Research Article

Formulation and evaluation of controlled release matrix tablets of Pentoxifylline

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ABSTRACT

Pentoxifylline is a vasodilator widely used in the treatment of the peripheral & cerebral vascular disorders & thus exerts a milder side effect on gastrointestinal mucosa. The objective of this work is two retardant polymers were employed with varying concentrations & also in combination in different ratio to get promising concentration for controlled release matrix tablets. Matrix tablets of pentoxifylline were formulated using hydrophilic swellable polymers hydroxyl propyl methyl cellulose & guar gum with lactose as diluent. Two retardant polymers HPMC & guar gum were used in different ratio to retard the drug release from the matrices. Talc, magnesium Stearate& starch were used as excipients. All the formulations prepared were found to comply with the weight variation, friability, drug content uniformity & in-vitro dissolution studies. Promising formulations F_3, F_6, F_8 were compared with marketed formulation, which shows that formulation F_3 exhibits drug release pattern which is similar with marketed formulation of pentoxifylline.

Key words: Pentoxifylline, Vasodilator, Controlled release, Matrix tablets

INTRODUCTION

Pentoxifylline[1,2,3] is a vasodilator[4,5] used in treatment of peripheral vascular diseases mainly atherosclerosis obliterans, raynaud's phenomenon & diseases. Its short biological half-life[6] 0.4-0.8hrs. The chief objective of controlled release matrix tablets is to increase the efficacy as well as bioavailability & to prevents its first pass metabolism. It also leads to reduction in frequency of dosing & drug toxicity which in turn improve patient compliance.One method of fabricating controlled release[7] dosage forms is by incorporating the drug in a matrix containing a hydrophilic, rate controlling polymer. The most commonly used polymers are cellulose ether derivatives which include HPMC[8].Drug release from these types of systems is controlled by the hydration of HPMC[9] which forms a gelatinous barrier layer at the surface of matrix through which the included drug diffuses. Water soluble drugs are released primarily by diffusion of dissolved drug molecules across the gel layer, while poorly water soluble drugs are released predominantly by erosion mechanisms[10]

MATERIALS & METHODS

A batch of 50 tablets was prepared. All the ingredients were initially passed through a 40# sieve separately. Weighed quantities of pentoxifylline[11,12,13,14] polymer & excipients (Table 1) were thoroughly mixed in a glass mortar, in different ratios and directly compressed in to tablets of weight 800mg with 400mg of drug (table 1). Tablets were compressed to an average hardness of 3-4 kg/cm² on tablet on tablet punching machine (Karnavati, Ahemdabad). The compressed tablets were evaluated for hardness, friability, uniformity of drug content & in-vitro drug release characteristics. In-vitro drug release studies[15,16,17] carried out in USP XXII tablet dissolution apparatus in 900mL of dissolution media, maintaining at 37°c ± 0.5°c.Aliquot samples were withdrawn every hour up to a period of 8hrs. The aliquots were diluted suitably, analyzed at 278nm & the in-vitro release from the tablets was determined.

RESULTS & DISCUSSION

Drug content[18] of the prepared matrices was found to be in range of 97.15-98.87%. Hardness[19,20] of tablets was found to be in the range of 3.16-3.84 kg/cm² & friability values of all the batches of tablets was less than 1%. It was observed that formulations F1, F2, F3 contains HPMC as release retarding polymer in 12.5%, 25%, 37.5% concentrations. Formulation F1 & F2 gave 96.90% & 91.73% of drug release in 8 hrs due to inadequate concentration of (HPMC) retardant polymer. The formulation F3 gave 84.37% of drug release in 8 hrs due to high concentration of retardant polymer (table 2).Guar gum, a natural retardant polymer was used in formulations F4, F5, F6 in 12.5%, 25%, & 37.5% concentrations gave 98.78%, 95.71%, & 91.59% of drug release in 8 hrs of dissolution study due to inadequate hydration (guar gum) of retardant as compared to HPMC.

Table 1: various formulations of controlled release matrix tablets of Pentoxifylline

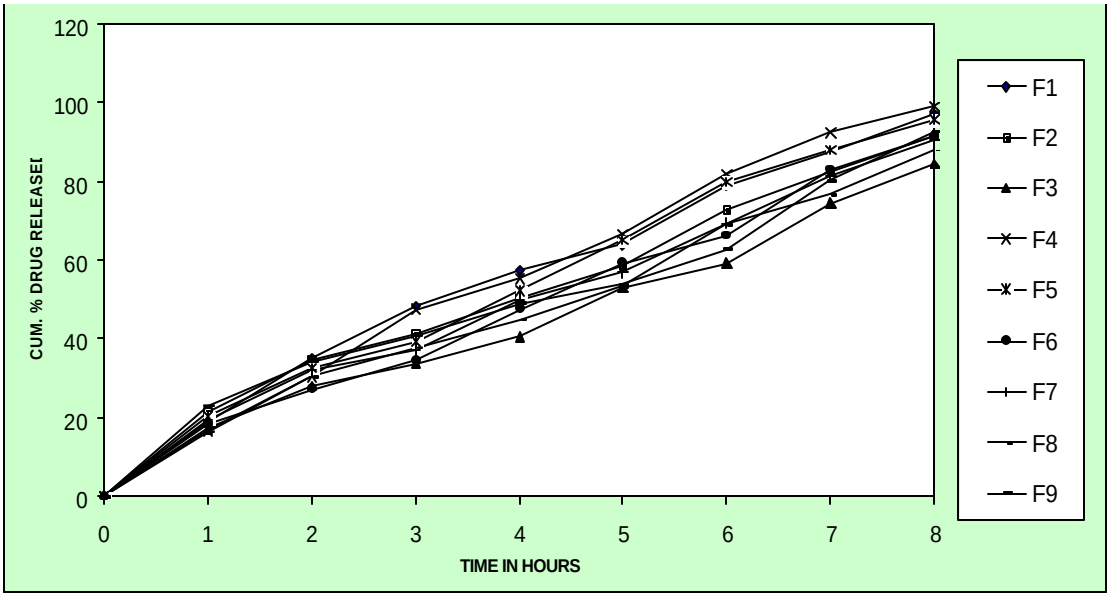
Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9
Pentoxifylline	400	400	400	400	400	400	400	400	400
Hydroxypropyl methyl cellulose	100	200	300	-	-	-	150	200	100
Guar gum	-	-	-	100	200	300	150	100	200
Lactose	236	136	36	236	136	36	36	36	36
Starch	40	40	40	40	40	40	40	40	40
Talc	16	16	16	16	16	16	16	16	16
Magnesium stearate	8	8	8	8	8	8	8	8	8
% of polymer to the total tablet weight	12.5	25	37.5	12.5	25	37.5	37.5 (1:1)	37.5 (2:1)	37.5 (1:2)

Each tablet contains 400mg of pentoxifylline, each tablet weighs 800mg.

Table 2:Cumulative % drug released v/s. time for formulations F1 TO F9 (Buffer pH 1.2 & 7.2)

Time	F1	F2	F3	F4	F5	F6	F7	F8	F9
1 hr	19.04	21.35	17.10	16.56	20.31	18.48	19.37	16.42	22.86
2 hr	34.93	34.80	28.12	30.36	32.85	27.42	31.95	30.53	34.22
3 hr	48.44	41.43	33.72	47.59	39.27	34.63	36.93	37.75	40.81
4 hr	57.24	50.66	40.45	55.26	52.21	47.66	49.72	44.70	49.23
5 hr	63.79	58.53	52.89	66.75	65.10	59.23	56.88	53.50	53.92
6 hr	79.17	72.99	59.31	81.67	79.90	66.18	69.40	69.13	62.70
7 hr	87.63	82.79	74.57	92.26	87.98	83.04	81.60	76.58	80.25
8 hr	96.90	91.73	84.37	98.78	95.71	91.59	90.84	88.16	92.69

Figure.1. Comparative plots of Drug Released v/s Time for controlled released matrix tablets of Pentoxifyline



retardant as compared to HPMC.

Combinations of two retardants, HPMC, guar gum in different ratio was also tried. Three Formulations F7, F8, F9 contain , HPMC: Guar gum in the ratio of 1:1, 2:1, 1:2 respectively. Among these formulations F7 gave 90.84% of release in 8 hrs due to inadequate concentration of HPMC. Formulation F9 gave 92.69% of drug release in 8 hrs due to inadequate hydration (guar gum) of retardant. The promising formulation F8 containing HPMC: Guar gum 2:1 gave 88.16% of release in 8 hrs due to high concentration of HPMC having advantage of better hydration & gelation properties as compared to guar gum.i.e Increase in concentration of retardant polymer resulted in reduction in the drug release rate.

The graphical representation of cumulative % drug retained as a function of time for formulations F3, F6, F8 were found to be nearly linear with correlation co-efficient (r) values which are -0.9935, -0.9974 & -0.9956 for F_3, F_6 & F_8 respectively. This linearity indicates that the release of pentoxifylline from the matrix tablets might have followed nearly zero order kinetics. Negative values of correlation coefficient indicates negative slope for the plot. The best selected formulations F_3, F_6 & F_8 were subjected to Higuchi's classical diffusion.

These Higuchi's plots were found to be nearly linear with correlation coefficient (r) values which are 0.9740, 0.9798 & 0.9832 for F_3, F_6 & F_8 respectively. This linearity suggests that the drug release may be by diffusion controlled mechanism.

From the above studies it is concluded that promising formulations F_3, F_6 & F_8 were compared with marketed formulation & among them F_3 exhibited fairly comparable control release pattern with marketed formulation.

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