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Research Article

Formulation and release kinetic study of Hydrogel containing Acarbose using polymers as Hydroxypropylmethyl cellulose and Guar gum

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ABSTRACT

Hydrogel matrix tablets of Acarbose was formulated using hydroxypropyl methyl cellulose and guar gum with the aim to study of release kinetic and to attain a near zero order release. *In-vitro* dissolution studies were carried out using USP type 2 dissolution test apparatus. The release of drug followed a typical Higuchian pattern. Matrix tablets formulated employing hydroxypropyl methyl cellulose and guar gum slow release of Acarbose over a period of 12 h and were found suitable for maintenance portion of oral controlled release tablets. Acarbose release from these tablets were diffusion controlled and followed zero order kinetics after a lag time of 1h.The most successful of the study, exhibited drug release pattern very close to theoretical release profile. A decrease in release kinetics of the drug was observed on increasing polymer ratio.

Key words:Formulation ;release kinetic study ; Hydrogel ; Hydroxypropylmethyl cellulose;Guar gum

INTRODUCTION

During the last two decades there has been remarkable increase in interest in controlled release drug delivery system.This has been due to various factor viz. the prohibitive cost of developing new drug entities, expiration of existing international patents, discovery of new polymeric materials suitable for prolonging the drug release, and the improvement in therapeutic efficiency and safety achieved by these delivery systems. Now-a-days the technology of controlled release is also being applied to veterinary products also.The basic rationale for controlled drug delivery is to alter the pharmacokinetics and pharmacodynamics of pharmacologically active moieties by using novel drug delivery system or by modifying the molecular structure and /or physiological parameters inherent in a selected route of administration. Carboxymethylcellulose sodium, hydroxypropylmethyl cellulose, polyethylene oxide, polyvinyl-107, and natural gums can be used as matrix materials. The matrix may be tableted by direct compression of the blend of active ingredient and certain hydrophilic carriers or from a wet granulation containing the drug and hydrophilic matrix material.Diabetes mellitus is a chronic disease that is characterized by disorders in carbohydrate, protein and lipid metabolism. Its central disturbance appears to involve an abnormality either in the secretion of or effects produced by insulin although other factors also may be involved. Diabetes mellitus is a metabolic disorder in which carbohydrate metabolism is reduced while that of proteins and lipids is increased.Acarbose(O-4,6-dideoxy-4-[[(1S,4R,5S,6S)-4,5,6-trihydroxy-3-(hydroxymethyl)-2-cyclohexen-1-yl] amino]-a-D-glucopyranosyl-(1->4)-O-a-?D-glucopyranosyl-(1->4)-D-glucose) (1) is an oral alpha-glucosidase inhibitor, especially sucrase. It is given by mouth in the treatment of type 2 diabetes mellitus. It has also been studied for the treatment of reactive hypoglycemia, the dumping syndrome and certain types of hyperlipoproteinaemia (2). Because of its higher water solubility and shorter half life, drug requires frequent dosing by oral route. Off various recent techniques for controlling drug release, matrix system offer various advantages of ease of formulation, better control on release profile of drug and better patient compliance.

MATERIALS AND METHODS

Acarbose was obtained as gift sample from Windlas biotech Ltd, Dehradun. Hydroxypropyl methyl cellulose procured from Suleb Lab ,Baroda. Guar gum was obtained as gift sample from S.D.Fine chemical Ltd, Mumbai. other materials used were of analytical grade, and procured from commercial sources.

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Fabrication of Controlled Release matrix Tablets of Acarbose

All the ingredients were sieved through sieve number 120. Weighed quantities of the drug, polymer, lubricants (Talc and Magnesium stearate) and diluent (lactose) were mixed in geometric proportion using a mortar and pestle. Required amount of 90% v/v Isopropyl alcohol was added as a granulating fluid. Controlled release tablets were prepared by wet granulation method. Hydroxypropyl methylcelluloses, Guar Gum were used as retardant material for preparation of tablets.

The resultant mixture were wetted with 4% starch paste and granulated through 10 mesh and than the damp mass was passed through sieve no. 60. The wet granules were dried in the oven at 50°C for half an hour. Remaining amount of lubricants were added to the dried granules.

After evaluating the precompression parameters, the lubricated granules were subjected to compression to form tablets with target weight of 350mg using hydraulic press having 10mm diameter flat punches. The hardness of all the tablets was maintained at 6 to 8 Kg/cm^2.

The formula for various formulations attempted have been given in table no.I

Dissolution study of controlled release matrix formulation of Acarbose:

A single tablet was placed in 40 mesh dissolution basket and immersed in 900ml of dissolution media, maintained at 37^{o}C±0.5^{o}C. Aliquot samples were withdrawn every hour up to a period of 12 hours. After each withdrawal, the withdrawn amount of dissolution media was replaced with buffer. The absorbance of the withdrawn samples, after appropriate dilution was measured at 278nm against appropriate buffer blanks. Results of in-vitro dissolution studies obtained were tabulated and shown graphically according to following modes of data treatment.

1.Cumulative Percentage Drug Released V/s. Time in Hours.
2.Cumulative Percentage Drug Retained V/s. Time in Hours.
3.Higuchi's Classical Diffusion Equation - Cumulative Percentage Drug Released V/s. Square Root T.

RESULTS AND DISCUSSIONS:

In present work an attempt has been made to formulate controlled release matrix tablets of Acarbose using two retardants namely hydroxypropyl methylcellulose and guar gum in different concentrations and combinations. The *formulation of tablets* was done by using wet granulation technique which was found acceptable.

The results of *evaluation studies* can be summarized as follows:

Figure no.I shows plots of cumulative percentage of Acarbose released V/s. time for promising formulations.Two retardants were employed with varying concentrations to get promising concentration for controlled release matrix tablets, which can be used for further studies.Formulations F1, F2, and F3 contains Hydroxypropyl methylcellulose as release retarding polymer in 14.3%, 28.6%, 42.9% of concentration respectively. Formulations F1 and F2 gave 93.44% and 88.46% of drug release respectively in 12 hours of dissolution study performed. It was found that drug release was not prolonged to desired level; this may be due to inadequate concentration of retardant polymer and also due to lactose, present in relatively large amount which alter drug release rate mainly by altering the gelation of retardant polymer. The formulation F3 gave 80.09% of drug release in 12 hours of study. This may be due to high concentration of retardant polymer level employed. The mechanism of release may be based on hydration and gelation due to cellulosic nature of retardant polymer at tablet liquid interface. The existence of gel barrier could be expected to retard drug release by limiting exposure of solid drug to dissolution liquid. The drug release may be due to diffusion controlled and swelling controlled mechanism because of inherent swelling characteristic of hydroxylpropyl methylcellulose. The tablets were found swollen at the end of 12 hours indicating a hydrophilic matrix system.Guar gum, a natural retardant polymer was used in formulations F4, F5, F6 in 14.3%, 28.6%, and 42.9% of concentrations, respectively. Formulations F4, F5, and F6 gave 94.91%, 89.56%, and 79.58% of drug release in 12 hours of dissolution study, respectively. It was found that the drug release was not prolonged to desired level this may be due to inadequate hydration of retardant (guar gum) as compared to hydroxypropyl methylcellulose. The tablets were found swollen at the end of 12 hours dissolution study this may be due to inherent swelling property of gum.In all the above formulations, it was observed that drug release rate was inversely proportional to the concentration of retardant polymer i.e., increase in concentration of retardant polymer resulted in a reduction in the drug release rate.Figure No.II shows the graphical representation of cumulative percentage drug retained as a function of time for Formulations F1 to F6. In all, F3 and F6 formulations were considerable (the best selected formulations). These plots were found to be nearly linear with correlation coefficient (r) values which are –0.9923, and -0.9902 for F3, & F6 respectively. This linearity indicates that the release of Acarbose from the matrix tablets might have followed nearly zero order kinetics. Negative values of correlation coefficient indicates negative slope for the plot.

Table.I: Composition of controlled release tablets of Acarbose

Ingredients	F1	F2	F3	F4	F5	F6
Acarbose	150	150	150	150	150	150
Hydroxypropyl methyl cellulose	50	100	150	-	-	-
Guar gum	-	-	-	50	100	150
Lactose	125.5	75.5	25.5	125.5	75.5	25.5
Starch	14	14	14	14	14	14
Talc	7	7	7	7	7	7
Magnesium stearate	3.5	3.5	3.5	3.5	3.5	3.5
% of polymer to the total tablet weight	14.3	28.6	42.9	14.3	28.6	42.9

Weight of each tablet = 350 mg ,Quantities in mgs

FIGURE I. COMPARATIVE PLOT OF DRUG RELEASE VS TIME FOR CONTROLLED RELEASE MATRIX TABLET OF ACARBOSE

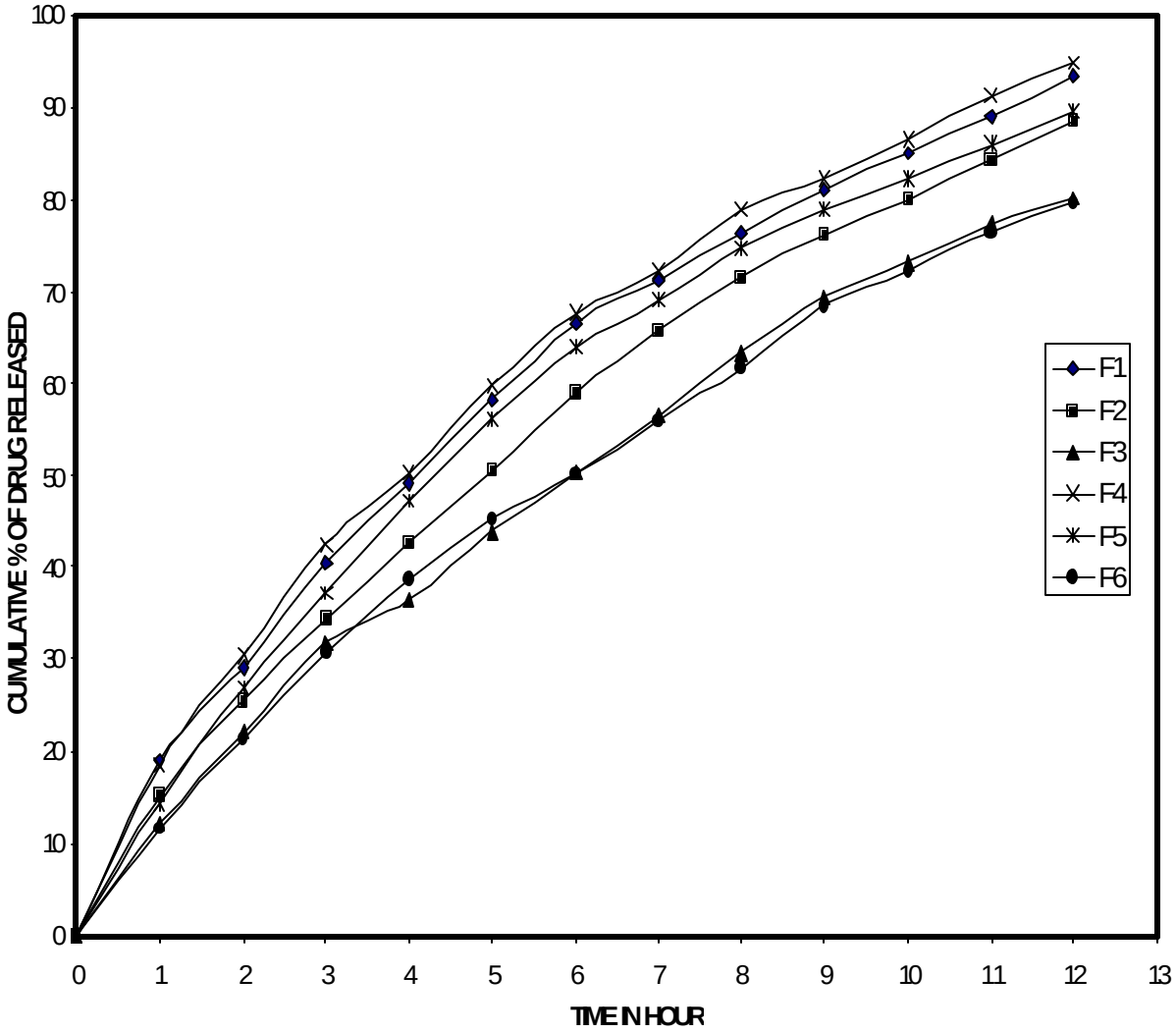

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FIGURE II. COMPARATIVE PLOT OF DRUG RETAINED V/S TIME FOR CONTROLLED RELEASE MATRIX TABLET OF ACARBOSE

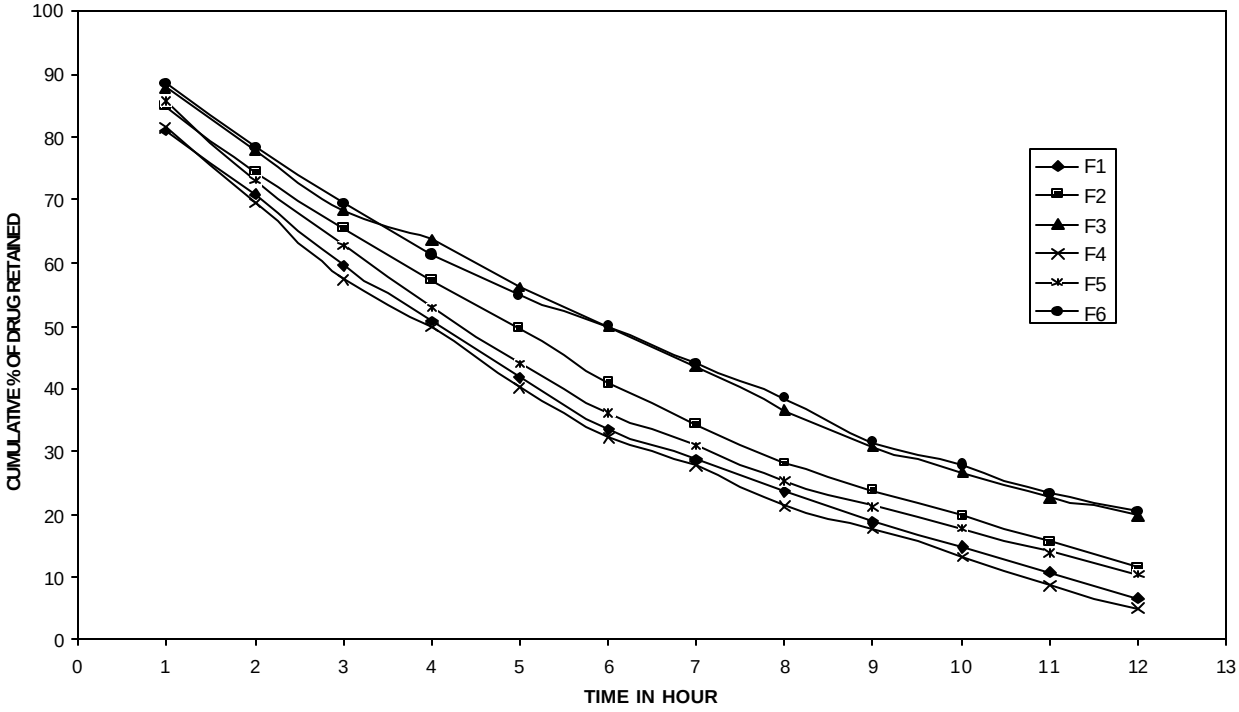

FIGURE III. COMPARATIVE PLOT OF DRUG RELEASE V/S SQUARE ROOT OF TIME FOR CONTROLLED RELEASE MATRIX TABLET OF ACARBOSE

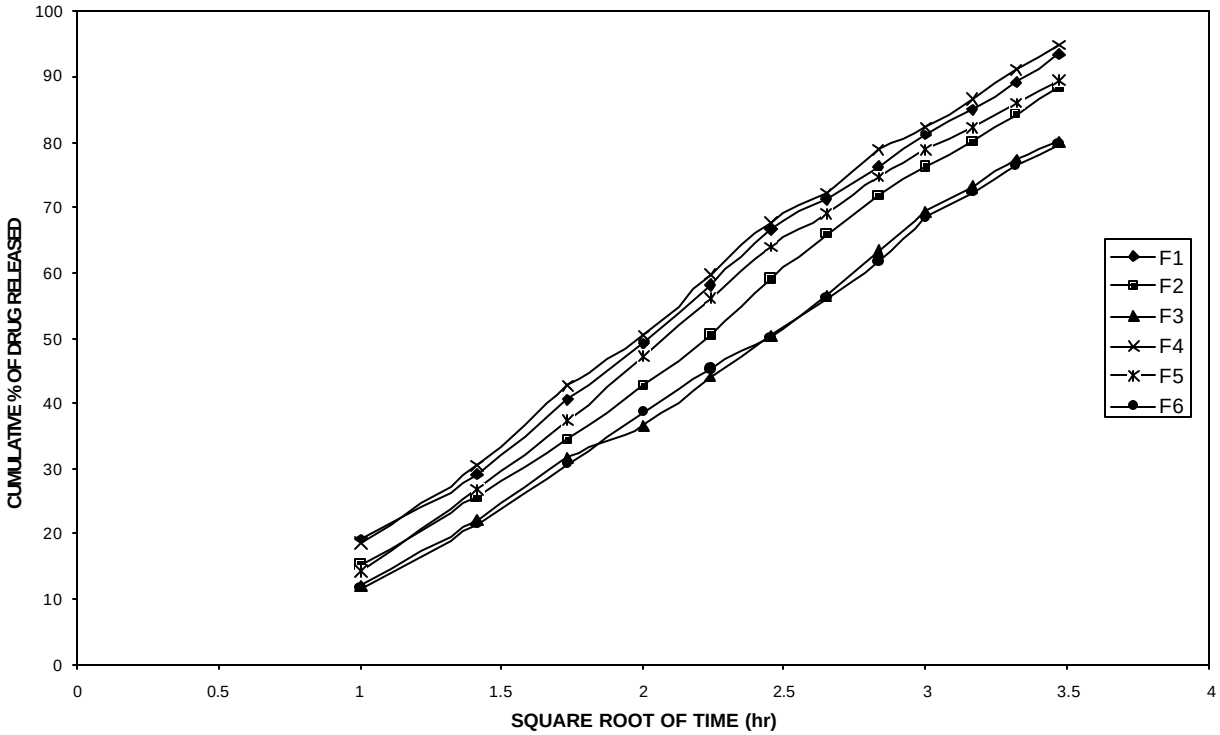

Figure No.III shows the graphical representation of cumulative percentage of Acarbose release as a function of square root of time. These Higuchi's plots were found to be nearly linear with correlation coefficient (r) values which are 0.9979, 0.9985, 0.9980, 0.9981, 0.9968 and 0.9992 for F1, F2, F3, F4, F5 and F6 respectively. This linearity suggests that the drug release may be by diffusion controlled mechanism.

CONCLUSION:

From the findings obtained so far, it can be concluded that,

- Hydroxypropyl methylcellulose and Guar gum in the concentration of 42.9% to the total tablet weight is promising concentration for oral controlled release tablets of Acarbose.
- In all the formulations, drug release rate is inversely proportional to the concentration of polymer and directly proportional to concentration of lactose.
- Formulated tablets exhibited nearly zero order kinetics and the release profile was of matrix diffusion type.
- From this study, it is possible to design promising oral controlled release matrix tablets containing Acarbose for the treatment of type 2 diabetes mellitus diseases with more efficacy and better patient compliance.
- In *in-vitro* dissolution study, formulations F3 to F6 wherein hydroxypropyl methylcellulose and guar gum were employed, it was found that increasing the concentration of the polymer resulted in linearization of drug release curve and formulation F3 and F6 gave satisfactory drug release pattern. The drug release mechanism may be of diffusion and swelling controlled, implies hydrophilic matrix system. The results obtained in the in-vitro dissolution studies for different formulations are recorded in Table No.II and Table no.III for F1 to F6 respectively.

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