SHORT COMMUNICATIONS

Preparation and *in vitro* Characterization of Eudragit RL 100 Microspheres Containing 5-Flurouracil

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A relatively simple technique of preparing Eudragit RL-100 microspheres containing 5-Fluorouracil is described. The technique described is based on a condensation process and does not involve use of any harmful organic solvent, antiadhesion agents and surfactants. Discrete microspheres were obtained in the colloidal size range (3.79 ± 2.55 microns) and were evaluated with reference to entrapment efficiency and leaching rate profile.

COPOLYMER of acrylic and methacrylic ester popularly known as Eudragit RL 100 is widely used for delayed release permeable film coatings. The basic aim of the proposed work was to exoplore the possibility of using Eudragit RL 100 microsphere for site specific delivery of 5-FU by the process of passive targeting. In this paper a relatively simple method of preparation of Eudragit RL 100 microspheres containing 5-FU is reported.

Most of the methods reported in literature for preparation of Eudragit microspheres involve techniques such as solvent evaporation[1-3], emulsification solvent evaporation[4-8] and the phase separation[9,10]. Kawashima et al[11,12] reported a quasiemulsification technique to prepare microspheres of Ibuprofen with acrylic polymers Eudragit S 100, Eudragit L 100-55, Eudragit RS 100 and Eudragit RL 100 using sucrose fatty acid ester as surfactant. The method adopted here is a slight modification on the method reported by Kawashima *et al*[11]. Eudragit RL 100 was dissolved in ethanol to produce a 0.5 %, 1% and 2% w/v solution. The drug was dissolved in 10 mL phosphate buffer saline (pH 7.2) to produce a 0.2 % w/v solution. The ethanolic solution of Eudragit RL 100 was added gradually to 5-FU solution with constant stirring at 1000 rpm at 35°. Stirring was continued for 45 minutes to allow complete evaporation of ethanol. Microspheres suspended in phosphate buffer saline were obtained. The unentrapped 5-Fu was separated from the microspheres by repeated centrifugation at 4,000 rpm for 30 minutes and washing of microspheres with phosphate buffer saline.

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The amount of drug loaded in the microspheres was determined indirectly. The phosphate buffer saline washings obtained during centrifugation were analysed spectrophotometrically at 226 nm for 5-FU content. The entrapment efficiency was expressed as percentage of initial amount of 5-FU added during preparation. The drug entrapment efficiency of various batches of Eudragit RL 100 microspheres is shown in Table 1. As the polymer to drug ratio increases the drug entrapment efficiency increases.

The particle size of microspheres was determined microscopically (Axiomat (Zeiss) Microscope) by taking an average of about 300 particles. The mean size of microspheres was found to be 3.79 ± 2.55 microns.

The microspheres (polymers to drug ratio 5) prepared were stored at room temperature in phosphate buffer saline medium and the amount of 5-FU leached out was

Table I : Drug entrapment efficiency of Eudragit RL 100 Microspheres

Polymer to Drug Ratio	Amount of 5-FU entrapped mg ± S. D. (n-1)	Percent 5-FU entrapped ± S.D. (n-1)
2.50	0.11 ± 0.04	0.55 ± 2.05
5.00	4.39 ± 0.63	22.00 ± 3.14
10.00	4.86 ± 0.51	24.33 ± 2.52

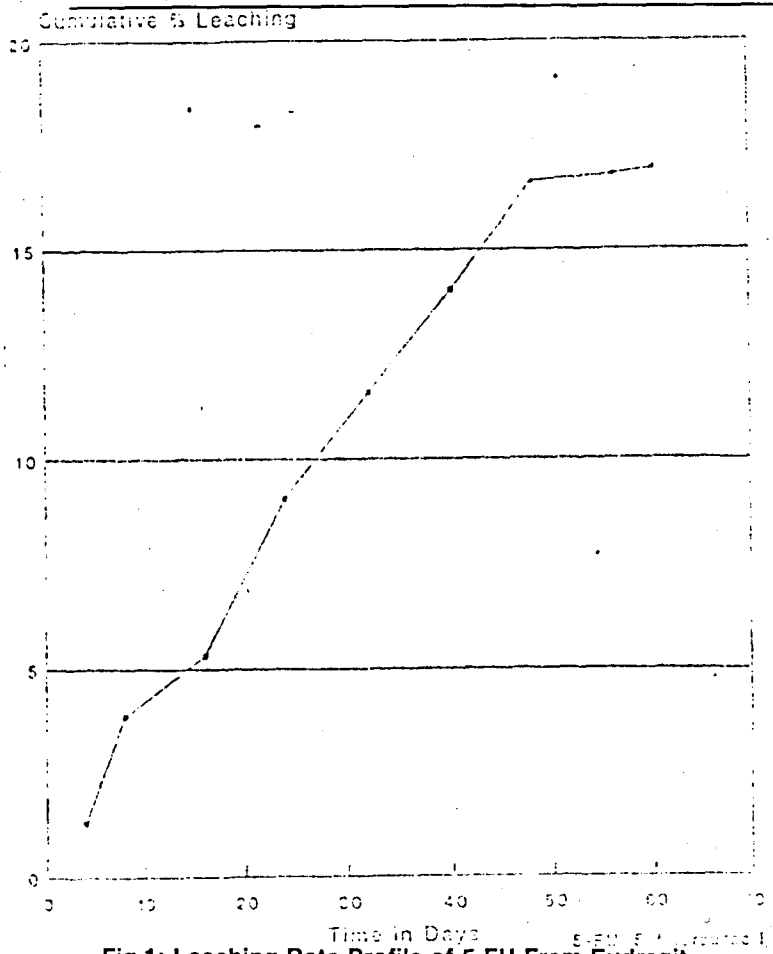

Fig.1: Leaching Rate Profile of 5-FU From Eudragit RL 100 Microspheres

studied over a period of 60 days at room temperature. An aliquot of the sample was withdrawn at different time intervals, centrifuged and the supernatant was analysed for 5-Fu content spectrophotometrically at 266 nm. The leaching rate profile of 5-FU from Eudragit RL 100 microspheres as shown in Fig.1, indicates that 16.90 % of drug was leached out from the microspheres during a period of 60 days. It shows an initial burst effect which may be due to saturation of membrane with available drug followed by a steady state release of the drug.

In this method discrete microspheres of very small size were formed spontaneously. Probably the presence of quarternary ammonium groups in the Eudragit RL 100 polymer stabilized the colloidal dispersion and microspheres could form even in absence of surfactant. The present method avoids the use of harmful solvents like methylene chloride, methanol, acetone, methyl acetate and use of antiadhesion agents like magnesium stearate and aluminium stearate[1-6]. It also avoids the use of any additives like surfactants in the process of preparation. The colloidal nature of the microspheres indicate the potential use of these microspheres as a colloidal drug delivery system. They can be further evaluated through *in vivo* studies.

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Polarographic determination of some Sulphonamide derivatives in pharmaceutical preparations

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A polarographic catalytic method is developed for the determination of sulpha drugs in presence of chromium (VI). The drugs produced a catalytic peak at - 1.7 V vs Saturated Calomel Electrode (SCE) in a buffer solution of pH 9.6. Optimum conditions are established for the analytical method. The method can be used for the determination of Cr (VI) as well as hydrolysed drug in micro quantities.

MANY organic compounds containing nitrogen and sulphur produce polarographic catalytic hydrogen waves in presence of certain metal ions such Co (II) and Ni (II)[1-3], Cr (VI) and W (VI)[4]. The waves produced due to evolution of hydrogen can be used for the determination of metal ions as well as sulpha drug in trace quantities[5,6]. The present communication describes a method for the determination of sulpha drugs such as sulfamoxole, sulphaacetamide and sulfadoxine.

Experimental solutions are prepared with double distilled water and Analar grade chemicals. A Lingane type of H-cell, digital pH meter and a pen recording Polarograph (ELICO make, Hyderabad) are used in these studies.

A stock solution of 1 x 10^{-3} M chromium (VI) is prepared in distilled water. All the three sulpha drugs are hydrolysed as indicated in the procedure given below. One hundred mg of the powdered drug is weighed into a 100 ml standard flask containing 50 ml of 5 M HCl. The flask is heated in a water bath for 30 minutes, cooled to room temperature, 20 ml of DMF is added and the solution is made up to the mark with distilled water. 10 ml of this solution is neutralised with 10 ml 5 M NaOH and diluted to 100 ml with distilled water. This solution is used in further studies after appropriate dilution.

Required quantity of the hydrolysed drug (HS) is transferred into a 25 ml standard flask containing 1o ml of buffer solution of pH 9.6. Three ml of NH_4Cl (0.4 M) is added as supporting electrolyte. Required quantity of Cr (VI) solution is added and the solution is made up to the mark with distilled water. It is shaken well and is transferred into a polarographic cell. Pure nitrogen gas is passed for 10 minutes and the polarogram is recorded.

Polarographic experiments were carried out with the following three solutions. (a) Cr (VI), (b) hydrolysed sulfa