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Formulation and Relative Evaluation of Cefazolin Sodium Microspheres with Guar gum in Different Ratios

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ABSTRACT

The objective of this study was to develop oral sustained release microspheres of Cefazolin sodium to attain prolonged action, which can reduce its side effects and provide more safety and efficacy. Microspheres were formulated by solvent evaporation method using the polymer Guar gum. Five formulations were prepared with 1:1, 1:2, 1:3, 1:4, 1:5 drug: polymer ratio. They were comparatively evaluated for their better release profile.

Keywords: Cefazolin Sodium, Guar Gum, and Sustained Release.

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INTRODUCTION

The goal of any drug delivery system is to provide therapeutic amount of drug to the proper site in the body to achieve promptly and 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. Here, the piece of interest is sustained release delivery system of Cefazolin sodium. This drug has low half life of 1.8 hr and which is rapidly eliminated. So Cefazolin sodium is lacking to maintain its concentration at the site of action, conventionally. Hence Sustained release oral drug delivery of cefazolin sodium will be able to maintain therapeutic concentration at the site of action. The calculated sustain release dose of Cefazolin sodium is 100mg,so frequency of dosing is reduced, as well as better control of plasma drug levels is possible with sustained release oral delivery system with less side effects, better efficacy and safety.

The objective of this work is to formulate and evaluate microspheres of Cefazolin sodium in different drug-polymer ratios using Guar gum and to study the release of drug from each formulation.

MATERIALS AND METHODS

Materials used

Cefazolin sodium (Orchid Pharma, Chennai), Guar gum (Merk Chemicals), Dichloromethane (SD fine Chemicals), Petroleum ether (SD fine Chemicals) Light liquid paraffin (Fischer Chemicals), Distilled water (Industrial Scientific Enterprises, Namakkal).

Formulation of microspheres

Solvent Evaporation Method

Non-aqueous solvent evaporation method was employed for formulation of microspheres. Guar gum was dissolved in 20ml of dichloromethane and stirred well until a homogenous solution was formed. Core material, Cefazolin sodium was added to the polymeric solution and mixed well. Resulting solution was then added in a thin stream to 100ml of light liquid paraffin in 450ml beaker while stirring at 2000rpm.

The solution was stirred for 4 hr to evaporate the solvent and microspheres collected by filtration. Microspheres were washed with petroleum ether (40-60 degree celcius) until free from oil. The collected microspheres were dried overnight and subsequently stored in desiccators over fused silica gel.

Different core: coat ratio,(1:1,1:2,1:3,1:4,1:5)of Guar gum was prepared by same methodology. Formulation Codes (Table- 1).

Method for Preparation of standard graph for the estimation of Cefazolin sodium in water

100mg of accurately weighed drug was transferred into 100ml standard flask (1000mcg/ml). To this a little quantity of distilled water was added and made to dissolve and made up to 100ml.This is stock solution. From this 10ml was pipetted out into a 100ml standard flask and made up to 100ml(100mcg/ml). From this 10 to 50mcg/ml solution was prepared and absorbances were determined at 235nm using Elico make UV-VISIBLE spectrophotometer.

Method for Preparation of Standard graph of cefazolin sodium in Hcl buffer pH 1.2.

100mg of the drug was accurately weighed and transferred to a 100ml(1000mcg/ml) standard flask. To this small quantity of Hcl buffer was added to dissolve the drug and made up to 100ml.This is stock solution. From this 10ml was pipetted out to 100ml standard flask and made up to 100ml(100mcg/ml). From this 10 to50mcg/ml solution was prepared and the absorbance were determined at 235nm by Elico make UV-VISIBLE spectrophotometer.

Method for Preparation of Standard graph of Cefazolin sodium in Phosphate buffer pH7.2

100mg of the drug was accurately weighed and transferred to a 100ml (1000mcg/ml) standard flask. To this small quantity of Phosphate buffer was added to dissolve the drug and made up to 100ml.This is stock solution. From this 10ml was pipetted out to 100ml standard flask and made up to 100ml(100mcg/ml). From this 10 to50mcg/ml solution was prepared and the absorbance were determined at 235nm by Elico make UV-VISIBLE spectrophotometer.

Method for Determination of Entrapment Efficiency of Cefazolin Sodium micro spheres by UV-spectrophotometer

25 mg of the sample was soaked in 25ml of water for injection for overnight, it was passed through membrane filter and the drug was diffused into the solution. Entrapment efficiency was estimated by measuring the absorbance in UV-visible spectrophotometer at 235nm. The entrapment efficiency of the microspheres was calculated from the absorbance.

The quantity of cefazolin sodium present in 25mg of the sample taken was calculated by the following formula.

$$\% \text{ Entrapment efficiency} = \frac{\text{Calculated drug content}}{\text{Theoretical drug content}} \times 100$$

In-Vitro Release of Cefazolin Sodium Microspheres

In-vitro release studies of the samples were carried out in specially designed dissolution apparatus. 500ml beaker containing 250ml of dissolution medium was placed over a magnetic stirrer and stirred at 100rpm with a constant temperature of 37.5°C. The release study of cefazolin sodium was carried out in acidic pH (1.2) for 2 hours for the other 6 hours it was continued at an alkaline pH (7.2) using phosphate buffer.

100mg of cefazolin sodium microspheres from each formulation were taken in muslin cloth for dissolution and the release rate were determined, at periodic time intervals (½ hour) up to 2 hours there after at 1-hour interval each. 5ml of sample was withdrawn, filtered and diluted suitably. The absorbance was measured at 235nm using UV-spectrophotometer. 5ml of fresh dissolution medium was added each time to maintain sink condition. Zero order, first order kinetics and higuchi plot for all the formulations were plotted.

RESULTS AND DISCUSSION

The oral sustained release microspheres of Cefazolin sodium were formulated by using guar gum as polymer. The standard graph for the estimation of cefazolin sodium in water, in Hcl buffer pH 1.2 and in Phosphate buffer pH7.2 was plotted. The entrapment efficiency and invitro release of cefazolin sodium was studied using UV, Dissolution Apparatus respectively.

Standard graph for the estimation of Cefazolin sodium in water

The graph was plotted to determine the Cefazolin sodium in distilled water by determining the absorbance at 235nm by using different concentrations, such as 10,20,30,40,50 μgm/ml, and the absorbance was found to be 0.231, 0.460, 0.720, 0.928 and 1.206 respectively (Figure-1).

Standard graph of cefazolin sodium in Hcl buffer pH 1.2

The graph was plotted to determine the Cefazolin sodium in Hcl buffer pH 1.2 by determining the absorbance at 235nm by using different concentrations, such as 10,20,30,40,50 μgm/ml, and the absorbance was found to be 0.137, 0.330, 0.553, 0.728 and 0.906 respectively (Figure- 2).

Standard graph of Cefazolin sodium in Phosphate buffer pH7.2

The graph was plotted to determine the Cefazolin sodium in Hcl buffer pH 7.2 by determining the absorbance at 235nm by using different concentrations, such as 10,20,30,40,50 μgm/ml, and the absorbance was found to be 0.226, 0.521, 0.774, 1.042 and 1.480 respectively (Figure- 3).

Entrapment Efficiency of Cefazolin Sodium micro spheres by UV-spectrophotometer

The entrapment efficiency of the 5 formulations was done and it was found that FG1 showed least percentage entrapment with 47.64% and FG3showed maximum with 90.52%. Entrapment efficiency is plotted in the (table – 2).

In-Vitro Release Of Cefazolin Sodium Microspheres

The percentage release of drug from Guar gum formulations it was 42.08, 39.38, 61.09, 61.95, 69.66 respectively.

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Zero order, First order and Higuchi square root kinetics were plotted for all the formulations. All the formulations were following slow first order kinetics. From Higuchi plot it was concluded that diffusion was the rate-controlling factor. Therefore it was concluded that on increasing the polymer ratio the release of the drug also increased. From all the release data the Guar gum formulation, FG5 showed the best release profile and an excellent release pattern. (Figures 4,5&6).

Table- 1
Table showing details of formulation codes of Cefazolin microspheres

1	FG 1	1:1 (Guar gum)
2	FG 2	1:2 (Guar gum)
3	FG 3	1:3 (Guar gum)
4	FG 4	1:4 (Guar gum)
5	FG 5	1:5 (Guar gum)

Table-2
Percentage Entrapment of Cefazolin Sodium Microspheres

S.No	Formula code	% Entrapment
1	FG 1	47.64
2	FG 2	78.03
3	FG 3	90.52
4	FG 4	78.60
5	FG 5	77.64

SUMMARY AND CONCLUSION

Cefazolin sodium microspheres were formulated by solvent evaporation technique, using Guar gum at 1:1, 1:2, 1:3, 1:4, 1:5 drug:polymer ratios, this method was most suitable as it requires no heating procedure and cefazolin sodium is a thermoliable drug, all the formulated microspheres were found to be discrete, spherical, free flowing and specific yield was obtained.

The standard graph of the pure sample was made using three media, such as distilled water, acidic buffer pH 1.2 and phosphate buffer pH 7.2.

The entrapment efficiency of the 5 formulations was done and it was found that FG1 showed least percentage entrapment with 47.64% and FG3showed maximum with 90.52%.

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Figure- 1

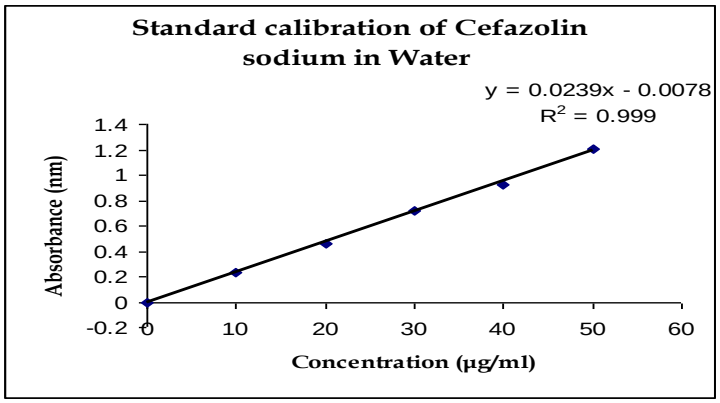


Figure-2

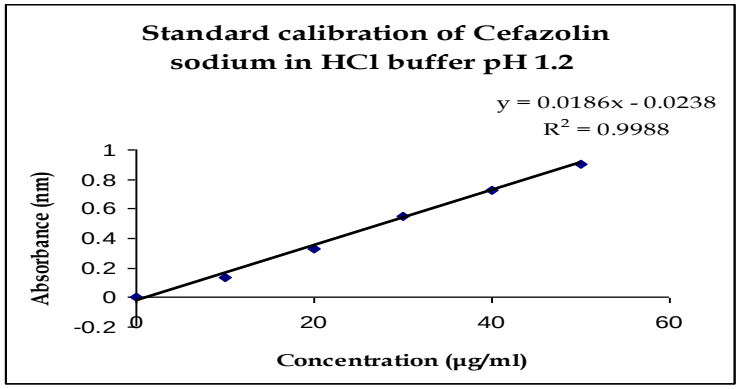
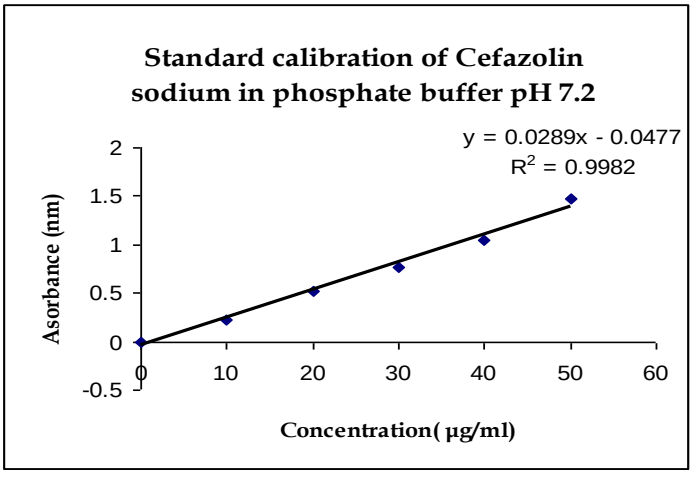


Figure- 3



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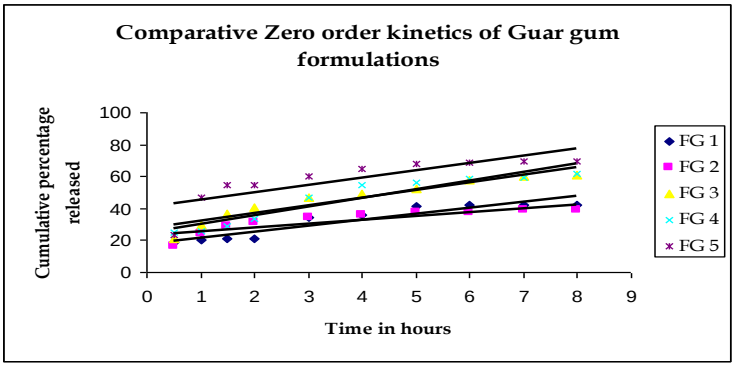

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Figure- 5

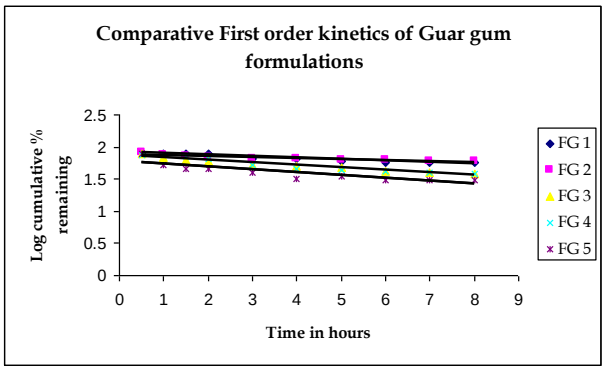
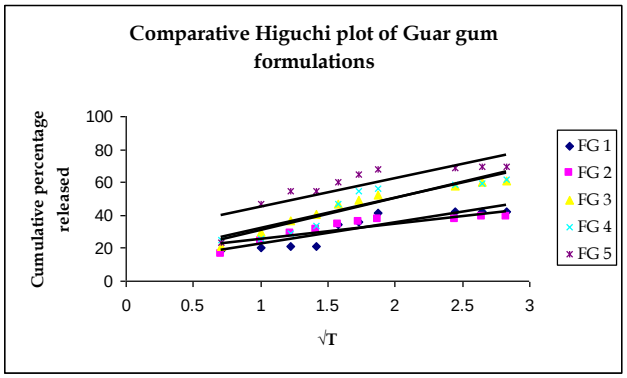


Figure - 6



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