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RESEARCH ARTICLE

DEVELOPMENT AND CHARACTERIZATION OF FACTORIALLY DESIGNED 5-FLUOROURACIL MICROSPHERES

Manjeet Kumar and Harish Dureja*

Department of Pharmaceutical Sciences, Maharshi Dayanand University, Rohtak - 124 001, Haryana, India

**E-mails*: harishdureja@gmail.com, ahlawat4880@gmail.com
Tel.: +91-9416357995, +91-1262-393228

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Microspheres of 5-fluorouracil were prepared for prolonged or controlled drug delivery, to improve bioavailability/stability and to target drug to specific sites. 5-Fluorouracil was encapsulated with eudragit RL 100 and ethyl cellulose using an *o/o* emulsion solvent evaporation method. Factorial design was used to study the effect of stirring speed, stirring time and phase ratio on cumulative percent of drug release. It was found that cumulative percent of drug release increases at the high level of stirring speed, stirring time and phase ratio. The effect was highest in case of stirring speed and lowest in case of phase ratio. Microspheres (batch MA-5) were characterized by spherical shape, absence of aggregates, a mean diameter of 107.92±1.12 μm, a recovery of 78.82±1.26% (*w/w*) and an encapsulation efficiency of 76.78±1.19% (*w/w*). ANOVA was applied on cumulative percent of drug release to study the fitting and significance of model. The estimated model may be further utilized as response surface for cumulative percent of drug release of 5-FU microspheres.

Key words: Eudragit RL 100, 5-Fluorouracil, Ethyl cellulose, Solvent evaporation method, Microspheres.

INTRODUCTION

Controlled drug delivery occurs when a polymer/drug system is designed to release the drug in a predetermined manner. The main purpose of these release systems is to achieve a more effective therapy *i.e.* a delivery profile that would yield a high blood level of the drug over a long period of time, avoiding the large fluctuations in drug concentration and reducing the need of several administrations (Duarte *et al* 2007). Microspheres are one of the multi-particulate delivery systems and are used for prolonged or controlled drug delivery, to improve bioavailability or stability and to target drug to specific sites. Microspheres can also offer advantages like limiting fluctuation within therapeutic range, reducing side effects, decreasing dosing frequency and improving patient compliance (Davis and Illum, 1988; Ritschel, 1989). One of the popular methods for the encapsulation of drugs within water-insoluble polymers is the emulsion solvent evaporation method. The technique of emulsion solvent evaporation is preferred to other preparation methods like spray-drying, sonication and homogenization, because it requires only mild conditions such as ambient temperature and constant stirring. Thus, a stable emulsion can be formed without compromising the activity of the core materials. The emulsion solvent evaporation method has been utilized successfully by various researchers for the preparation of microspheres using various biocompatible polymers such as ethyl cellulose, poly(D-L-lactide-coglycolide) (PLGA) (Murakami *et al* 2000; Choi *et al* 2002), poly(ε-caprolactone) (PCL) and Eudragit(s) (Lamprecht *et al* 2000; Arshady, 1990; Esposito *et al* 1996; 2005; Lorenzo-Lamosa *et al* 1998; Kim *et al* 2002; Yang *et al* 2001). In the present study, factorially designed microspheres of 5-fluorouracil (5-FU)