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Original Article

Formulation and in-vitro characterization of lamivudine controlled release tablet

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ABSTRACT

The goal of any drug delivery system should deliver drug at a rate dictated by the needs of the body over a specified period of treatment. In the present work, an attempt has been made to develop controlled release tablets of Lamivudine to improve its oral bioavailability, to reduce its dosing frequency and to optimize by taking of optimum concentration of various Controlled release polymers of HPMC with different grades and Guar gum. All the formulations were prepared by direct compression method using 12mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed good flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F3 formulation showed maximum % drug release i.e., 97.3 % in 8 hours hence it is considered as optimized formulation. Whereas the formulations containing HPMCK 100 M showed more retarding with increasing concentration of polymer.

Key words: Lamivudine, HPMCK 100 M, oral bioavailability and % drug release.

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INTRODUCTION

The goal of any drug delivery system is to provide a therapeutic amount of drug in the proper site in the body to achieve promptly and then to maintain the desired drug concentration. That is, the drug delivery system should deliver drug at a rate dictated by the needs of the body over a specified period of treatment. [1, 2]

Oral drug delivery: This is the most widely utilized route of administration among all the routes that have been explored for systemic delivery of drugs via pharmaceutical products of different dosage form. Solid dosage forms are popular because of ease of administration, accurate dosage, self medication, pain avoidance and most importantly patient compliance. The most popular solid dosage forms are tablets and capsules. But the important drawback of these dosage forms is the difficulty to swallow. The most common solid dosage forms in contemporary use are tablets. Tablet may be defined as a solid dosage form, containing a unit dose of one or more medicaments. Tablets are solid, flat or biconvex discs prepared by compressing a drug or a mixture of drugs with or without suitable excipients. Tablets may be swallowed whole or being chewed. Some are dissolved or dispersed in water before administration. Some are kept in oral cavity, where the active ingredient Is liberated at a predetermined rate. Implants or pessaries may also be presented in the form of tablet. Tablet may vary in shape , differ greatly in size, weight depending on the amount of medicinal substance and the intended mode of administration. The term modified-release drug product is used to describe products that alter the timing and/or the rate of release of the drug substance. A modified-release dosage form is defined "as one for which the drug-release characteristics of time course and/or location are chosen to accomplish therapeutic or convenience objectives not offered by conventional dosage forms such as solutions, ointments, or promptly dissolving dosage forms as presently recognized. [3]

Classification of tablets

Tablets are classified as follows:

A) According to the drug release rate from the tablet

B) According to the method of manufacturing

C) According to the route of administration or function.

A) According to the drug release rate from the tablet:

(a)Immediate release (conventional) tablets: The tablet is intended to be released rapidly after administration or the tablet is dissolved and administered as solution. It is the most common type and includes:

Eg : Disintegrating tablet, e.g. Acetaminophen tablet

Chewable tablet, e,g. Antacid tablet [4]

(b) Modified – release tablets: They have release features based on time, course or location. They must be swallowed intact.

Extended – release tablet: allowing the reduction in dosing frequency[5,6]

Delayed - release tablet: drug release is delayed due to physiological conditions

E.g.: pH (a lag period followed by normal release). The best example is enteric coated tablets; the drug is released in the upper part of small intestine after which the preparation will pass the stomach. If the drug is sensitive to acid or irritant to the stomach lining, an enteric coating can be used. [7,8]

Lamivudine: act as anti-HIV Agent, as Reverse Transcriptase Inhibitors.It is used to treat Human Immunodeficiency Virus Type 1 (HIV-1) and hepatitis B (HBV).

Objective of work: To formulate Diffusion Controlled release matrix tablets of Lamivudine to improve its oral bioavailability and to reduce its dosing frequency,To optimize optimum concentration of various Controlled release polymers and to perform various quality control evaluation parameters for the prepared tablets

MATERIALS AND METHODS

Materials: The materials to be used in this present experiment were Lamivudine acts as a drug from Hetero Laboratories, Mahabubnagar , hydroxy propyl methylcellulose K15M, hydroxy propyl methylcellulose K100M, Guar gum acts as polymorphs, Magnesium stearate acts as lubricant , Talc is used as adsorbent and Microcrystalline cellulose pH 102 is used as from Sd Fine Chemicals, Hyderabad.

Equipments: The equipments, which are used in the present experiment are as followed as

Electronic balance model Wensar, Tablet compression machine from company Karnavati, Rimek Mini Press II, Tablet hardness tester model is Monsanto hardness tester, Dissolution test apparatus Ds 8000(USP), Disintegration test apparatus, Friability test apparatus, UV-Visible Spectrophotometer, pH meter from Lab India Dissolution Apparatus and Hot air oven from VJ Instruments.

Methodology:

Determination OF UV Absorption maxima: Lamivudine solution was prepared in 0.1 N HCL and diluted suitably. The UV spectrum of the solution was taken on UV-Visible

Spectrophotometer .The Solution exhibited UV maxima at 298 nm. The procedure was repeated with pH 6.8 phosphate buffer. The spectrums of both were showed in fig nos: 3.1 & 3.2 by conducting of Standard Calibration Curve of Lamivudine by using 0.1 N HCl (pH 1.2) and pH 6.8 phosphate buffer.

Fourier Transform Infra Red (FTIR) spectroscopy: The physical properties of the mixture were compared with those of plain drug. Samples was mixed thoroughly with 100mg potassium bromide IR powder and compacted under vacuum at a pressure of about 12 psi for 3 minutes. The resultant disc was mounted in a suitable holder in Perkin Elmer IR spectrophotometer and the IR spectrum was recorded from 3500 cm to 500 cm. The resultant spectrum was compared for any spectrum changes and was showed by the fig no 3.2.1.and 3.2.2. respectively.

Formulation of Lamivudine Controlled release Tablet by Direct- Compression: Composition of preliminary trials for Lamivudine Controlled release Tablet by direct compression is shown in table. All the ingredients were weighed. Required quantity of drug and excipient mixed thoroughly in a polyethylene bag. The blend is compressed using rotary tablet machine-8 station with 12mm flat punch. Each tablet contains 100mg of Lamivudine and other pharmaceutical ingredients.

Evaluation parameters:

I) Pre compression parameters: The evaluation parameters like pre formulation parameters were performed to the all formulations as bulk density, tapped density, Angle of Repose , Carr's index (or) % compressibility, Hausner's ratio were performed and were showed by the table no:3.3.1; respectively.

II) Post compression parameters:

The post compression parameters performed like Weight variation, Hardness of tablet was measured using tablet hardness tester, Thickness of tablets was measured by using Vernier Caliper and Friability of the tablet determined using Roche friabilator finally the assy was performed for all formulations and the results obtained were taken in the table no:3.3.2; respectively.

III) In-Vitro drug release: In vitro dissolution studies were carried out by using 900ml of 0.1 N HCl in USP dissolution apparatus by using paddle method for about 2 hours. After 2 hours the dissolution medium was withdrawn keeping the tablet in the dissolution basket. Then pH 6.8 phosphate buffer was added to the dissolution medium (900ml) and the dissolution was carried out for about 6 hours. The samples were withdrawn at regular time intervals of 30 min,1 hour,2 hr,3,5,5,6,7 & 8 hours respectively and the data was shown by following fig nos: 3.3.3.1, 3.3.3.2; and 3.3.3.3; respectively.

RESULTS & DISCUSSION

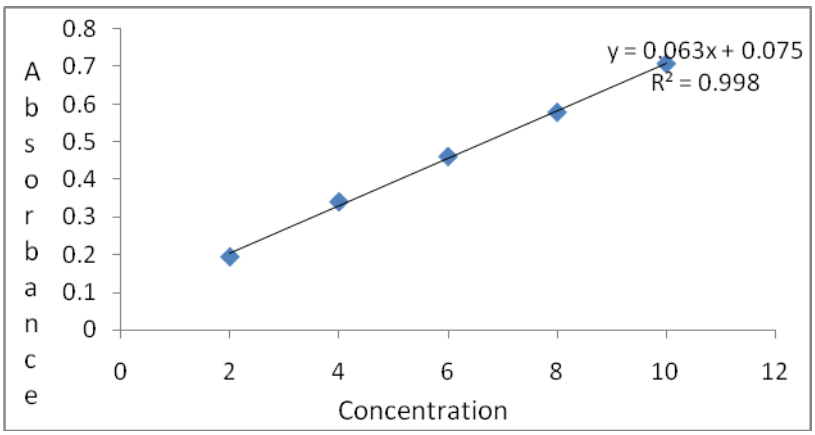

Fig 1: Standard graph of Lamivudine in 0.1 N HCl

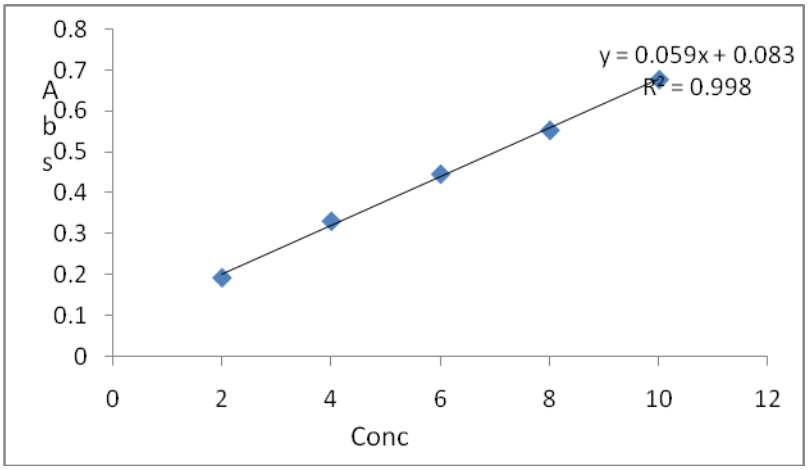

Fig 2: Standard graph of Lamivudine in pH 6.8 Phosphate buffer

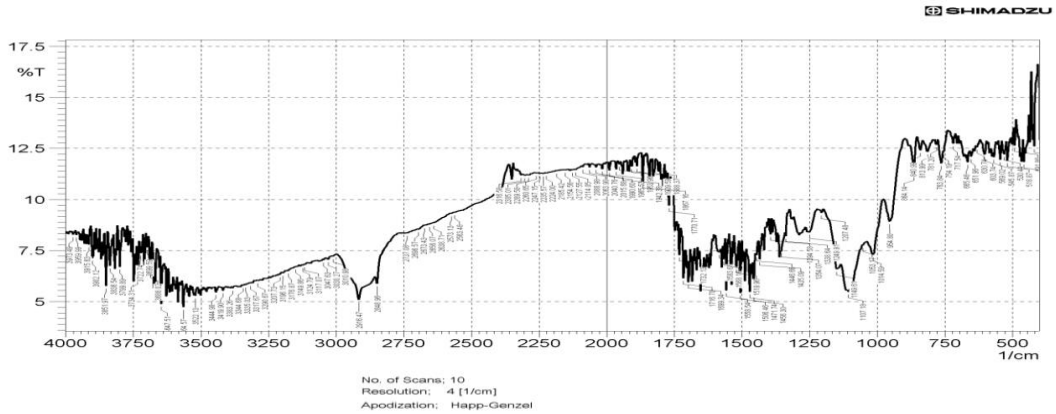

Fig 3. FTIR spectrum of pure drug

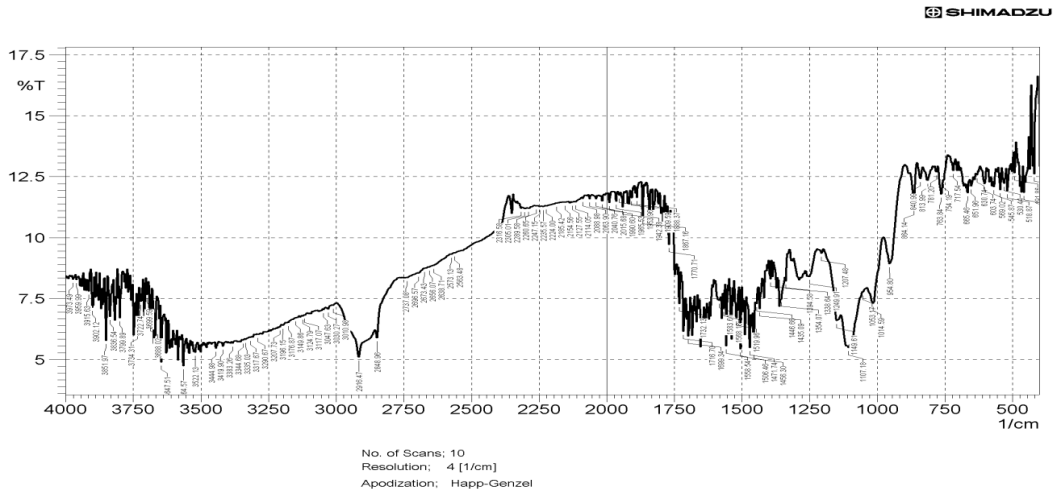

Fig 4. FTIR spectrum of optimized formula

Evaluation Parameters for Controlled release tablets of Lamivudine:

Pre-compression parameters:

Formulations	Bulk Density (gm/cm^2)	Tap Density (gm/cm^2)	Carr's Index (%)	Hausner ratio	Angle Of Repose(Ɵ)
F_1	0.45	0.55	18.18	1.22	27.91
F_2	0.47	0.55	14.54	1.17	28.23
F_3	0.50	0.58	13.79	1.16	29.34
F_4	0.46	0.55	16.36	1.19	26.71
F_5	0.50	0.58	13.79	1.16	29.34
F_6	0.47	0.55	14.54	1.17	28.23
F_7	0.50	0.58	13.79	1.16	29.34
F_8	0.41	0.50	18	1.21	26.78
F_9	0.41	0.50	18	1.21	26.78
F10	0.42	0.51	18.24	1.20	26.68
F11	0.48	0.56	18.12	1.21	26.70
F12	0.41	0.54	18.11	1.22	26.71

Table 1: Pre-compression parameters of all lamivudine controlled released tablets

Post compression Parameters:

Formulation	Weight variation (mg)	Hardness (kg/cm^2)	Thickness (mm)	Friability (%)	Assay (%)
F_1	494	4.5	5.5	0.43	97.23
F_2	504	4.3	5.5	0.34	98.55
F_3	510	4.2	5.5	0.49	98.16
F_4	495	4.2	5.4	0.47	99.34
F_5	502	4.3	5.5	0.49	98.16
F_6	508	4.3	5.5	0.34	98.55
F_7	510	4.4	5.4	0.49	98.16
F_8	494	4.5	5.5	0.34	99.25
F_9	506	4.4	5.5	0.34	99.25
F10	501	4.4	5.5	0.43	98.6
F11	502	4.3	5.5	0.54	98.7
F12	504	4.5	5.5	0.43	98.5

Dissolution profile of formulations :

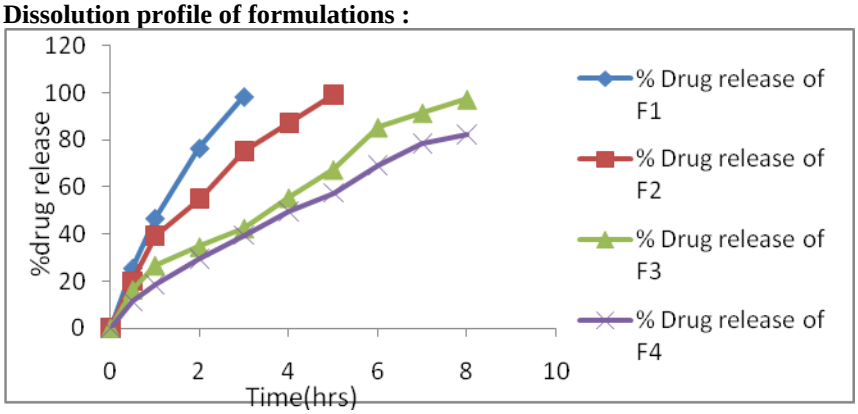

Fig 1; Dissolution profile of formulations prepared with HPMC K15M polymer

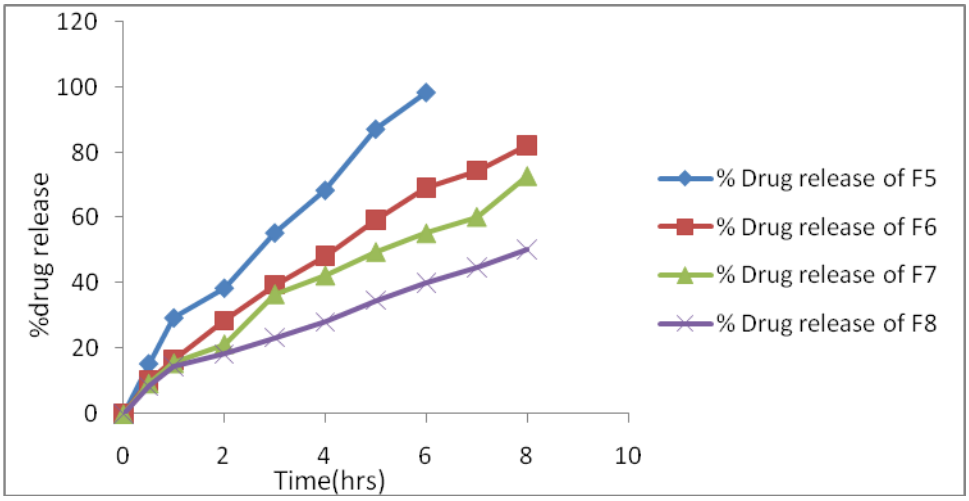

Fig no: 3.3.3.2; Dissolution profile of formulations prepared with HPMC K100M polymer

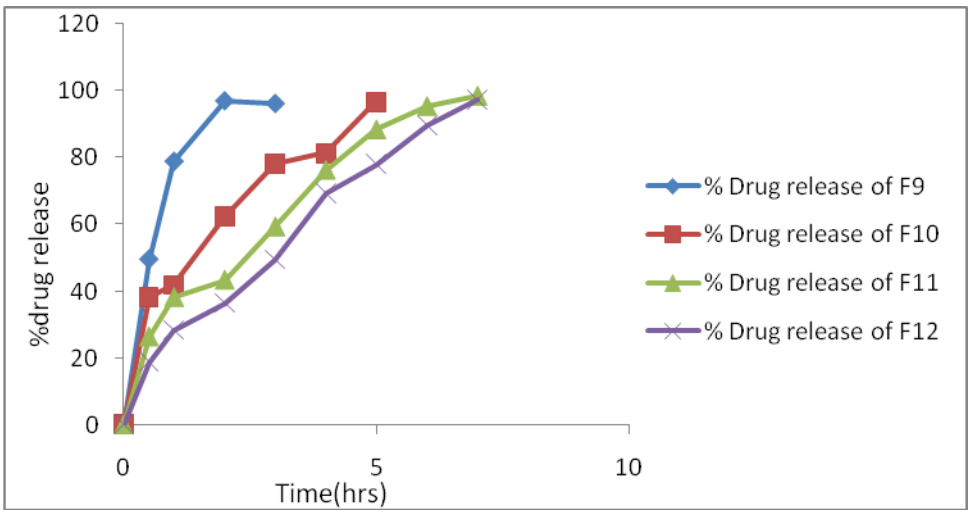

Fig no:3.3.3.3; Dissolution profile of formulations prepared with Guar gum as polymer

Application of Release Rate Kinetics to Dissolution Data: Various models were tested for explaining the kinetics of drug release. To analyze the mechanism of the drug release rate kinetics of the dosage form, the obtained data were fitted into zero-order, first order, Higuchi, and Korsmeyer-Peppas release model.

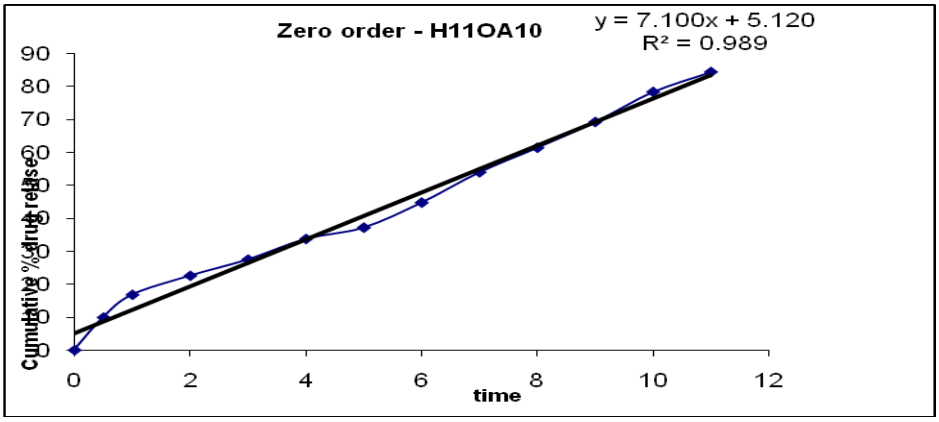

Fig 3.3.3.4: Zero order release kinetics graph

The optimized formulation F3 was followed Zero order release mechanism.

CONCLUSION

In the present work, an attempt has been made to develop controlled release tablets of Lamivudine by selecting different grades of HPMC and Guar gum as retarding polymers. All the formulations were prepared by direct compression method using 12mm punch on 8 station rotary tablet punching machine. The blend of all the formulations showed god flow properties such as angle of repose, bulk density, tapped density. The prepared tablets were shown good post compression parameters and they passed all the quality control evaluation parameters as per I.P limits. Among all the formulations F3 formulation showed maximum % drug release i.e., 97.3 % in 8 hours hence it is considered as optimized formulation. Whereas the formulations containing HPMCK100M showed more retarding with increasing concentration of polymer. The formulations with Guar gum were unable to produce the desired rug release pattern.

REFERENCES

1. Ansel H., Allen L &Jr.popovich N. Ansel's pharmaceutical Dosage Forms and Drug delivery systems, 8th edition, 2004; 260-268.
2. Aulton M. The science of dosage form design, International student edition, published by churchil Livingston, 2002;304-321,347-668.
3. Banker GS. Modern pharmaceutics, 3rd edition marcel dekkerinc , newyork . 576-820.
4. Bramhanker DM, .Jaiswal SB. Controlled release medications. In: Biopharmaceutics and Pharmacokinetics a treatise, 1995; 335-375.
5. Chien YW. Controlled and modulated-release drug delivery systems, 1995;281-313.
6 Donald L. Hand book of pharmaceutical controlled release technology,2002; 466-471,738-739.
7. Durgacharan A Bhagwat., Pravin S Kawtikwar., Dinesh M Sakarkar. "Formulation and the *in-vitro* and biopharmaceutical evaluation of sustained release tablet of verapamil HCL using precirol ATO 5 through melt granulation technique." 2009; 278-285.
8. Government of India Ministry of Health and Family Welfare.,1999.*The* Pharmacopoeia of India. Delhi, India, Controller of Publication.312-314.
9. Higuchi T. 1963. "Mechanism of sustained action medication, theoretical analysis of rate of release of solid drugs dispersed in solid matrices." *J Pharm Sci*.52:1145-1149.
10. Kuchekar., "Indian journal of pharma education." 2nd edition. 2001;150-152
11. Lachman L.,. The Theory of practice of Industrial pharmacy, 3rd edition, published by Lea &Febiger, 1986; 293-345,346-373.