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FORMULATION, CHARACTERIZATION AND *IN-VITRO* EVALUATION OF ACRYLIC POLYMER LOADED ACECLOFENAC MICROSPHERES

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ABSTRACT

Microspheres can be utilized for precise delivery of drugs and reduce the drug concentrations at sites other than the target organ. The present study is aimed to prepare and evaluate the aceclofenac microspheres using an acrylic polymer Eudragit–S 100. Aceclofenac microspheres were prepared by o/w solvent evaporation method and evaluated for its percentage yield, particle size, entrapment efficiency and its *in-vitro* release. Percentage yield and entrapment efficiency of formulated microspheres were found to be high. The mean diameter of microspheres were found to be within 91 – 109µm. *In-vitro* release study on phosphate buffer pH 6.8 showed 58 – 67%.

KEY WORDS

Aceclofenac, Microsphere, Eudragit–S 100, Solvent Evaporation.

INTRODUCTION

Microencapsulation techniques are widely used in pharmaceutical research. Stability and Release profile of drug substance can be modified according to the needs and unpleasant taste can be masked by microencapsulation of drugs.[1] Microspheres can be utilized for precise delivery of drugs and reduce the drug concentrations at sites other than the target organ[2]. Microspheres are solid, approximately spherical particles (1 to 1000 µm) and have large surface to volume ratio. Rheumatoid[3] arthritis is traditionally considered a chronic, inflammatory autoimmune disorder that causes the immune system to attack the joints. Circadian rhythm of levels of interleukin-6 might correspond to the rhythm of symptoms of rheumatoid arthritis. Non steroidal anti inflammatory drugs are considered to be the first line drugs in the symptomatic treatment of rheumatoid arthritis. Aceclofenac[4-5], is a non-steroidal anti-inflammatory drug (NSAID) used extensively in the treatment of rheumatoid arthritis, osteoarthritis and ankylosing spondylitis. Aceclofenac directly blocks prostaglandin E2 secretion at the site of inflammation by inhibiting IL-Beta and Tumour necrosis factor in the inflammatory cells. Recommended dose of Aceclofenac is 100mg twice daily, due to short biological half-life of the drug (3-4h) makes it suitable candidate for the modified release dosage forms. The objective of the present work is to formulate and evaluate the aceclofenac microsphere using Eudragit–S 100 as polymer. Aceclofenac is practically insoluble drug this makes the choice of formulation of o/w type microencapsulation method using solvent evaporation technique.

MATERIALS AND METHODS

Aceclofenac and Aerosil were generously supplied by Biotrans, Chennai as a gift sample. Eudragit S100 by Evonik Degussa India Pvt. Ltd., Mumbai. Polyvinyl Alcohol (PVA) Loba Chemie, Bombay, India. All other chemicals used in the study were of analytical grade.

Preparation of Microspheres by O/W solvent evaporation method[6-11]

Aceclofenac loaded Eudragit-S100 microspheres were prepared by solvent evaporation method. Polymer dissolved in the mixture of Ethanol and Dichloromethane at 3:2 ratio to get a clear solution. This solution is added drop wise into 1% w/w PVA aqueous continuous phase**.** Aerosil is dispersed into this continuous phase previously as anti-sticking agent to prevent the large agglomeration of microspheres. The solution was stirred for 1 hour at 800 rpm at 40^0C. The prepared microspheres were filtered and washed with distilled water. The microspheres obtained were then air dried at room temperature 24 hours and stored in dessicator until further used. Details of the microsphere formulations were shown in Table 1

Table 1
Compositions of Microspheres Formulation

Formulation Code	Drug : Polymer Ratio	Solvent Ratio Ethanol : Dichloromethane
F1	1:3	3:2
F2	1:4	3:2
F3	1:5	3:2
F4	1:6	3:2

Percentage Yield[12]

The percentage yield of all the batches were calculated on dry weight basis with respect to the solid materials added at the initial stage was calculated by using the following equation and the results were shown in Table 2

Percent Yield = (the amount of microspheres obtained / the theoretical amount) X 100

Particle Size Distribution

The particle size distribution was done by the optical microscopy method using a calibrated stage micrometer around 200 particles were calculated and mean diameter was calculated and shown in Table 2.

Drug Entrapment efficiency

Accurately weighed 25mg of dried microspheres dissolved in methanol and sonicated for 15 mins then the solution was filtered and diluted appropriately then the filtrate was analyzed for drug concentration by spectrophotometerically by the following equation and tabulated in Table 2.

% Entrapment = (Actual content / Theoretical content) X 100

Table 2
Evaluations of Formulations

Formulation Code	Percentage Yield	Mean Particle Size (µm)	Percent Entrapment efficiency
F1	72	91.45	73
F2	76	98.27	76
F3	79	104.57	78
F4	84	109.78	83

SCANNING ELECTRON MICROSCOPY

Scanning Electron Microscopy (JEOL-6360) was carried out to study the morphological characteristics of the microspheres. The dried microspheres were coated with gold foil (100A°) under an argon atmosphere in a gold coating unit and scanning electron microscopy in both higher and lower resolution were observed. Figure 1 shows the SEM image of formulation F3

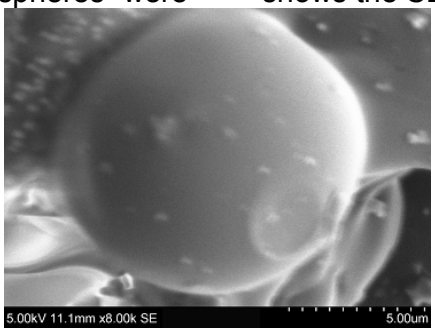

Figure 1
SEM image of Formulation F3

In-vitro Release Studies[13-14]

In vitro dissolution studies were carried out on the formulated aceclofenac microsphere at 37°C ± (0.5°C) at 100 rpm with paddle type dissolution apparatus. The *in vitro* dissolution studies were performed by using Phosphate buffer pH 6.8. An accurately weighed sample (100mg) was placed in dissolution media consisting 900 ml of pH 6.8 Phosphate buffer and the dissolution was carried out for 6 hours. The sample (5 ml) was withdrawn at each hour interval and replaced with the same volume of buffer and the withdrawn samples were diluted and estimated for aceclofenac concentration at 275 nm spectrophotometrically (Shimadzu Pharmspec UV-1700 series, Japan). Figure 2 shows the cumulative percentage release of all the formulations.

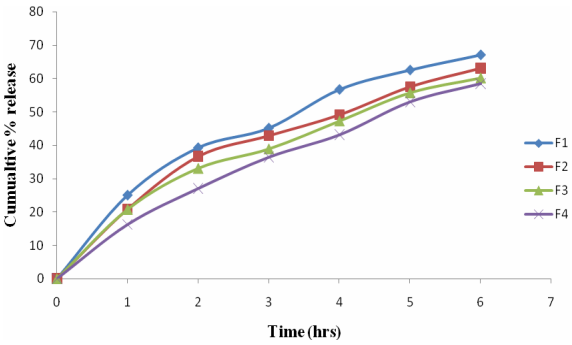

Figure 2
Cumulative percentage release profiles of Formulations

RESULTS AND DISCUSSION

Microspheres of aceclofenac with Eudragit-S 100 polymer in various ratios were formulated by solvent evaporation method. Addition of aerosil to the continuous phase agglomeration of particles were reduced which showed larger in the initial trials. It was seen that as the ratio of drug to the polymer increased the production yield also increased and was found to be 72 – 84%. Due to increase in polymer concentration which leads to increase in viscosity of the phase the particle size of the formulation also found to be increased and the mean diameter of the microspheres were 91 – 109µm. Entrapment efficiency was in the range from 73 to 83%. It was observed that as the polymer ratio increases, entrapment efficiency also increases. The surface morphology of formulation F3 was evaluated to its texture as well. From the the image obtained it revealed that the morphology of the microspheres were spherical and that the texture was almost smooth. The *in-vitro* drug release was carried out using Phosphate buffer pH 6.8 upto 6 hours. The cumulative percentage of release for all the formulations were found to be 58 to 67%. The effect of polymer on release rate of the formulations were found to be decreasing with increasing the concentration of polymer. The burst effect of *in-vitro* may be due to the adherence of the drug particles at the surface of the microspheres.

CONCLUSION

It can be concluded that aceclofenac microspheres could be successfully prepared using Eudragit –S 100 as polymer by utilizing solvent evaporation method. Further evaluation by this polymer may be studied to bring out a sustained release microspheres.

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