JOURNAL OF DRUG DELIVERY RESEARCH

eISSN 2319-1074

RESEARCH ARTICLE

FORMULATION AND EVALUATION STUDY OF AZITHROMYCIN TABLETS BY VARIOUS NATURAL POLYMERS AND THEIR COMPARATIVE PREFORMULATION STUDY

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ABSTRACT

The present study was to formulate Azithromycin matrix tablet using Xanthan gum, and guar gum as natural polymers and to elucidate the effect of type of polymers and its concentration on release pattern of drug from sustained release matrix tablets. Azithromycin matrix tablets were prepared in two batches (batch number F1 to F2) by direct compression method using xanthan gum and guar gum as natural polymers and microcrystalline cellulose as a binder and pyrolidone as a water soluble polymer. The in vitro drug release studies of all the batches indicated that optimized formulation pertaining to Batch no. F2 was a promising system to provide sustained release effect of drug. The release pattern of the above formulation was best fitted to zero-order model and first order model. Mechanism of drug release followed was non-Fickian (super case-II) transport mechanism. Based on the above studies it can be concluded that this Azithromycin drug can be effectively formulated using different classes of natural polymers which can have greater bioavailability with less dose related side effects having better patient compliance.

KEYWORDS: Azithromycin, Guar gum, Xanthan gum, microcrystalline cellulose, Pyrolidone, Talc.

INTRODUCTION

Drug delivery is the method or process of administering a pharmaceutical compound to achieve a therapeutic effect in humans or animals.[1][2] Drug delivery technologies modify drug release profile, absorption, distribution and elimination for the benefit of improving product efficacy and safety, as well as patient convenience and compliance. Drug release is from: diffusion, degradation, swelling, and affinity-based mechanisms.[3] Most common routes of administration include the preferred non-invasive peroral (through the mouth), topical (skin), transmucosal (nasal, buccal/sublingual, vaginal, ocular and rectal) and inhalation routes.[4][5] Many drugs, peptide and protein, antibody, vaccine and gene based, in general may not be delivered using these routes because they might be susceptible to enzymatic degradation or cannot be absorbed

eISSN 2319-1074

into the systemic circulation efficiently due to molecular size and charge issues to be therapeutically effective. For this reason many protein and peptide drugs have to be delivered by injection or a nano-needle array.

To achieve and maintain the concentration of administered drug within the therapeutically effective range needed for a medication, it is often necessary to administer conventional dosage forms several times a day. These results in rise of drug level after each administration with subsequent fall which results in fluctuated drug level. [20][29][25]

The concept of sustained release was introduced in the early 1950s and the first patent on sustained release was obtained by Israel Lipowski who worked on coated pellets. There has-been more than 50 years of research and development on sustained release dosage forms to prolong drug levels in the body[17,21,23]. Successful fabrication of sustained release product is usually very difficult and involves consideration of physico-chemical parameters and pharmacokinetic behavior of drug, route of administration, disease state to be treated and, most important placement of the drug in the dosage form that will provide the desired temporal and spatial delivery pattern for the drug. Types of sustained release formulations include liposome's, drug loaded biodegradable microspheres and drug polymer conjugates. Basically there are three basic modes of drug delivery, i.e. targeted delivery, controlled release and modulated release.

MATERIALS AND METHOD:

Materials Azithromycin was gift sample by Medico Remedies Pvt.Ltd.Juhu, Mumbai. Guar gum, Xanthan gum was procured by Merck Specialties private Limited., India. Talc, Magnesium stearate was purchased from Apex Chemicals, Ahmadabad, India. Microcrystalline cellulose (MCC) Polyvinyl pyrolidone was purchased from Loba chemie Private Ltd. Mumbai.

Method

Method for preparation matrix tablet of Azithromycin

The controlled release matrix tablets of azithromycin were prepared by the direct compression method. The drug, polymers and other excipients were passed through sieve # 80. The controlled release tablets containing drug, matrix materials, diluents, binder and lubricants were mixed uniformly and compressed on 10 station tablet machine using 8 mm round and flat punches with hardness between 5-7 kg cm-2.

Table 1: Formulation trials of 250 mg azithromycin matrix tablets

Formulation Code	Drug (mg)	Xanthan gum (mg)	Guar gum (mg)	MCC	PVP	Talc	Magnesium Stearate	Total
F1	250 mg		100 mg-	208 mg	30 mg	6 mg	6 mg	600
F2	250 mg	100 mg		208 mg	30 mg	6 mg	6 mg	600

Each formulation contains 10 tablets.

Table: 2 Micromeritic properties of formulation blends.

Formulation Code	Angle of Repose	Bulk Density	Tapped Density	Carr's Index	Hauner's Ratio
F1	24.03 ± 0.78	0.425 ±0.03	0.512 ±0.017	16.99 ±2.25	1.20 ±0.03
F2	26.61 ± 0.98	0.467 ±0.1	0.551 ±0.1	15.24 ±1.68	1.17 ±0.02

eISSN 2319-1074

The obtained micromeritic properties are given in Table no.5.The value of Angle of repose of formulation within the range of 30°, indicating good flow properties for the granules. The tapped density values ranged between 0.510 ±0.08 to 0.608 ±0.04 g/ cm^3 and the bulk density values ranged between 0.425 ±0.03 to 0.516 ±0.07 g/ cm^3. The result of Carr's Index range from 14.09 ±0.86 to 17.69 ±1.95 % suggests good flow characteristics of the granules. Hausner's Ratio range from1.16 ±0.01 to1.21 ±0.09 % which indicates good flow property of microspheres.

RESULT AND DISCUSSION

Preformulation Studies

1. **Standard Calibration Curve**
   The λ_{max} was found at 215nm in 0.1 N HCl , and phosphate buffer (P^H-6.8) and The standard calibration curve for Azithromycin with regression value of 0.983 and 0.993 are shown in figure 1 and 2 respectively. The relation between drug concentration and absorbance is linear and the curve obeys Beer-lamberts law within the concentration range of 5 to 25 µg/ml of Azithromycin.
2. **Differential Scanning Calorimetry Thermogram**
   The supplied gift sample was identified by DSC thermogram. Identification of the drug can be described from the fig.8-10 **.**
3. **Drug Polymer Interaction Studies**
   The FT-IR spectra analysis of losartan potassium and the physical mixtures shows that there was no significant interaction between drug and polymers as shown in Fig no.5-6.

Physico-chemical properties of matrix tablets of losartan potassium

The thikness (mm), weight variation (%), Hardness (kg/cm2) Friability (%) and content uniformity (%) were calculated and the results are tabulated in table-3

Table:3 Physico-chemical properties of matrix tablets of azithromycin.

Formulation Code	Thickness (± S.D) (mm)	Hardness (± S.D) (kg/cm2)	Friability (± S.D) (%)	Weight variation (± S.D) (%)	Percentage Content (± S.D) (%)
F1	0.574±0.054	6.73 ± 0.16	0.45 ±0.01	±2	99.79± 0.36
F2	0.596±0.070	6.79 ± 0.28	0.35 ±0.07	±1	99.96 ± 0.23

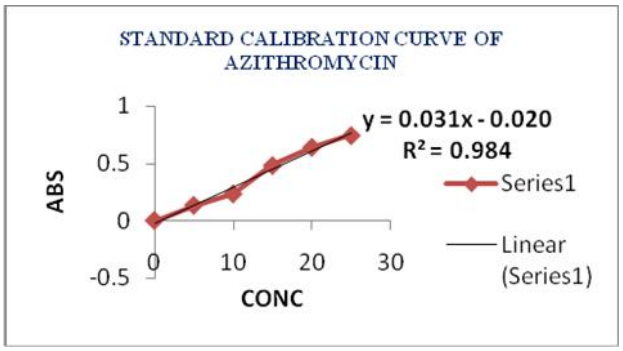

Fig.1. Standard curve of Azithromycin in phosphate buffer 0.1N Hcl (P^H 1.2)

eISSN 2319-1074

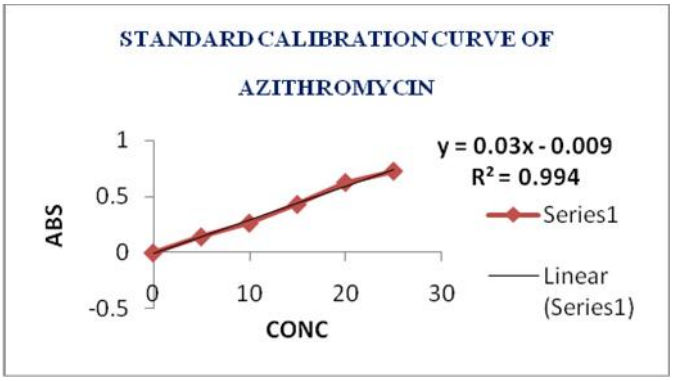

Fig.2. Standard curve of Azithromycin in phosphate buffer (P^H 6.8)

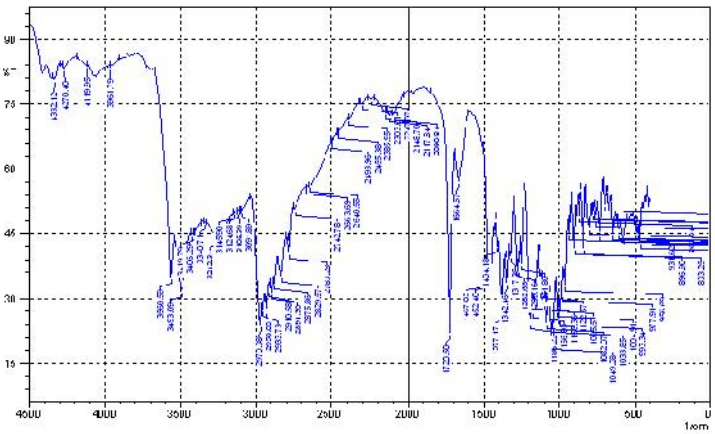

Fig. 3. FTIR spectra of Azithromycin

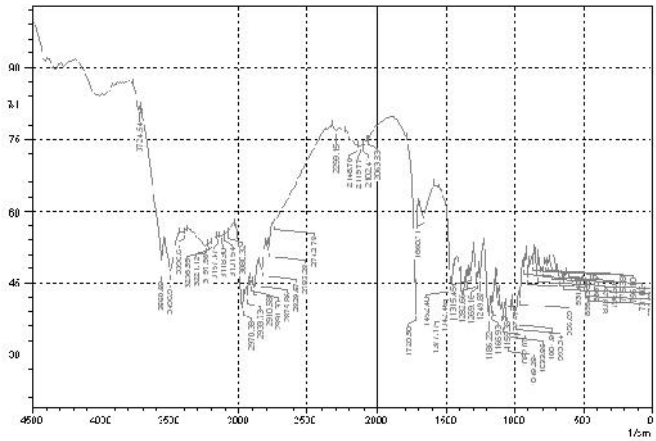

Fig. 4. FTIR spectra of Azithromycin and polymers (Xanthan gum and Guar gum)

eISSN 2319-1074

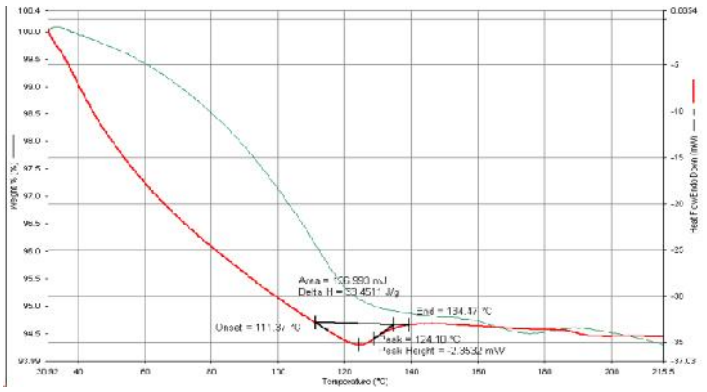

Fig. 5: DSC Thermogram of Azithromycin

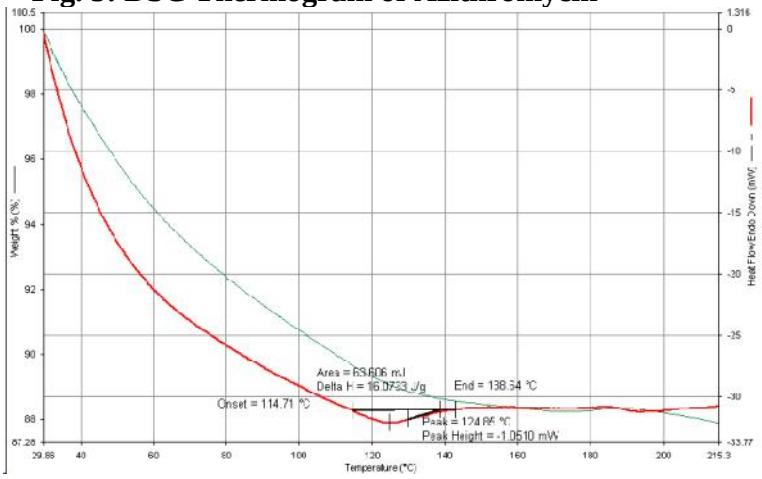

Fig. 6: DSC Thermogram of Azithromycin and polymers

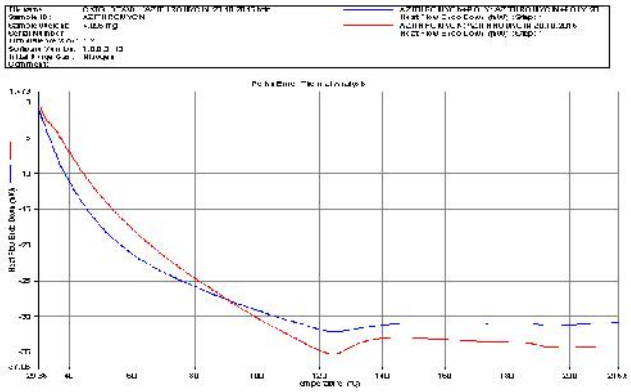

Fig:7. DSC Thermogram of Azithromycin and polymers comparison

***In- Vitro* Drug Release Studies**

It includes the dissolution of the matrix type tablet formulations study of all of the formulations by fitting the data obtained from dissolution study. In vitro release was carried out for all the formulations in 0.1 N HCl for 2 hours and phosphate buffer PH 6.8 for 6 hours.

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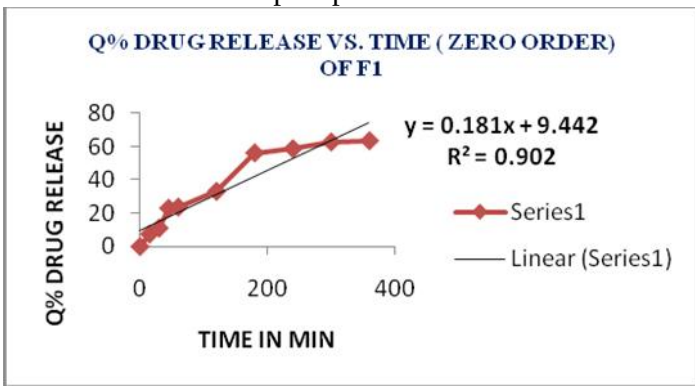

Fig 8: Release Data to be Fitted in Zero order Release Kinetics for Formulations F1

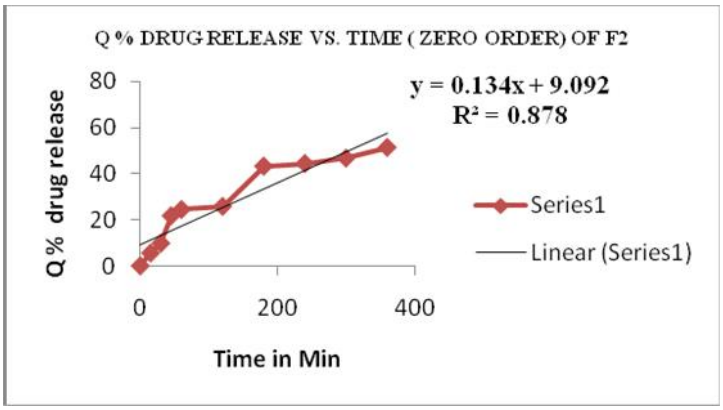

Fig 9: Release Data to be Fitted in Zero order Release Kinetics for Formulations F2

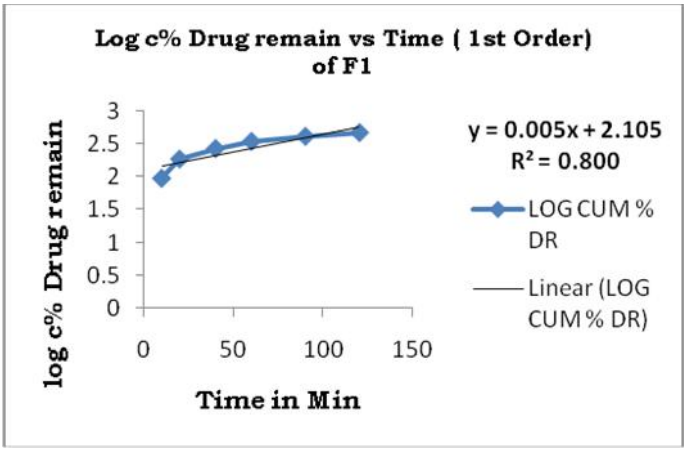

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Fig 10: Release Data to be Fitted in First order Release Kinetics for Formulations F1

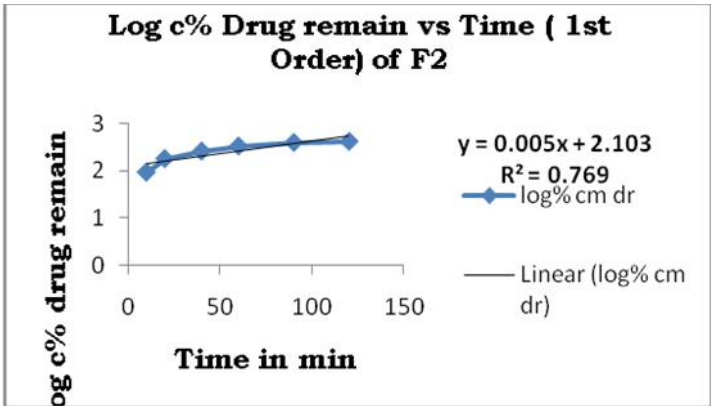

Fig 11: Release Data to be Fitted in First order Release Kinetics for Formulations F2

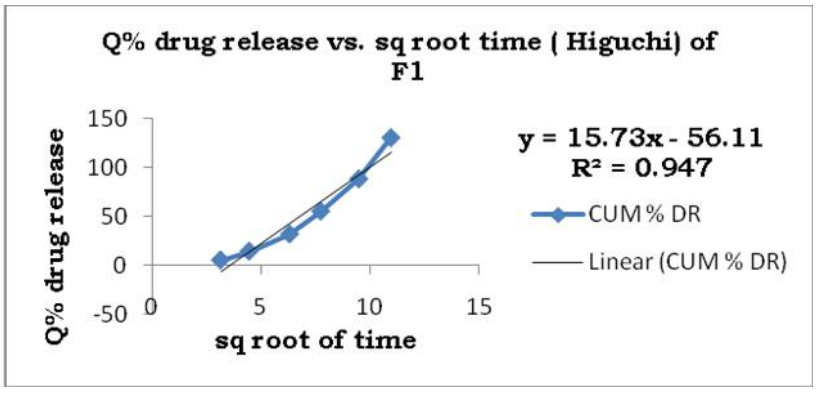

Fig: 12. Release Data to be Fitted in Fitted in Higuchi Release Kinetics for Formulations F1

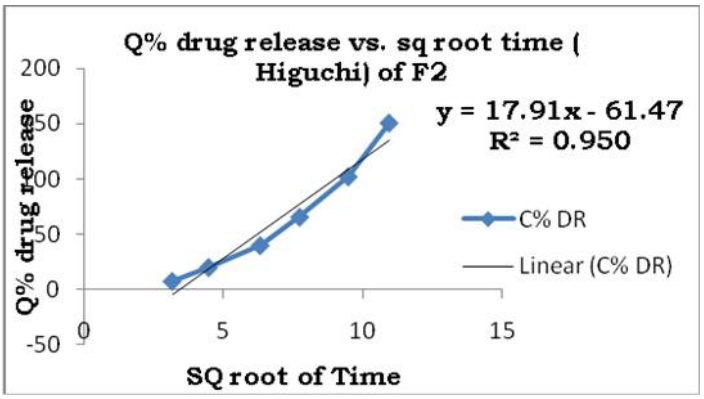

Fig: 13. Release Data to be Fitted in Fitted in Higuchi Release Kinetics for Formulations F2

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Statistical Evaluation of Release Data

	Zero Order Model		1st Order Model		H-M Model	
Formulations	**R^2**	**Ko**	**R^2**	**K_1**	**R^2**	**K_h**
F1	0.902	4.35	0.800	0.208	0.947	11.88
F2	0.878	4.74	0.769	0.206	0.950	14.33

DISCUSSION:

From the dissolution profile study of two formulations of Azithromycin formulations namely: **F1 & F2,** it was found that the **F2** formulations release profile best predicted by Higuchi Matrix named found to be the best released with R^2 value of 0.950,which is nearer to 0.999. These properties and the viscous nature of the Guar gum retards release of the drug from the dosage form. This natural polymer is also appealing for use in drug delivery for a wide range of molecular weights, varying chemical compositions, low toxicity and biodegradability. The matrix tablets of xanthan gum, are given sustained release pattern of drugs from tablets.

So it can be concluded from the above experiment that among al two formulations **F2** shows best release profile in our laboratory atmosphere and set up.

ACKNOWLEDGEMENT

The author Acknowledge the support of School of Pharmacy (Seacom Skills University), Kendradangal, Bolpur for providing infrastructural facilities to carry out this research work.

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