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Research Article

FORMULATION AND *IN VITRO* EVALUATION OF NELFINAVIR MESYLATE MICROCAPSULES USING CELLULOSE ACETATE

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ABSTRACT

Nelfinavir Mesylate is a protease inhibitor used in the treatment of human immunodeficiency virus infection.Microcapsules of Nelfinavir Mesylate were developed as sustained release dosage form and release kinetics were studied.The desired microencapsulation was achieved by solvent evaporation method using cellulose acetate in different drug:polymer ratios of 1:1,1:2,1:3,1:4 and 1:5.Characterization of five formulations FCA-1, FCA-2, FCA-3, FCA-4, FCA-5 was performed by size, shape, entrapment efficiency, infrared spectroscopy and *in vitro* drug release analysis. The prepared microcapsules were free flowing, spherical in shape, with particle size in the range 80-1000µm. FCA-5 had maximum entrapment efficiency of 95.03%. The *in vitro* release profile of FCA-5 was found to give 81.68% release of the drug which was more than the release of drug in FCA-1, FCA-2, FCA-3 and FCA-4. Release kinetics showed it followed zero-order kinetics and the correlation coefficient in Higuchi model indicated diffusion controlled mechanism.

Keywords: Nelfinavir Mesylate, Cellulose acetate, Microcapsules, Release kinetics.

INTRODUCTION

Sustained release dosage forms have many advantages in comparison to conventional dosage forms.They maintain blood levels of the drug for long duration of time, minimize undesirable side effects and reduce the dosing frequency[1].Nelfinavir Mesylate is a protease inhibitor used in the treatment of human immunodeficiency virus (HIV) infection[2].Nelfinavir Mesylate is available as a conventional dosage form and the dosing frequency is three times a day.Nelfinavir Mesylate was microencapsulated[3] using cellulose acetate[4] as polymer by solvent evaporation method [5,6] to give a sustained release dosage form with increased bioavailability and to reduce dosing frequency with minimal side effects.

MATERIAL AND METHODS

Nelfinavir Mesylate was obtained as a gift sample from Macleods Pharma, Daman, India and cellulose acetate from Loba Chemicals, Mumbai, India. All other chemicals were of analytical reagent grade.

Nelfinavir Mesylate microcapsules were prepared by solvent evaporation method according to the formula in Table1.Formulations of FCA-1, FCA-2,FCA-3,FCA-4,FCA-5 were prepared in the drug:polymer ratio of 1:1, 1:2,1:3,1:4 and 1:5. Polymer cellulose acetate was dissolved in acetone and stirred until a homogenous solution was formed. Core material,Nelfinavir Mesylate was added to the polymer solution and mixed thoroughly.The resulting mixture was then added in a thin stream to liquid paraffin while stirring at 600 rpm.The resultant mixture was stirred for 4 hours until the solvent evaporated completely.The liquid paraffin was decanted, the microcapsules were collected, washed twice in petroleum ether to remove any adhering oily phase, and was air dried for at least 12 hours to obtain discrete microcapsules.The percentage yield of formulations was obtained.

The particle size of developed formulations was determined by microscopy[7] method using calibrated eye piece micrometer.The particles were arranged on the basis of size ranges.The number of particles in each size range were then converted and tabulated.The percent number of particles in each interval and percent undersize were calculated.Histogram and cumulative undersize curve were plotted.

Scanning electron microscopy[8] was performed on the developed microcapsules to assess their surface and morphological characteristics using SEM(Philips/FEI XL30 ESEM). For drug entrapment efficiency[8] 25mg of the microencapsulated product was crushed into powder and 25ml water was added.The resulting mixture was kept for 24 hours and the solution was filtered.The drug entrapped was determined by measuring the absorbance at 254.6 nm after appropriate dilution with water. Infrared spectra of the pure drug and the formulations were obtained by potassium bromide pellet method using Shimadzu FTIR-8400S spectrophotometer in order to rule out drug-carrier interactions.

Standard calibration curve was determined in pH 1.2 and phosphate buffer pH 6.8. *In vitro* release studies of the formulated microcapsules was studied in USP XXIII type-2 dissolution apparatus (Electrolab Dissolution Tester TDT-08L) employing a paddle stirrer at 50 rpm using 900ml of 0.1 N HCl pH 1.2 for 2 hours and phosphate buffer pH 6.8 for 6 hours at 37 ± 0.5°c as dissolution medium[9]. 100mg of microcapsules from each formulation was used in each test. Aliquots of dissolution medium were withdrawn at specific intervals of time and analyzed for drug content by measuring the absorbance at 250nm.The volume withdrawn at each time interval was replaced with fresh quantity of dissolution medium. Cumulative percent of drug released was calculated and plotted against time.The release kinetics of Nelfinavir Mesylate from various formulations was determined by comparing respective correlation coefficients of zero-order,first-order and Higuchi model[10].

RESULTS AND DISCUSSION

The percentage yield of the microcapsules for FCA-1,FCA-2,FCA-3,FCA-4 and FCA-5 was 60.30%, 67.14%, 71.25%, 79.12% and 86.03% respectively.The particle size of the formulation was in the range of 80-100µm. Scanning electron microscopy (SEM) studies revealed that the microcapsules are almost spherical in shape as shown in Fig1.The drug entrapment efficiency of microcapsules in formulations FCA-1,FCA-2,FCA-3,FCA-4 and FCA-5 was 37.22%, 42.50%, 54.18%, 72.56% and 95.03% respectively.The maximum drug entrapment was seen in formulation FCA-5.

The IR spectrum of the formulations showed all the characteristic peaks of pure drug Nelfinavir Mesylate thus confirming that no interaction of drug occurred with the polymer.*In vitro* drug release studies of the microcapsules at the end of 8 hours showed release profiles which are graphically presented in Fig 2.Release of Nelfinavir Mesylate from the polymeric microcapsules was slow and spread over a longer period of time. The release profiles of microcapsules in phosphate buffer pH 6.8 was better than the release profiles in pH 1.2.The percentage cumulative release profile of formulation FCA-5 was 81.68% which gave maximum release compared to formulations FCA-1, FCA-2, FCA-3 and FCA-4.So FCA-5 was taken as the best formulation. The release kinetics of microcapsules from FCA-5 was determined by comparing their correlation coefficients.It followed zero-order kinetics and it was diffusion controlled as in Table 2.

Table 1: Ingredients used for the formulation of Nelfinavir Mesylate microcapsules

Formulations	FCA-1	FCA-2	FCA-3	FCA-4	FCA-5
Nelfinavir Mesylate(mg)	1000	1000	1000	1000	1000
Cellulose Acetate (mg)	1000	500	333.33	250	200
Acetone (ml)	25	25	25	25	25
Liquid Paraffin (ml)	100	100	100	100	100
Speed (r.p.m)	600	600	600	600	600

Table 2: Coefficient coefficient (R^2) of different kinetic models for Nelfinavir mesylate microcapsules

Microcapsule	Zero order	First order	Higuchi equation
	R^2	R^2	R^2
FCA-5	0.9989	0.9661	0.9743

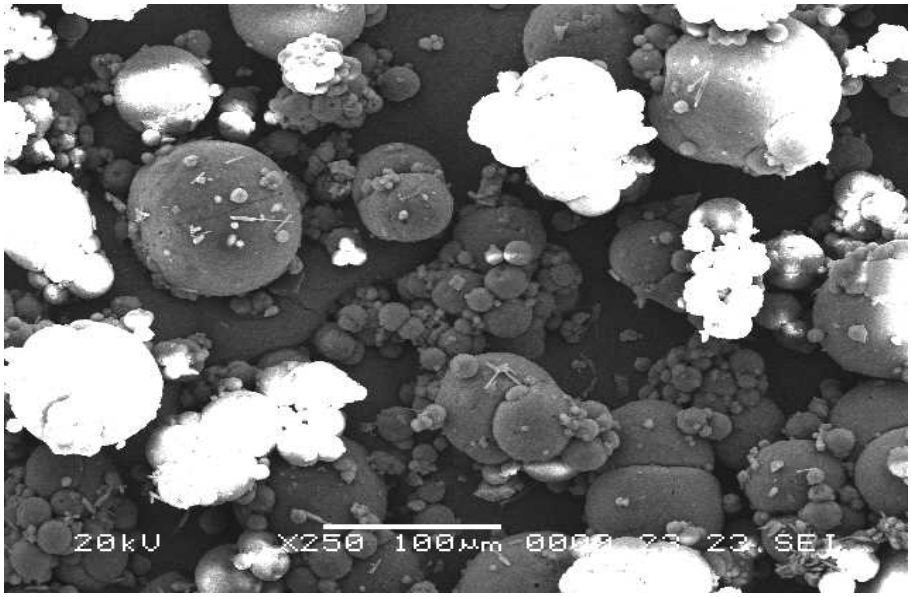

Fig. 1: Scanning electron microscopy of FCA -5 (250X, 100µm)

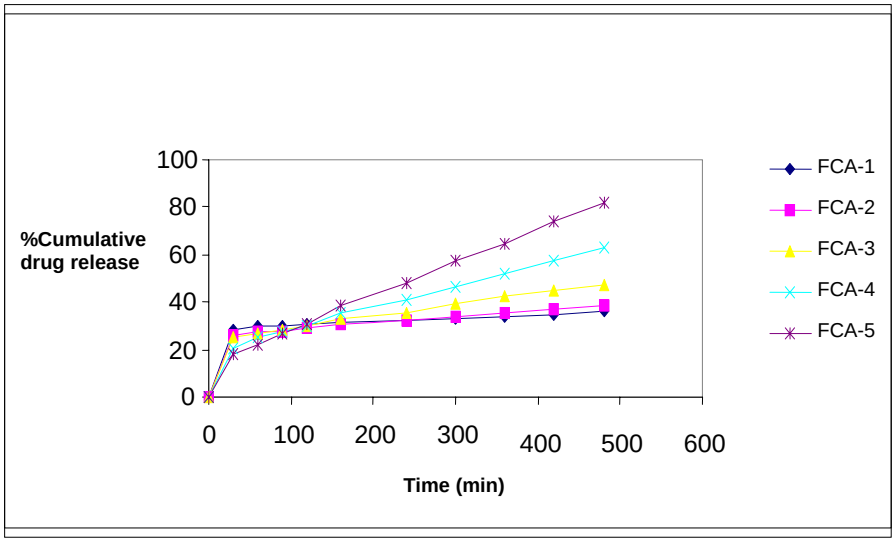

Fig. 2: Comparative release profile of Nelfinavir Mesylate microcapsules FCA-1 to FCA-5

CONCLUSION

It can be concluded that the solvent evaporation technique is a simple and reproducible method for the preparation of Nelfinavir Mesylate microcapsules. The prepared microcapsules of FCA-5 were spherical with high entrapment efficiency and *in vitro* release using cellulose acetate as the retardant material. *In vivo* studies have to be done to confirm enhanced bioavailability and reduced dosing frequency with lesser side effects.

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