7]. The release data were fitted to corresponding equations to determine release rates and mechanism of drug release from these tablets. It was observed that the release of drug was more with in 40 min due to the presence of fast releasing layer after that slow release was observed due to the presence of matrix materials, the release data followed zero order kinetics. The release parameters of tablets formulated were summarized in Table 2. Plots of amount release *vs* square root time were found to be linear with r>0.984 and the Korsemeyer model indicating that the drug release mechanism form these matrix tablets was Fickian diffusion controlled.

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REFERENCES

1. Benowitz NL, Katzung BG. Basic and clinical pharmacology. 6th ed. New York: Prentice-Hall Iinternational Inc; 1995, 157.
2. Siepmann J, Aninaoui A, Vernaud JM. J.Pharm.Sci. 1998; 87: 827.
3. Reynolds JE. Martindale:The extra Pharmacopoeia. 30th ed. London: Pharmaceutical press; 1993,354.
4. Abraham MA, Shirwaikar A. Formulation of multilayered sustained release tablets using insoluble matrix system. Indian J. Pharm. Sci. 1997; 59:312-315.
5. Vercammen JP, Dauwe D, Brioen P. Possibility of use of Eudragit RS as a sustained release matrix agent for the incorporation of water soluble active compounds at high percentages. STP Pharma. Sci. 1997; 7:491-497.
6. Leon Lachman, Lieberman HA and Kanig JL. The theory and practice of Industrial pharmacy, 3rd ed. Bombay: Varghese publishing house; 1987, 67.
7. Indian Pharmacopoeia. Vol I. The controller of Publications, New Delhi. 1996, 736.
8. United States Pharmacopoeia, United States Pharmacopoeial Convention, Rockville, MD. 1997,1475.
9. Higuchi T. J.Pharm.Sci. 1961; 50: 874.