INTERNATIONAL JOURNAL OF RESEARCH IN PHARMACY AND CHEMISTRY

Available online at www.ijrpc.com

Research Article

FORMULATION AND EVALUATION OF THEOPHYLLINE BILAYERED TABLETS USING HPC AS MATRIX MATERIAL

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ABSTRACT

Theophylline, an asthmatic drug is based on the relaxation of bronchi. This drug has a great variability in clearance (elimination t½ 3-4 h, adults 6-12 h) and a narrow therapeutic range (7.5-20 µg/ml). The aim of the present work is to formulate theophylline bilayered controlled release dosage[4]form using HPC as matrix[3] material with other commonly used tablet excipients. The release profile of the above dosage form aims to improve patient compliance, prolong the drug action and to avoid kinetics resulting in effective therapy along with better control of plasma drug levels. The formulation of theophylline bilayered tablets[5] were intended for reducing the time for onset of action and to give 12 hours release profile by reducing dosing frequency. The different grades of Hydroxy Propyl Cellulose i.e, EXF, MXF and HXF are intended for the formulation of theophylline bilayered tablets. The release profile of the bilayered tablets should abide by the USP standards of releasing the drug upto 12 hours in the required intervals of time.

Keywords: Theophylline, Bilayered tablet, HPC.

INTRODUCTION

The term drug delivery can be defined as techniques that are used to get the therapeutic agents inside the human body. Another role of the delivery systems is to allow the safe application of the drug. This includes that the drug in the formulation must be chemically, physically and microbiologically stable. Side-effects of the drug and drug interactions should be avoided or minimized by the use of suitable drug delivery systems. The delivery systems also need to improve the patient's compliance with the pharmacotherapy by the development of convenient applications.

EXPERIMENTAL

Materials used

Table 1: Materials used

S. No.	Ingredients/chemicals/solvents
1	Theophylline
2	HPC EXF
3	HPC MXF
4	HPC HXF
5	Lactose monohydrate
6	Povidone
7	Cross Povidone
8	Microcrystalline cellulose(MCC pH 101)
9	Talc
10	FD&C BlueNo:2
11	Hydrochloric acid
12	Monobasic potassium phosphate
13	Sodium hydroxide
14	Magnesium Stearate USP/NF

Formulation of Bi-layered tablets

Bi-layer tablets of Theopylline were prepared by wet granulation method.

Table 2: Composition of Sustained Release layer

Formulation code		TF1	TF2	TF3	TF4	TF5	TF6	TF7
Ingredients (in mg)	Theopylline	542	542	542	542	542	542	542
	HPC EXF	12.5	25	37.5	50	62.5	---	---
	HPC MXF	---	---	---	---	---	12.5	37.5
	HPC HXF	---	---	---	---	---	---	----
	Microcrystalline cellulose(MCC pH 101)	64.25	51.75	39.25	26.75	14.25	64.25	39.25
	Magnesium stearate	6.25	6.25	6.25	6.25	6.25	6.25	6.25
Total wt of layer		625	625	625	625	625	625	625

Formulation code		TF8	TF9	TF10	TF11	TF12	TF13
Ingredients (in mg)	Theopylline	542	542	542	542	542	542
	HPC EXF	---	---	----	---	---	---
	HPC MXF	50	62.5	---	---	---	---
	HPC HXF	---	---	12.5	25	37.5	50
	Microcrystalline cellulose	26.75	14.25	64.25	51.75	39.5	26.75
	Magnesium stearate	6.25	6.25	6.25	6.25	6.25	6.25
Total wt of layer		625	625	625	625	625	625

Dissolution for bi-layer tablets

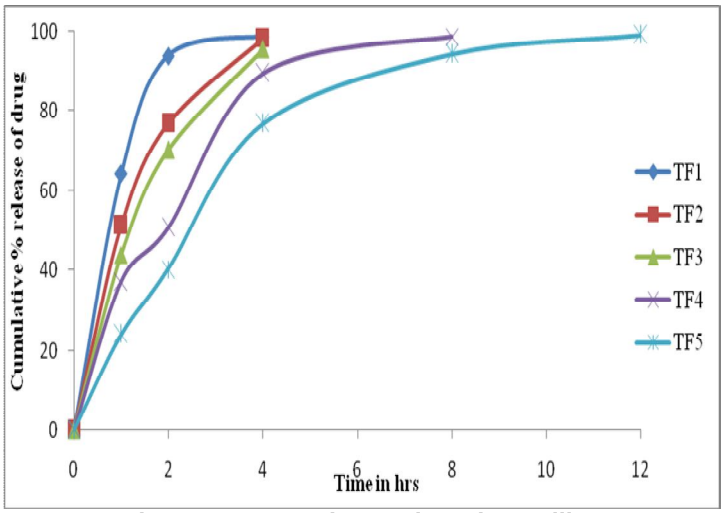

Fig. 1: Compatrative In-vitro Theopylline release of Formulations (TF1-TF5)

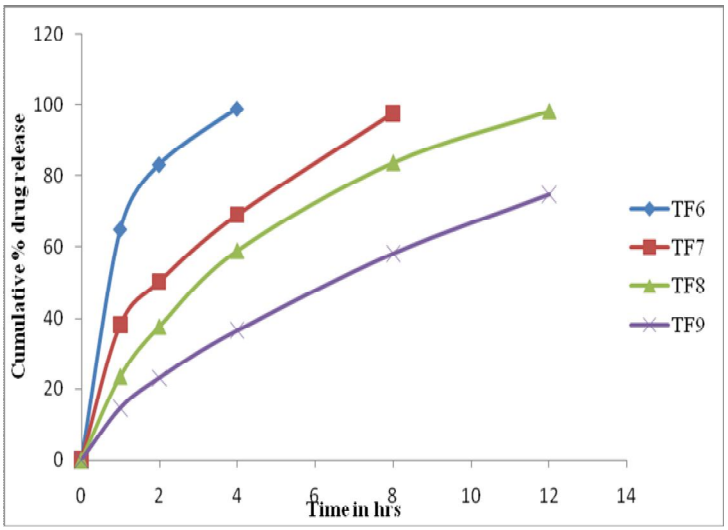

Fig. 2: Compatrative In-vitro Theopylline release of Formulations (TF6-TF9)

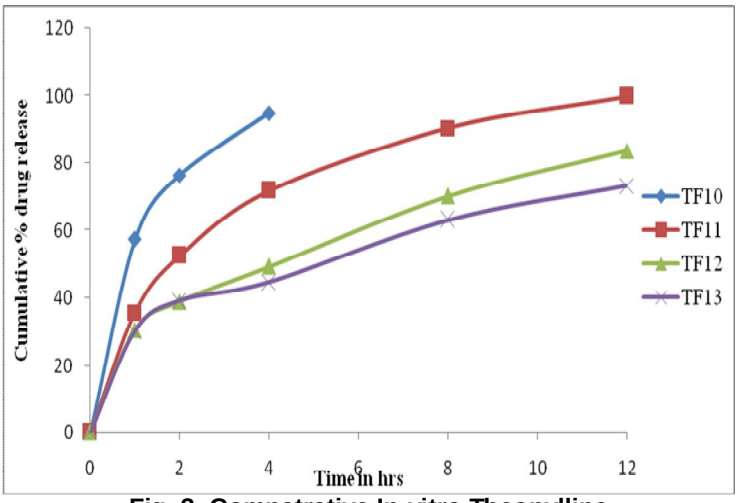

Fig. 3: Compatrative In-vitro Theopylline release of Formulations (TF10-TF13)

RESULTS AND DISCUSSION

Theophylline, an asthmatic drug is based on the relaxation of bronchi. This drug has a great variability in clearance (elimination t½ 3-4 h, adults 6-12 h) and a narrow therapeutic range (7.5-20 µg/ml). Once or twice daily administration of controlled release preparations in patients with chronic obstructive pulmonary disease (COPD) is recommended for better patient compliance. Hence, in the present investigation, an attempt has been made to fabricate a controlled release dosage form of theophylline using HPC as matrix material with other commonly used tablet excipients.

The objective of designing a controlled release system is to deliver drug at a rate necessary to achieve and maintain a constant drug blood level. The multilayered tablet concept has been long utilized to develop sustained release formulations. Such a tablet has a fast releasing layer and may contain bi- or triple layers to sustain the drug release.

The invitro release studies were conducted for all the formulations and an attempt has been made to study the drug release kinetics from the formulations.

Bi-layer sustained release tablets in which an immediate release layer i.e. loading dose and sustained release layer i.e. maintenance dose of theophylline was prepared. The theophylline

bi-layer sustained release tablets were prepared by wet granulation method by using different polymers such as hydroxylpropylcellulose HPC(EXF),HPC(MXF) and HPC(HXF) as sustained release polymers and Polypladone XL10 (Crospovidone) as super disintegrants along with Povidone (plasdone k29/32) as binding agent.

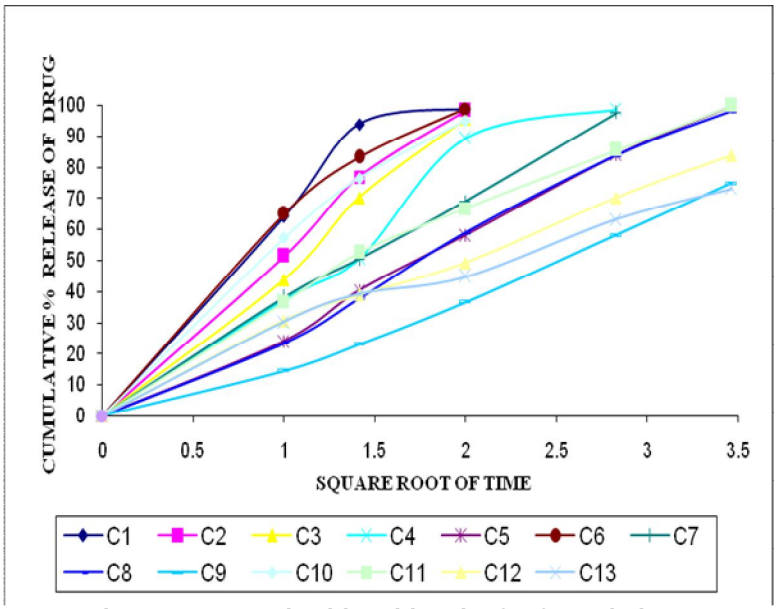

Fig. 4: Comparative higuchi's plot for formulations (TF1-TF13)– Theophylline

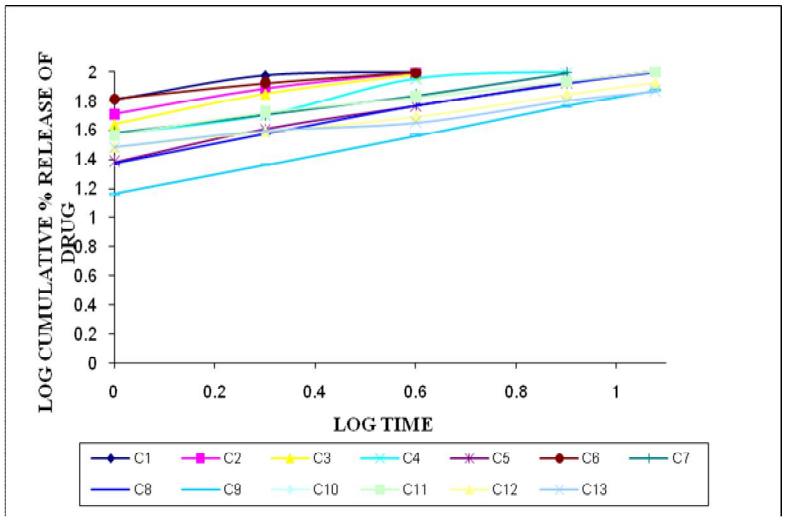

Fig. 5: Comparative peppa's plot for formulations (TF1-TF13)– Theophylline

Table 3: Diffusion characteristics of (Theophylline) Bi-layer tablet formulations

Formulation code	Kinetic models			
	Zero order	Higuchi	Peppas Model	
	R^2	R^2	R^2	N
TF1	0.993284	0.994543	0.999107	0.862871
TF2	0.988728	0.986065	0.997845	0.830548
TF3	0.990547	0.982154	0.998496	0.854898
TF4	0.993362	0.981429	0.997421	0.88629
TF5	0.992405	0.996123	0.991883	0.862572
TF6	0.992386	0.987373	0.998588	0.874863
TF7	0.990818	0.995043	0.996796	0.842754
TF8	0.988223	0.993593	0.991625	0.836326
TF9	0.987906	0.989781	0.995699	0.832864
TF10	0.991822	0.997257	0.999269	0.863822
TF11	0.992753	0.99157	0.993117	0.872231
TF12	0.988625	0.988853	0.952731	0.830746
TF13	0.987360	0.99787	0.999791	0.842742

CONCLUSION

Once or twice daily administration of controlled release preparations in patients with chronic obstructive pulmonary disease (COPD) is recommended for better patient compliance. Hence Theophylline has been made to fabricate a controlled release dosage form using HPC as matrix material with other commonly used tablet excipients. Theophylline is used in the treatment of asthma. Having different release profiles which improves patient compliance, prolongs the drug(s) action, avoid saw tooth kinetics resulting in effective therapy along with better control of plasma drug levels.

The theophylline bi-layer sustained release tablets were prepared by wet granulation method by using different polymers such as hydroxyl propyl cellulose EXF, MXF, HXF as sustained release polymers and Polypladone XL10 (Crospovidone) along with (PLASDONE K29/32) as binding agent.

The theophylline sustained release and immediate release was evaluated for morphological characteristic, physical characteristic, chemical characteristic and stability. The results obtained were satisfactory and within specified limits

The formulation of theophylline bilayered tablets were intended for reducing the time for onset of action and to give 12 hours release profile by reducing dosing frequency. So the above criteria was found to be followed by the formulation i.e, 10% of EXF ,8% of MXF and 4% of HXF.

These results are evident that the viscosity of the polymer has great influence on the release parameters of the dosage form. It can also be concluded that the release is retarded more by the higher viscosity polymer (HXF) grade at lower concentration compared to lower viscosity polymer (EXF) grade at the same concentration.

ACKNOWLEDGEMENTS

We are very thankful to the management for providing necessary requirements for fulfilling this project.

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