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FORMULATION AND EVALUATION OF SUSTAINED RELEASE MICROSPHERES OF ACETAZOLAMIDE BY SOLVENT EVAPORATION TECHNIQUE

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Abstract

Sustained release microcapsules of acetazolamide, a short half life carbonic anhydrase inhibitor, was developed to reduce the frequency of drug administration, ease of dose adjustment and improve patient compliance. In this study, sustained release microcapsules of acetazolamide was prepared by solvent evaporation techniques using Eudragit RL/RS as polymer and particle size, encapsulation efficiencies and in vitro release of the fabricated microcapsules were evaluated. The results showed that the encapsulation efficiencies were desired for all the formulations of microcapsules developed. Particle sizes of the microcapsules were influenced by the concentration of Eudragit and stirring speed. From the results of the in vitro study shows that the desired release rate is achieved by the combination of Eudragit RL and Eudragit RS.

Key words: Acetazolamide, Sustained release, Eudragit,

INTRODUCTION:

Acetazolamide is a carbonic anhydrase inhibitor and it is widely used in the treatment of glaucoma and also used as diuretics. The drug has a relatively short half life (3-4 hr) and usually administered 3 – 4 times daily in the form of an immediate release formulation [1]. A sustained release formulation reduces the frequent drug administration and thus improves patient compliance.

Micro encapsulation by solvent evaporation techniques is widely used in pharmaceutical industries. It facilitates sustained release of a drug, which has many clinical benefits. Water insoluble polymers like Eudragit RS and Eudragit RL are used as encapsulation matrix using this technique [2].

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Eudragit polymers are series of acrylate and methacrylate polymers available in different ionic forms. Eudragit RL and Eudragit RS are insoluble in aqueous media but they are permeable and both have pH independent release profiles [3].

The purpose of this study was to formulate and evaluate microspheres of acetazolamide.

MATERIALS AND METHODS

MATERIALS

Acetazolamide (Micro labs, Bangalore), Eudragit RS, Eudragit RL (S.D fine chemicals, India) were obtained from commercial sources. All other reagents used were analytical grade.

METHODS

PREPARATION OF MICROSPHERES [4]

Acetazolamide microspheres were prepared by solvent evaporation

technique. Various proportions of polymers like Eudragit RS and Eudragit RL were dissolved in acetone. Acetazolamide was powdered and dispersed in polymer solution. This solution was added slowly to a jacketed flask containing 300ml of petroleum ether and light liquid paraffin (40:60 w/w) and 1% w/w span 80 under constant stirring (400, 500 and 750 RPM). After evaporation of acetone, the microspheres formed were collected by filtration in vacuum, washed 3-4 times with 50ml of petroleum ether each and dried at room temperature for one day.

PARTICLE SIZE ANALYSIS: [5]

Particle sizes of micro spheres were measured by a particle size analyzer. For this analysis, the sample was prepared by suspending 50mg of microspheres in 5ml of filtered distilled water containing 2% w/v of Tween 80 and then sonicating in a water bath for 3 mins to prevent aggregation between microspheres. The particle size was expressed as the volume mean diameter in micrometer.

Table: 1 Formulation of Acetazolamide Microspheres

Bath No.	Drug (g) (Acetazolamide)	Eudragit RS (g)	Eudragit RL (g)	Stirring speed (rpm)
1	1.5	1.5	---	600
2	1.5	1.5	---	900
3	1.5	---	1.5	600
4	1.5	3	---	600
5	1.5	3	---	900
6	1.5	4.5	---	600
7	1.5	4.5	---	900
8	1.5	---	3	600
9	1.5	---	3	900
10	1.5	---	4.5	600
11	1.5	---	4.5	900
12	1.5	2.5	0.5	900
13	1.5	2.2	0.8	900
14	1.5	2	1	900

DETERMINATION OF YIELD AND DRUG CONTENT: [6,7]

The yields of the formulations were calculated by the ratio between the experimental weight of product and the sum of the weight of all components, discounting the weight of acetone and span 80.

To determine the drug content, the microspheres were powdered and content equivalent to 30mg of acetazolamide was transferred into 100ml volumetric flask. The contents was dissolved by using 0.01M sodium hydroxide solution and made up to 100 ml. From the above solutions, 5ml was diluted to 50ml using the 0.01M sodium hydroxide solution. The resulting solution was measured the absorbance at 240nm. The amount of acetazolamide present in the fabricated microspheres was calculated by the reference standard of acetazolamide.

INVITRO RELEASE [8,9]

The release pattern of the acetazolamide microspheres were determined by using USP XXV dissolution test apparatus. 900 ml of dissolution medium (0.1N HCl) was taken and maintained at the temperature of 37±5˚ C. Acetazolamide microspheres was accurately weighed and taken in each basket and rotated at 100 rpm. 5ml of sample was withdrawn at each time interval and made up to 100ml with dissolution medium. Absorbance was measured at 265 nm and the percentage release was calculated.

RESULTS AND DISCUSSION

The present study was taken to formulate and evaluate sustained release microspheres of acetazolamide by solvent evaporation method. Various batches were made and these formulations are shown in table 1. When drug and polymer ratio was too low (1:1), no spherical particles were obtained. These results indicates that the amount of solid, thus the viscosity of the inner phase is and important factor for the formulation of microspheres. Spherical particles were obtained, when

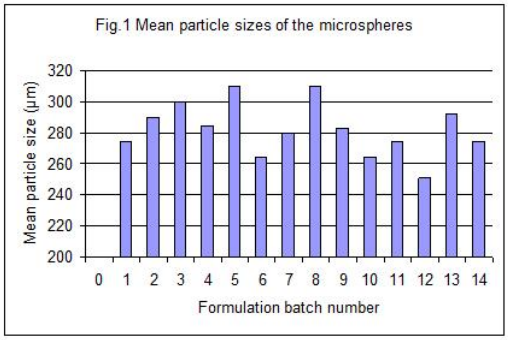


Fig. 2. In vitro release of Acetazolamide from Eudragit RS and Eudragit RL microspheres

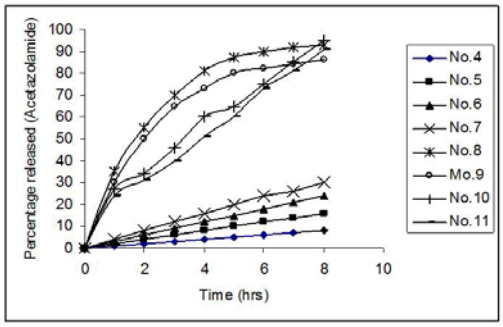
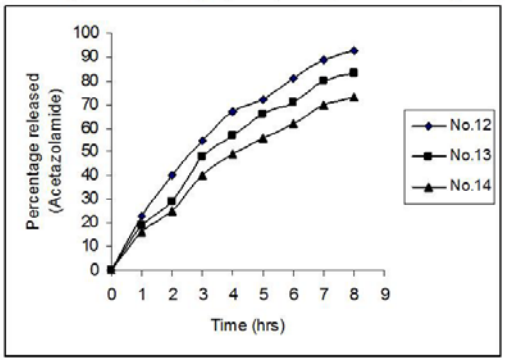


Fig.3. In vitro release of Acetazolamide from microspheres containing combination of polymers (Eudragit RS and Eudragit RL)



the polymer and drug ratio was increased (2:1, 3:1) at stirring speed 750rpm. But the shapes of particles in the above ratio were irregular.

The average size of the microspheres was found as 250µm in all the formulations. The particle size distribution and mean particle size of the microspheres are shown in the fig.1. The yield of microspheres and encapsulation efficiencies were high for all the formulations and were not affected by the type of polymer and drug polymer ratio and stirring speed.

The in vitro releases of the drug from microspheres were studied at pH 1.2 using USP XXIV basket method. The results are given in the fig .2 and fig.3. From this study, it shows that the release rates were very slow in Eudragit RS and the release rate is fast in the microspheres made by Eudragit RL. So the combination of the polymers Eudragit RS and Eudragit RL gives desired release of drug from the microspheres.

CONCLUSION:

The sustained release microspheres were successfully developed by solvent evaporation technique using Eudragit as polymers. From this study it is concluded that the drug polymer ratio and stirring speed were important for obtained desired spherical particles. The yield and encapsulation efficiencies ere found to be high in all the formulations. The release rate of acetazolamide from the microspheres were depend upon the amount and type of polymers used. Microspheres containing Eudragit RS gives very slow release of drug whereas the desired release rate is achieved by combination of the Eudragit RS and Eudragit RL

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