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Research

Design, Development and Evaluation of Extended Release Acetazolamide Tablet

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Abstract

In the study, antiepileptic drug was selected for designing extended release matrix tablets. Pre-Formulation studies were done with Acetazolamide. Compatibility was done before choosing the excipients for the study with physical observation and FTIR studies. The samples were charged in stability chambers at conditions 30°C/65%RH and 40°C/75%RH for 30 days. All the pre-formulation studies and compatibility studies were found to be satisfactory. So formulation trials were followed with the selected excipients. Blend for ER formulation was prepared by wet granulation method. Hypromellose K4M and Hypromellose K15M were used as release retarding polymers for optimizing the formula.Six trials were taken to optimize the release of Acetazolamide in ER form to be within specifications. F5 is the optimized formula with 11.66% concentration of HPMC K15M polymer which optimized the drug release profile as per predetermined specificatons. A reproducibility trial F6 was performed to check the reproducibility of process of drug release as per F5.For the ER form, Other excipients include povidone as binder, Lactose monohydrate as diluent, colloidal silicon dioxide as glidant and Magnesium stearate as Lubricant. Instacoatyellow was used as ready mix. Post-Compression analysis of all formulations like Hardness, Weight variation, Friability and Assay were within the limits for all the formulations. In- vitro dissolution studies were performed by HPLC method revealed that the formulation F5 released the drug as per the specifications. Kinetic Model fitting was done by plotting graphs for Zero-Order kinetics, First-Order kinetics, Higuchi's Kinetic model and Korsemeyer - Peppas kinetic model. The formulation selected was F5 which has shown the release rate of the drug by First order kinetics and follows matrix diffusion controlled mechanism. Accelerated stability studies are being performed.

Keywords: Extended release matrix tablets, antiepileptic drug, Acetazolamide, wet granulation method.

INTRODUCTION

Oral route is most common and popular route of administration of drug is oral route because of its systemic effect, patient compliance, less expensive to manufacture. Tablet provides high precision dosing. Tablet form is the most widely used dosage form because of self-administration and ease in manufacturing. The ideal dosage regimen is that by which an acceptable therapeutic concentration of drug at the site(s) of action is attained immediately and is then maintained constant for the desired duration of the treatment.

Conventional drug products like tablets and capsules are formulated to release the active drug immediately to obtain Acetazolamide and complete systemic absorption of the drug. The conventional dosage form maintains the constant plasma drug concentration for the long period of time by administering in a particular dose and at particularfrequency. The frequency of administration or the dosing interval of any drug depends upon its half-life or mean residence time (MRT) and its therapeutic index. In most cases, the dosing interval is much shorter than the half-life of the drug resulting in a number of limitations. These limitations can overcome by formulating into Modified-Release dosageforms. Modified-release products provide either delayed-release or extended-release of the drug.

The terms sustained release, prolonged release or extended release are used to identify drug delivery systems that are designed to achieve a prolonged therapeutic bloodor tissue levels of the drug by continuous releasing of the medication for an extended period of time after administration of a single dose.

Extended release dosage forms release drug slowly, so that plasma concentrations are maintained at a therapeutic level for a prolonged period of time (usually between 8 and 12 hours).

MATERIALS AND METHODOLOGY

List of chemicals used with grade and supplier

Materials used Grade Manufacturer Acetazolamide IP Gift Sample of Sun Pharma Hypromellose K4m USP/NF Colorcon, Hypromellos K15m ,USP/NF Colorcon Carboxy Methyl Cellulose, Sodium IP FMC ,Lactose Monohydrate ,USP DMV Fonterra, Povidone USP BASF Ltd, Colloidal Silicon Dioxide, Magnesium Stearate USP Amishi drugs and chemicals.

List of ingredients with their functional category

Excipients functional category

Drug Active Ingredient, HPMC K15M/K4M Matrix forming Polymer, Lactose monohydrate Diluent, Povidone Binder, Colloidal silicon dioxide Glidant, Magnesium Stearate Lubricant Purified Water Solvent for granulation List of ingredients with their functional category Drug Active Ingredient ,HPMC K15M/K4M Matrix forming Polymer, Lactose monohydrate Diluent Povidone Binder ,Colloidal silicon dioxide Glidant, Magnesium Stearate Lubricant, Purified Water Solvent for granulation.

PRECOMPRESSION PARAMETERS

Table 1: Precompression Parameter

Formulation Code	Bulk density (gm/cm3)	Tapped density (gm/cm3)	Hausner's ratio (HR)	Carr's index (CI)	Angle of repose (θ)
FT-1	0.465	0.609	1.373	26.78	32.06
FT-2	0.448	0.666	1.451	32.05	38.23
FT-3	0.615	0.689	1.14	11.89	45.24
FT-4	0.589	0.660	1.109	10.60	44.98
FT-5	0.548	0.597	1.18	14.61	29.99
FT-6	0.553	0.640	1.169	14.653	32.37

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Calibration Curve in various solvent

Standard Preparation For Acetazolamide

Weigh accurately about 0.1 g of Acetazolamide working standard into 50ml volumetric flask, add about 30ml of methanol, sonicate for 15minutes to dissolve with intermittent shaking and dilute to 50ml with methanol, and mix well. Pipette and dilute 5ml of resulting solution into 25mlvolumetric flask, and dilute to 25ml with diluent and mix well. Centrifuge a portion of this solution at 3000rpm for 10minutes and use this as standard solution.

Sample Preparation for Acetazolamide

Weigh and powder 20 tablets. Accurately weigh and transfer tablet powder equivalent to 50 mg of Acetazolamide into a 100ml volumetric flask, add about 70ml of methanol, sonicate for about 30 minutes to dissolve the contents and dilute to 100ml with methanol and mix well. Centrifuge a portion of this solution at 3000 rpm for 10 minutes. Pipette and dilute 5ml of resulting into 25ml volumetric flask, and dilute to 25ml with diluents.

From the prepare stock solution, dilutions were made so as to obtain 2, 4, 6, 8, 10 µg/ml with water. Absorbance of each dilution was measured at 288 nm. A graph is plotted by taking absorbance on y –axis and concentration on x-axis.

Table 2: Absorbance of Acetazolamide Standard Solution

S. No.	Concentration	Absorbance
1	0	0
2	2	0.126
3	4	0.253
4	6	0.312
5	8	0.423
6	10	0.561

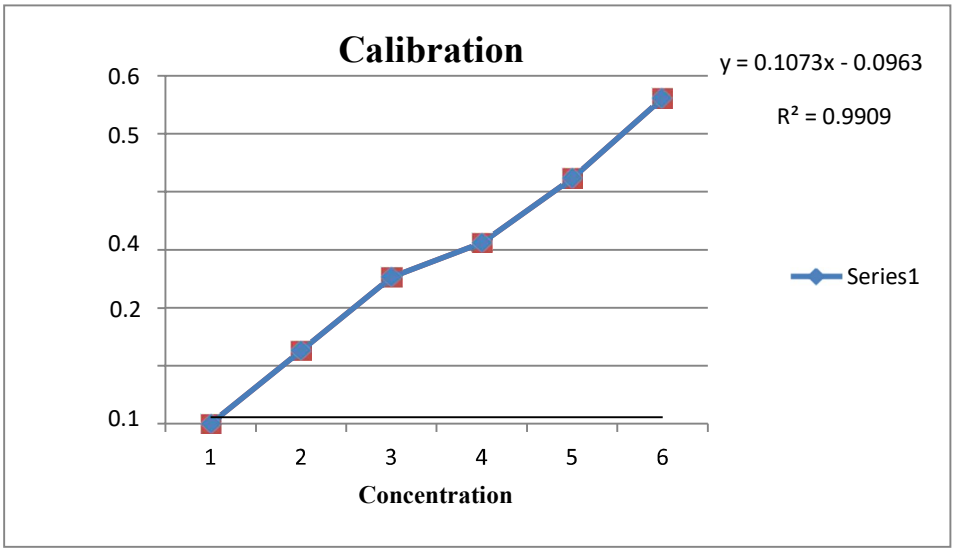

Fig 1: calibration curve of Acetazolamide Standard Solution

Formulation design

Table 3: Formula for extended release tablets

INGREDIENTS	QUANTITY USED IN THE FORMULATION (mg per tablet)					
	F1	F2	F3	F4	F5	F6
Acetazolamide	250	250	250	250	250	250
HPMCK15M	-	-		50	35	35
HPMCK4M	30	35	37.5		-	-
CMC Sodium	15	10	10	-	-	-
Lactose monohydrate	80	80	80	80	80	80
Povidone (PVPK30)	5	5	5	5	5	5
Colloidal Silicon dioxide	1	1	1	1	1	1
Magnesium stearate	2.5	2.5	2.5	2.5	2.5	2.5
Purified Water	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Total weight	383.5	383.5	386	388.5	373.5	373.5

RESULT

FTIR study

The samples that were charged in 30^0C/65%RH and 40°C/75% RH stability chambers were analysed by IR spectroscopy after 30 days. The graphs of the samples were given below.

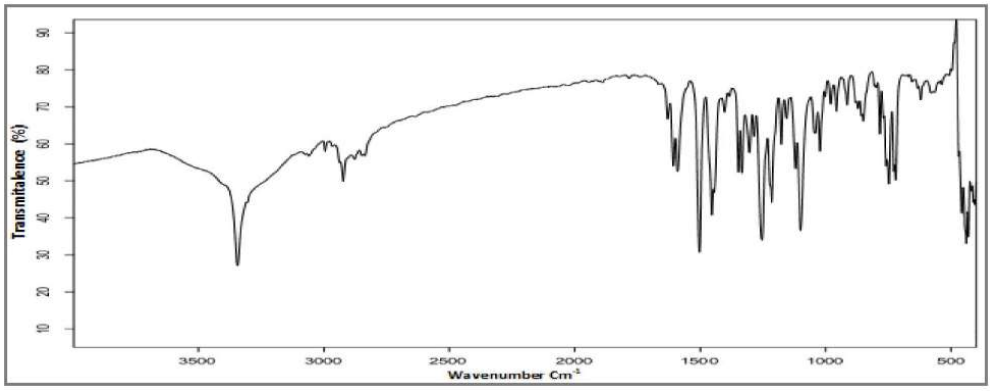

Fig 2: FTIR of acetazolamide

Table 4: Results of Compatibility studies

Particulars	Ratio	Description	Parameters				Remarks
			30ºC/ 65% RH		40ºC/ 75% RH		
			15 days	30 days	15 days	30 days	
Acetazolamide	-	Yellow Powder	No change	No change	No change	No change	Compatible
Acetazolamide : HPMC K15M Premium	**1:1**	Off white to yellow Powder	No change	No change	No change	No change	Compatible
Acetazolamide : HPMC K4M Premium	**1:1**	Off white to Yellow Powder	No change	No change	No change	No change	Compatible
Acetazolamide : Povidone	**1:0.5**	Off White to yellow Powder	No change	No change	No change	No change	Compatible
Acetazolamide : Lactose monohydrate	**1:5**	Off White to Yellow Powder	No Change	No change	No change	No change	Compatible
Acetazolamide : Aerosil	**1:0.1**	Off White to yellow Powder	No change	No change	No change	No change	Compatible
Acetazolamide : Magnesium stearate	**1:0.1**	Off White to yellow Powder	No change	No change	No change	No change	Compatible

Post-compression properties

Table 5: Post-Compression Properties

TRIALS	PHYSICAL PARAMETERS			
	Weight variation (mg)	**Hardness** (N)	**Thickness** (mm)	**Friability** (%)
F1	299 ± 5	120± 10	4.21 ± 0.02	0.197
F2	298 ± 5	130± 10	4.20 ± 0.02	0.099
F3	298 ± 5	140± 10	4.20 ± 0.02	0.162
F4	300 ± 5	140± 10	4.18 ± 0.02	0.97

F5	300 ± 5	150± 10	4.19 ± 0.02	0.08
F6	299 ± 5	150± 10	4.19 ± 0.01	0.09

Comparitive in-vitro dissolution profile from f1-f6

Table 6: Comparative In-vitro dissolution profile from F1-F6

Time(hours)	% Cumulative drug release Average % drug release for all trials						Specifications
	F1	**F2**	**F3**	**F4**	**F5**	**F6**	
2hr	21	17	16	15	14	12	NMT 30%
6hr	75	67	70	33	45	43	30-60%
12hr	83	88	84	79	92	87	NLT 85%

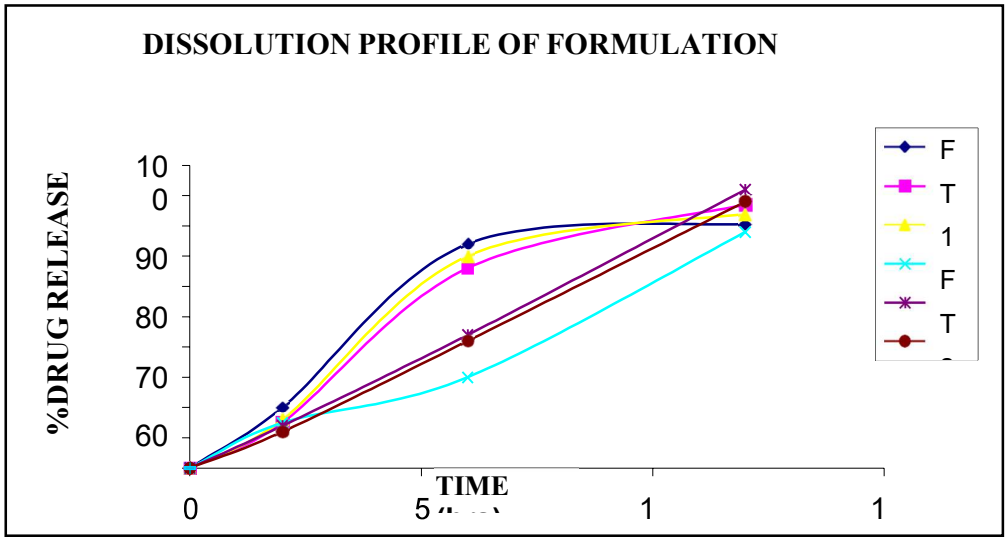

Fig 3: Comparative dissolution profile from F1 to F6

Data analysis

Formulation-5 was found to be the desired *In-vitro* dissolution rate, so this formulation was selected for determining the nature of drug release from dosage form.

Table 7: Different Kinetic models

Time (in hours)	Square root of time	Log Time	% CDR	Log(100 % - CDR)	Log %CDR
2	1.414213562	1.411	14	1.99492	1.146128036
6	2.449489743	2.44	44	1.99280	1.643452676
12	3.464101615	3.46	92	1.99138	1.963787827

Table 8: Regression coefficients from all the Kinetic model graph

Formulation	Zero-order kinetics	First-order kinetics	Higuchi's kinetics	Korsmeyer-Peppas
F5	0.963	1	0.981	0.986

Kinetic models

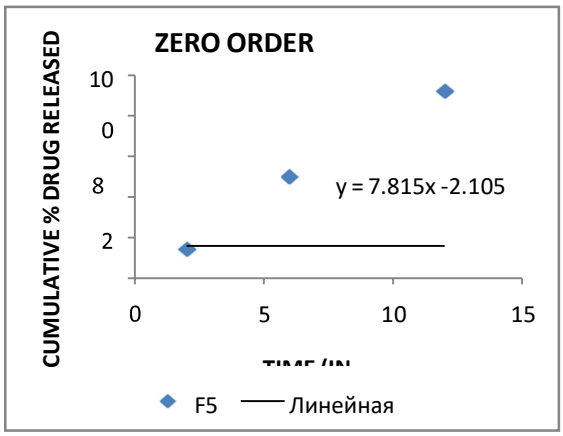

Fig 4: Zero order kinetics

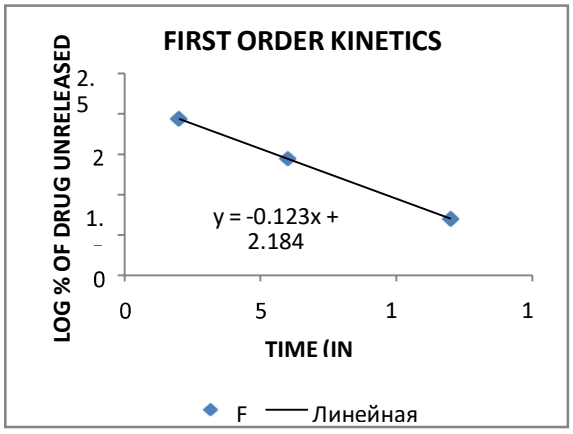

Fig 5: First order kinetics

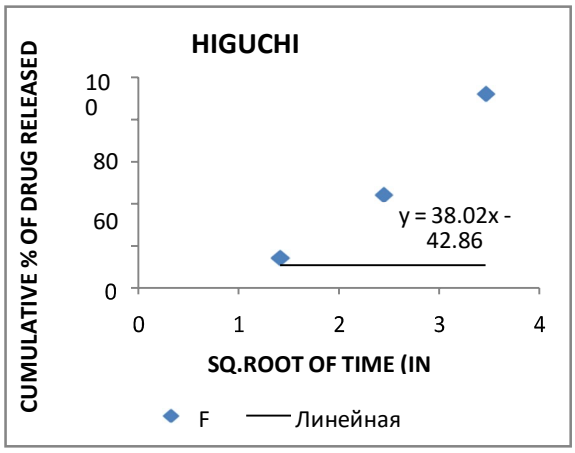

Fig 6: Higuchi model

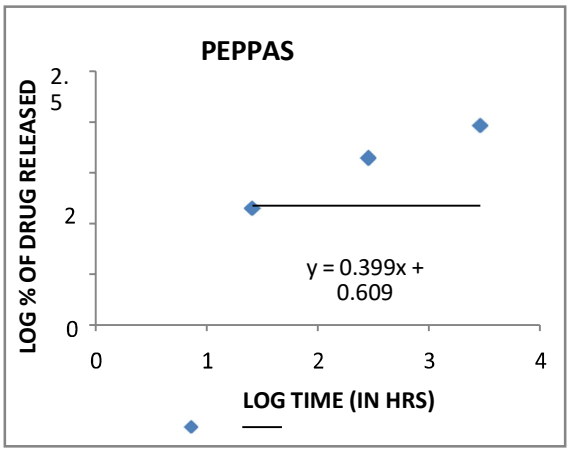

Fig 7: Peppas model

CONCLUSION

The aim of the study is was design and develop extended release matrix tablets. Hypromellose, water swellable polymer was selected for the extended release of Acetazolamide. The formulation was optimized to obtain the release of Acetazolamide for a sustained period of 12hours. In the initial trials, Hypromellose K4M of low viscosity grade was used, then Hypromellose K15M of high viscosity grade was selected to check the feasibility of the polymer to sustain the release of Acetazolamide. With HPMC K4M the drug release was not controlled to the desired limit of 30-60% at 6th hour. So, a still high viscous polymerHypromellose K15M was used in the formulations F-4 to F-6. The incorporation of the Polymer intra- granularly at concentration 11.66% gave an optimum release profile within specifications. From graphs plotted for various Kinetic models, it can be concluded that the F5 follows First-order kinetics as the plots of that model had shown higher regression value. F5 formula extended the release and follows matrix diffusion controlled mechanism.

REFERENCES

1. Bhavani A, Hemalatha B, Padmalatha K. Formulation development and in vitro Evaluation of sustained release matrix tablets of Cefpodoxime proxetil. Asian Journal of Pharmacy and Technology. 2021;11(4):273-8. https://www.indianjournals.com/ijor.aspx?target=ijor:ajpt&volume=11&issue=4&article=003
2. Patel KB, Vyas JR, Upadhyay UM. Formulation and evaluation of sustained release matrix tablets of

nateglinide. Journal of Drug Delivery and Therapeutics. 2015 Sep 21;5(5):19-25. http://www.jddtonline.info/index.php/jddt/article/view/1130

3. Chen W, Desai D, Good D, Crison J, Timmins P, Paruchuri S, Wang J, Ha K. Mathematical model-based accelerated development of extended-release metformin hydrochloride tablet formulation. AAPS PharmSciTech. 2016 Aug;17:1007-13. https://link.springer.com/article/10.1208/s12249-015-0423-9
4. Rheims S, Ryvlin P. Once-daily lamotrigine extended release for epilepsy management. Expert Review of neurotherapeutics. 2009 Feb 1;9(2):167-73. https://www.tandfonline.com/doi/abs/10.1586/14737175.9.2.167
5. Chaudhary A, Pacharane S, Jadhav KR, Kadam VJ. Formulation and development of extended release tablet of Lamotrigine. Int. J. Pharm. Sci. 2011;2:975-6299.
6. Huang Y, Khanvilkar KH, Moore AD, Hilliard-Lott M. Effects of manufacturing process variables on in vitro dissolution characteristics of extended-release tablets formulated with hydroxypropyl methylcellulose. Drug development and industrial pharmacy. 2003 Jan 1;29(1):79-88. https://www.tandfonline.com/doi/abs/10.1081/DDC-120016686
7. Furlanetto S, Cirri M, Maestrelli F, Corti G, Mura P. Study of formulation variables influencing the drug release rate from matrix tablets by experimental design. European journal of pharmaceutics and biopharmaceutics. 2006 Jan 1;62(1):77-84. https://www.sciencedirect.com/science/article/pii/S0939641105001980
8. Bialer M. Extended-release formulations for the treatment of epilepsy. CNS drugs. 2007 Sep;21:765-74. https://link.springer.com/article/10.2165/00023210-200721090-00005
9. Atef E, Belmonte AA. Formulation and in vitro and in vivo characterization of a phenytoin self-emulsifying drug delivery system (SEDDS). European journal of pharmaceutical sciences. 2008 Nov 15;35(4):257-63. https://www.sciencedirect.com/science/article/pii/S0928098708003369
10. Madhavi N, Sudhakar B, Ravikanth PV, Mohon K, Ramana Murthy K. Formulation and evaluation of Phenytoin sodium sustained release matrix tablet. J Bioequiv Availab. 2012;4:128-33. Doi: 10.4172/jbb.1000125
11. Rompicharla Bhargavi et al.(2013) Formulation, Development and Evaluation of Acetazolamide matrix tablets. American.J.Pharmtech Research. ISSN: 249-3387.