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Formulation and Evaluation of 5-FU Loaded Eudragit Microspheres: Effect of Various Eudragit on Micromeretic Properties of Microspheres

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The aim of the present study was to prepare and evaluate microspheres of Eudragit (RS, RL and RSPO) containing an anticancer drug 5-FU. Microspheres were prepared by O/O solvent evaporation method using a acetone/liquid paraffin system. Magnesium stearate was used as the droplet stabilizer and n-hexane was added to harden the microspheres. The prepared microspheres were characterized for their micromeretic properties and entrapment efficiency; as well by Fourier transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), X-ray powder diffractometry (XRPD), thin layer chromatography (TLC) and scanning electron microscopy (SEM) revealed the crystalline nature of drug in a final state. The *in vitro* release studies were performed in a Phosphate Buffer Solution (PBS) pH 7.4. The best fit release kinetics was achieved with a Higuchi plot. The yields of preparation and entrapment efficiencies were very high with a larger particle size for all the formulations. Mean particle size, entrapment efficiency and production yield were highly influenced by the type of polymer and polymer concentration. It is concluded from the present investigation that various Eudragit are promising controlled release carriers for 5-FU.

Keywords: 5-Fluorouracil, Eudragit RS 100, Eudragit RL 100, Eudragit RSPO, microspheres, controlled release

1. Introduction

5-Fluorouracil (5-FU) is an antimetabolite of the pyrimidine analog class, which is widely used alone or in combination with chemotherapy regimens. It interferes with nucleic acid synthesis, inhibits DNA synthesis, and eventually inhibits cell growth (1). It has been the only agent with clinical activity against colorectal cancer. It is also used for malignancies, such as those of the breast, head and neck (1). 5-FU is poorly absorbed after oral administration with extremely variable bioavailability (2). These disadvantages make it an appropriate candidate for microencapsulation. Microspheres are one of the multiparticulate delivery systems and are prepared to obtain 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 site effects, decreasing dosing frequency and improving patient compliance (3). Eudragit polymers are a series of acrylate and methacrylate polymers available in different ionic forms. Eudragit RL, Eudragit RS and Eudragit RSPO are insoluble in aqueous media, but they are permeable and have pH-independent release profiles. The permeability of all the tree polymers in aqueous media is due to the presence of quarternary ammonium groups in their structure; Eudragit RL has a greater proportion of these groups and as such is more permeable than Eudragit RS and Eudragit RSPO, while Eudragit RS and Eudragit RSPO have same the permeability due to their structural similarity. They differ in the physical forms where the previous has a granular form and the latter has a powder form. The aim of this study was to prepare Eudragit microspheres containing 5-FU to achieve a controlled drug release profile suitable for peroral administration. The microspheres were prepared by a solvent evaporation technique using Eudragit as a matrix polymer. Liquid paraffin and acetone systems were used for the preparation of microspheres. Magnesium stearate was used as a droplet stabilizer to prevent droplet coalescence in the oil medium and n-hexane was added as a non-solvent to the processing medium to solidify the microspheres (4). Firstly, we investigated formulation variables (polymer type and drug:polymer ratio) to obtain spherical particles. The effects of various Eudragit on the yield of production, particle size distribution,

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Table 1. Formulae for 5-FU loaded Eudragit microspheres

	Polymers (mg)		
Formulation	*RS100*	*RL100*	*RSPO*
S1	200	–	–
S2	400	–	–
S3	600	–	–
S4	800	–	–
S5	1000	–	–
S6	1200	–	–
L1	–	200	–
L2	–	400	–
L3	–	600	–
L4	–	800	–
L5	–	1000	–
L6	–	1200	–
P1	–	–	200
P2	–	–	400
P3	–	–	600
P4	–	–	800
P5	–	–	1000
P6	–	–	1200
SL1	570	30	–
SL2	540	60	–
SL3	510	90	–

encapsulation efficiency, surface properties and 5-FU release rate from microspheres were investigated. The influences of formulation variables on the microsphere properties were examined. The prepared spherical microspheres were evaluated for micromeritic properties and drug content, and also by FTIR, DSC, XRPD, and SEM, as well as for *in vitro* drug release studies (4).

2. Experimental

2.1. *Materials*

Eudragit RS, Eudragit RL and Eudragit RSPO, Rohm Pharma; 5-FU, Biochem; Magnesium sterate, Ottokemi; *n*-hexane, Spectrochem; Liquid paraffin Light, Central Drug House; Acetone, Central Drug House; Petroleum ether, Labort; Toluene, Merck; Other substances used were all of pharmaceutical grade.

2.2. *Preparation of microspheres*

The technique used in preparation of microspheres is a "O/O emulsion solvent evaporation technique". As shown in Table 1, six different formulations of each polymer (Eudragit RS 100, Eudragit RL 100 and Eudragit RSPO) and three formulations of a mixture of Eudragit RS and Eudragit RL with drug (5-FU, 200 mg) were prepared. The polymers were dissolved in 10 ml of acetone separately. Pure 5-FU was dissolved in 1 ml of Di-Methyl Formamide (DMF). Both the solutions were mixed and 40 mg of mg-sterate was dispersed in solution containing polymer and 5-FU. The dispersion was then stirred for 15 min using a magnetic stirrer. The resultant dispersion was then poured into a 500 ml beaker containing the external phase (135 ml liquid paraffin light + 15 ml n-hexane) while stirring, using a three blade mechanical stirrer. Stirring (at 750 rpm) was continued for 9 h until acetone and DMF had evaporated completely. After evaporation of the solvents, the microspheres formed were filtered using Whatman no. 41 filter paper. The residue was washed 4–5 times in 25 ml *n*-hexane followed by 4–5 times in 50 ml petroleum ether (40°C–60°C). Thereafter, the microspheres were dried in a desiccator for 24 h at room temperature. The microspheres were then stored in the desiccator (4).

2.3. *Production yield*

The yield was calculated by dividing the weight of the collected microspheres by the weight of all the non-volatile components used for the preparation of microspheres and expressed in the terms of percentage (5).

$$\text{Percent Yield} = (\text{the amount of microspheres obtained} / \text{the theoretical amount}) * 100$$

2.4. *Particle size distribution analysis*

Formulations of the microspheres were analyzed for particle size by optical microscope. The instrument was calibrated and found that 1 unit of eyepiece micrometer was equal to 7.5 μm. 300 microspheres' sizes were calculated under 10 X magnification (6).

2.5. *Drug entrapment efficiency (DEE)*

About 10 mg, accurately weighed, 5-FU loaded microparticles were dissolved in 100 ml of PBS (pH 7.4) by shaking with magnetic stirrer for 24 h. The solution was filtered through Whatman no. 41 filter paper. An aliquot was assayed spectrophotometrically (UV-1601 Schimadzu Corporation, Japan) for 5-FU at 266 nm. Drug entrapment efficiency was determined by using the following relationship.

$$\% \text{ Entrapment} = (\text{Actual content}/\text{Theoretical content}) * 100$$

2.6. *In vitro drug release study*

The dissolution rate of 5-FU from the microspheres were studied at pH 7.4 using the paddle method (USP XXIII). Accurately weighed microspheres (equivalent to 10 mg of 5-FU) were taken for dissolution studies. The dissolution medium was kept at 37 ± 0.5°C. Aliquots of sample were withdrawn at predetermined intervals of time and analyzed for drug release by measuring the absorbance at 266 nm.

Table 2. Percentage production yield, mean particle size and percentage entrapment efficiency of formulations S1-SL3

Formulations	*% yield**	*Mean Particle Size* (μm)*	*% entrapment Efficiency**
S1	61.65 ± 2.219	516.3 ± 14.816	73.02 ± 2.869
S2	67.01 ± 2.656	531.3 ± 12.1	77.93 ± 3.980
S3	73.27 ± 3.347	554.1 ± 6.669	83.01 ± 3.407
S4	78.63 ± 2.175	575.9 ± 8.586	87.74 ± 2.217
S5	82.33 ± 1.602	722.7 ± 16.344	94.08 ± 1.826
S6	87.92 ± 3.435	734.8 ± 8.454	95.53 ± 1.286
L1	65.35 ± 5.319	374.9 ± 9.714	70.42 ± 1.940
L2	73.30 ± 2.866	420.4 ± 9.141	75.07 ± 1.603
L3	76.49 ± 4.178	427.2 ± 8.154	83.76 ± 2.157
L4	81.43 ± 2.920	479.4 ± 11.704	84.72 ± 3.904
L5	87.60 ± 2.086	488.6 ± 9.297	86.00 ± 5.001
L6	90.63 ± 2.728	514.3 ± 9.362	91.47 ± 0.997
P1	61.24 ± 3.273	347.5 ± 10.00	62.91 ± 2.516
P2	64.87 ± 2.269	366.0 ± 9.670	69.22 ± 3.319
P3	69.45 ± 4.227	380.4 ± 18.867	74.51 ± 2.966
P4	74.84 ± 2.742	391.9 ± 6.978	80.39 ± 2.993
P5	77.80 ± 4.576	401.2 ± 7.948	86.53 ± 2.152
P6	82.75 ± 2.638	434.4 ± 4.276	90.12 ± 3.350
SL1	81.98 ± 10.906	787.9 ± 28.443	85.00 ± 7.618
SL2	78.48 ± 8.2	821.6 ± 11.421	72.42 ± 11.078
SL3	78.26 ± 2.632	938.0 ± 14.724	66.44 ± 19.596

*Indicates average of three readings ± SD.

The volume withdrawn at each time intervals was replaced with the same amount of fresh dissolution medium.

2.7. *Release kinetics*

Data obtained from *in vitro* release studies were fitted to various kinetics equations to discover the mechanism of drug release from microspheres. The kinetic models used were Zero order, First order, Higuchi and Korsemeyer-Peppas models. The rate constants were also calculated for the respective models (4).

2.8. *FTIR study*

Drug-polymer interactions were studied by FTIR spectroscopy. IR spectra for drug and drug loaded Eudragit microspheres were recorded in a Fourier transform infrared (FTIR) spectrophotometer (FTIR-8400 S, Shimadzu, Japan) with KBr pellets. The scanning range was 40–4000 cm^{-1}.

2.9. *Differential scanning calorimetry*

DSC scans of about 10 mg, accurately weighed 5-FU and drug loaded Eudragit RS microspheres were performed by using an automatic thermal analyzer system (DSC 60,

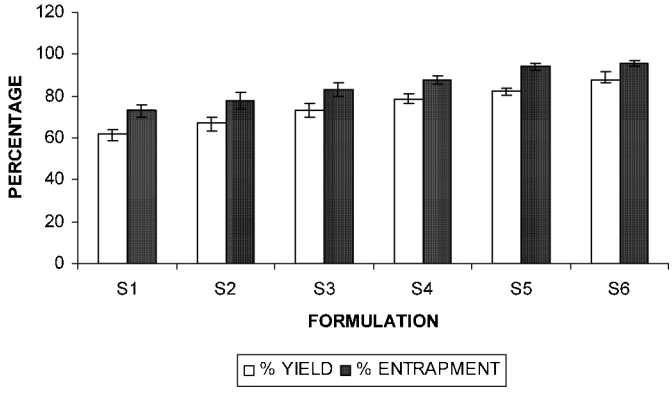

Fig. 1. Yield of preparation and encapsulation efficiency data (n = 3) of formulations S1–S6.

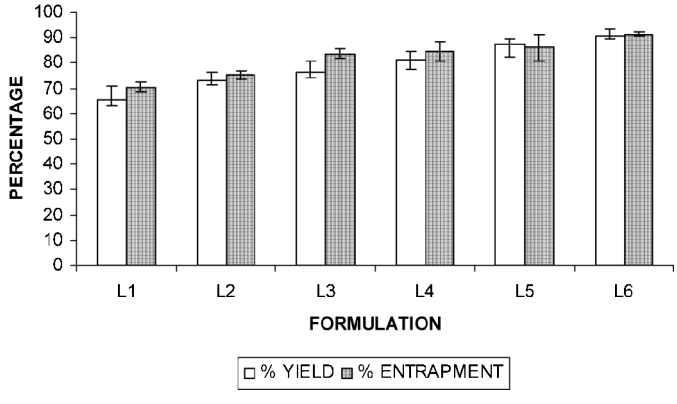

Fig. 2. Yield of preparation and encapsulation efficiency data (n = 3) of formulations L1–L6.

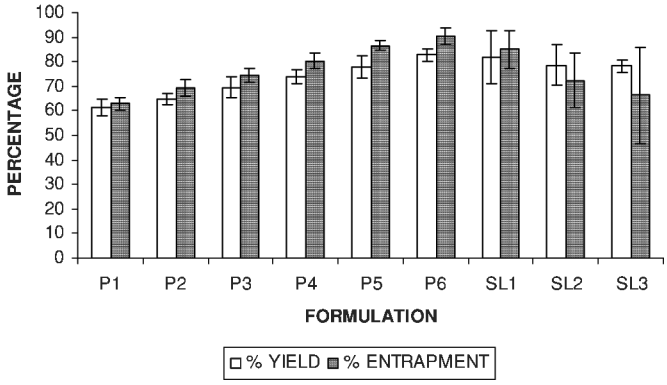

Fig. 3. Yield of preparation and encapsulation efficiency data (n = 3) of formulations P1–SL3.

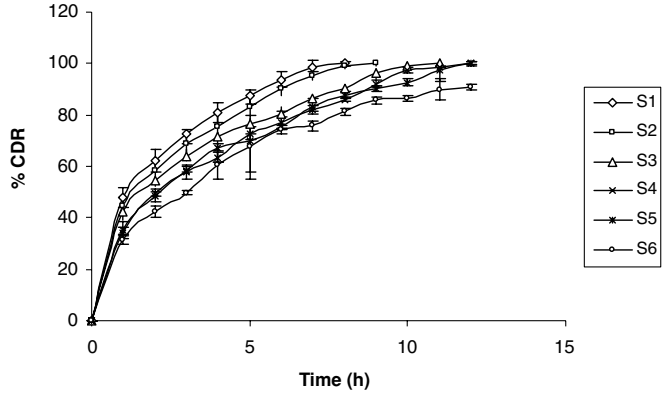

Fig. 4. *In Vitro* release profile of 5-FU (n = 3) from S1, S2, S3, S4, S5 and S6 formulations.

Shimadzu, Japan) with TDS tread line software. Sealed aluminum-lead pans were used in the experiments for all the samples. All the samples were run at a scanning rate of 10°C/min from 50–350°C.

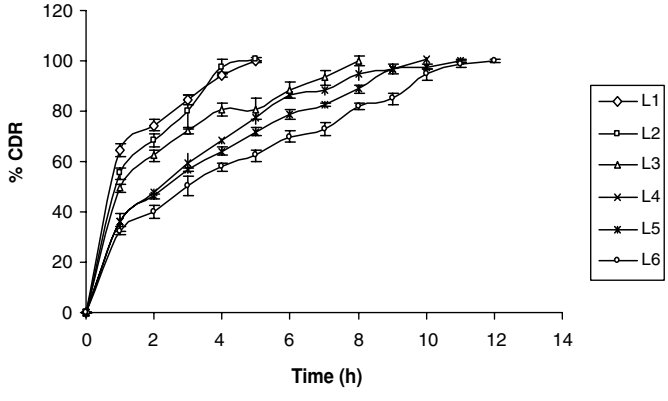

Fig. 5. *In vitro* release profile of 5-FU (n = 3) from L1, L2, L3, L4, L5 and L6 formulations.

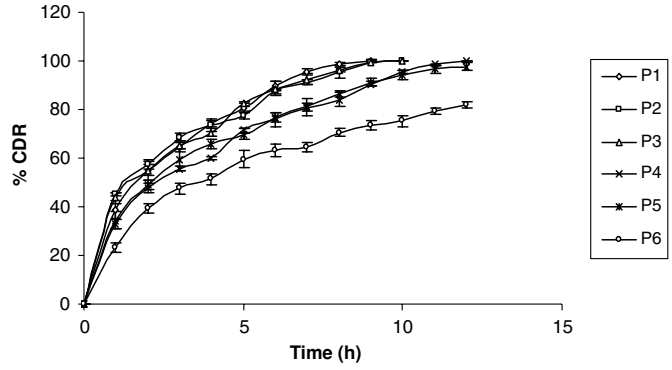

Fig. 6. *In vitro* release profile of 5-FU (n = 3) from P1, P2, P3, P4, P5 and P6 formulations.

2.10. *X-ray powder diffractometry (XRRD)*

The powder X-ray diffraction study was carried out to characterize the polymorphic forms of 5-Fluorouracil and 5-Fluorouracil loaded Eudragit RS microspheres. A Philips X'Pert PW 3040/60 (Almelo, Netherlands) was used as a X-ray generator for Cu Kα radiation ($\lambda = 1.54178$ Å). Data was collected in the continuous scan mode using step size of 0.01° 2θ. The scanned range was 5–50°.

2.11. *Thin layer chromatography (TLC)*

Pure 5-FU and drug loaded microspheres were dissolved in methanol separately and about 10 μg samples were spotted on precoated silica gel G plate. The solvent used was methanol. The plates were developed for at least 10 cm and then air dried. The R_f values were calculated and compared with the monographs (7).

2.12. *Scanning electron microscopy (SEM)*

Scanning electron microscopy was used to examine the surface morphology of microspheres. Dried microspheres were mounted onto stubs by using double-sided adhesive tape.

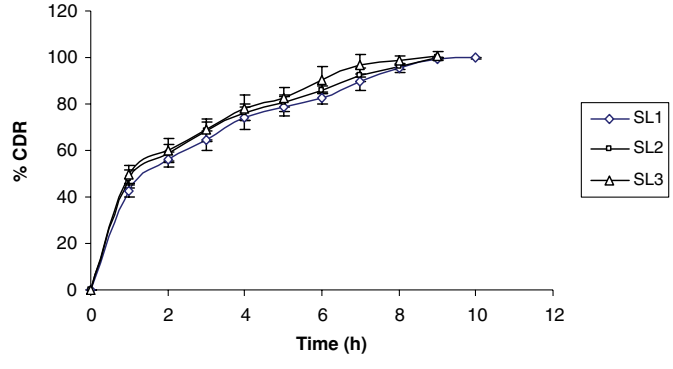

Fig. 7. *In vitro* release profile of 5-FU (n = 3) from SL1, SL2 and SL3 formulations.

Table 3. Correlation coefficients of different mathematical models for 5-FU microspheres

		Zero order	*First order*	*Higuchi*	*Korsemeyer Peppas*	
Sl.	*Formulations*	R^2	R^2	R^2	*n*	R^2
01	S1	0.8131	0.9120	0.9904	0.3634	0.9974
12	S2	0.8299	0.9117	0.9904	0.3813	0.9969
03	S3	0.829	0.8986	0.9952	0.3642	0.9986
04	S4	0.8692	0.9002	0.9936	0.4289	0.9954
05	S5	0.8573	0.9468	0.9915	0.4152	0.9955
06	S6	0.8597	0.9928	0.9817	0.4430	0.9904
07	L1	0.9899	0.9649	0.9936	0.2776	0.9848
08	L2	0.9724	0.8994	0.9908	0.3893	0.9770
09	L3	0.9535	0.9143	0.9918	0.3267	0.9906
10	L4	0.9461	0.9708	0.9883	0.4628	0.9935
11	L5	0.9677	0.9158	0.9956	0.4470	0.9968
12	L6	0.9288	0.8016	0.9903	0.4752	0.9888
13	P1	0.8641	0.9194	0.9895	0.4399	0.9951
14	P2	0.8138	0.8499	0.9894	0.3540	0.9949
15	P3	0.8205	0.8484	0.9937	0.3826	0.9915
16	P4	0.8852	0.8955	0.9938	0.4488	0.9950
17	P5	0.8529	0.9689	0.9886	0.4182	0.9935
18	P6	0.8634	0.9801	0.9905	0.4725	0.9752
19	SL1	0.8349	0.8266	0.9953	0.3780	0.9968
20	SL2	0.8107	0.9641	0.9975	0.3399	0.9978
21	SL3	0.8167	0.9301	0.9958	0.3383	0.9938

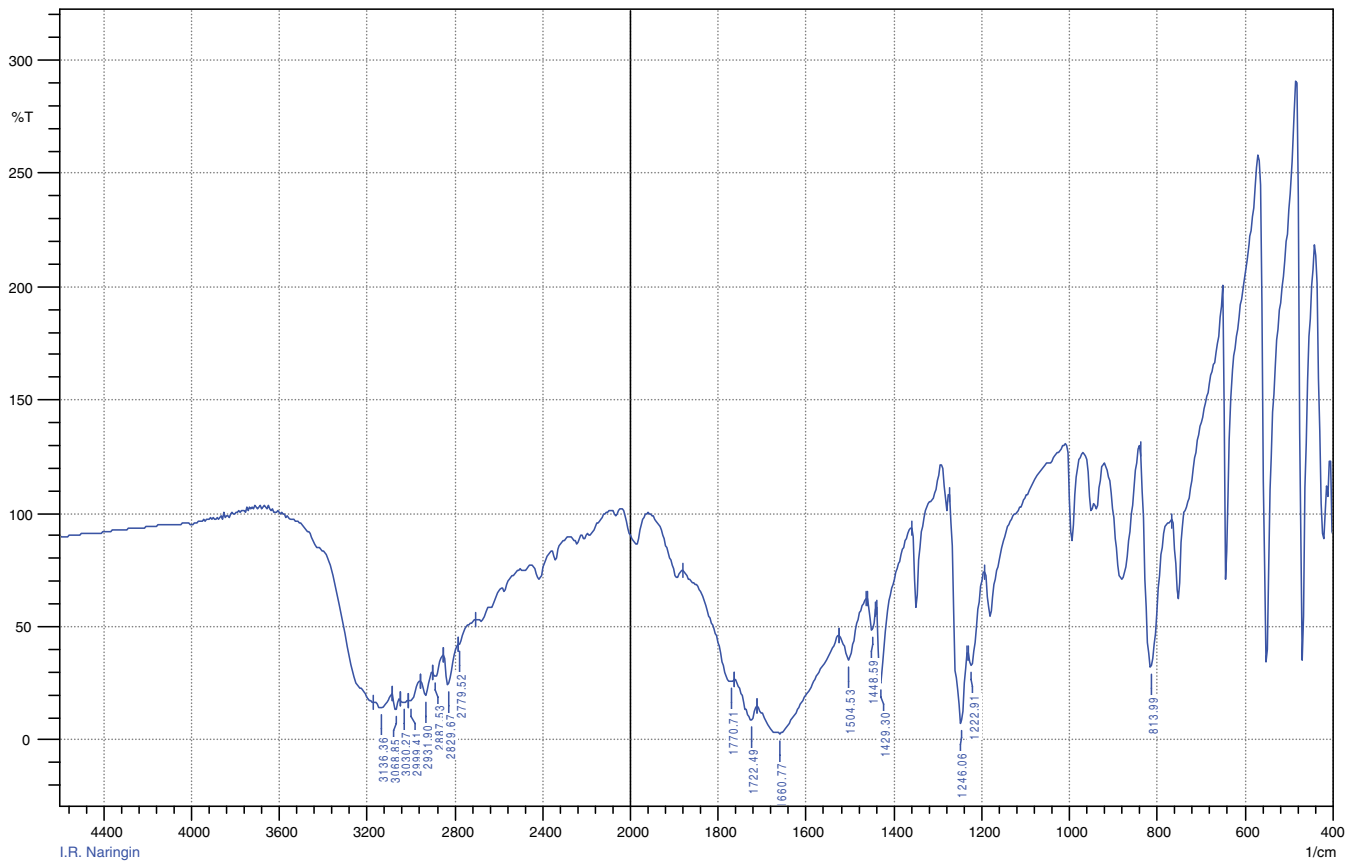

Fig. 8. FTIR spectra of pure 5-FU.

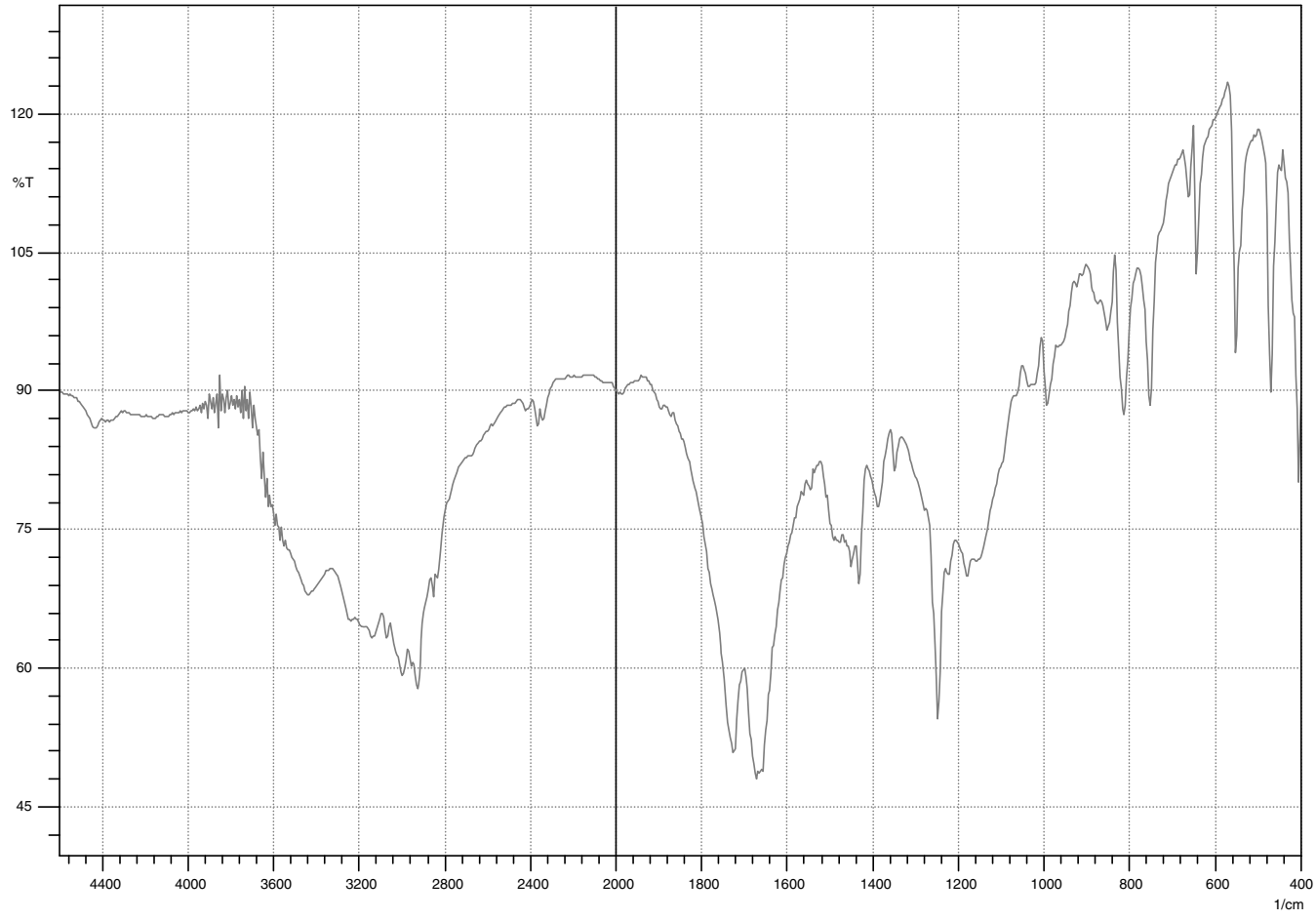

Fig. 9. FTIR spectra of formulation S5.

The microspheres were coated with gold and observed under a scanning electron microscope (Joel, JSM-5600 LV, Japan) for surface characteristics.

3. Results and discussion

3.1. *Mean particle size*

In the present work, the microspheres of Eudrgit RS, Eudrgit RL and Eudragit RSPO were prepared by a "O/O-emulsification solvent evaporation" technique using acetone/liquid paraffin system. The drug was dissolved in 1 ml DMF and polymers (Eudragit RS, RL and RSPO) were dissolved in acetone separately, then 40 mg Mg-stearate was dispersed into it. It was then dispersed into the external phase containing 135 ml light liquid paraffin and 15 ml n-hexane. The effects of parameters like the type of polymer and polymer concentration on the production yield, entrapment efficiency, particle size distribution, *in vitro* drug release, surface characteristics and drug polymer interaction were studied. As shown in Table 2, the mean particle size of the formulations of Eudragit RS (S1-S6) found in the range of 516.3 ± 14.816 μm to 734.8 ± 8.454 μm, for Eudragit RL, it was in the range of 374.9 ± 9.714 μm to 514.3 ± 9.362 μm, for Eudragit RSPO it was in the range of 347.5 ± 10.00 μm to 434.4 ± 4.276 μm and for Eudragit RS and RL combination the range was 787.9 ± 28.443 μm to 938.0 ± 14.724 μm. The mean particle size was found to be increased with the concentration of polymer in this method also. The formulations of combinations of Eudragit RS and Eudragit RL (SL1-SL3) showed an extreme increase in mean particle size as compared to Eudragit RS and Eudragit RL alone and it showed a lack of sphericity.

The data revealed that particle size was highly influenced by the type of polymer and polymer concentration (3,8,9,10,11).

3.2. *Production yield*

The production yields obtained were very high for all the formulations. As shown in Table 2 and Figures 1, 2 and 3, the % yield of the formulations of Eudragit RS (S1-S6) found in the range of $61.65 \pm 2.219\%$ to $87.92 \pm 3.435\%$, for Eudragit RL, it was in the range of $65.35 \pm 5.319\%$ to $90.63 \pm 2.728\%$, for Eudragit RSPO, it was in the range of

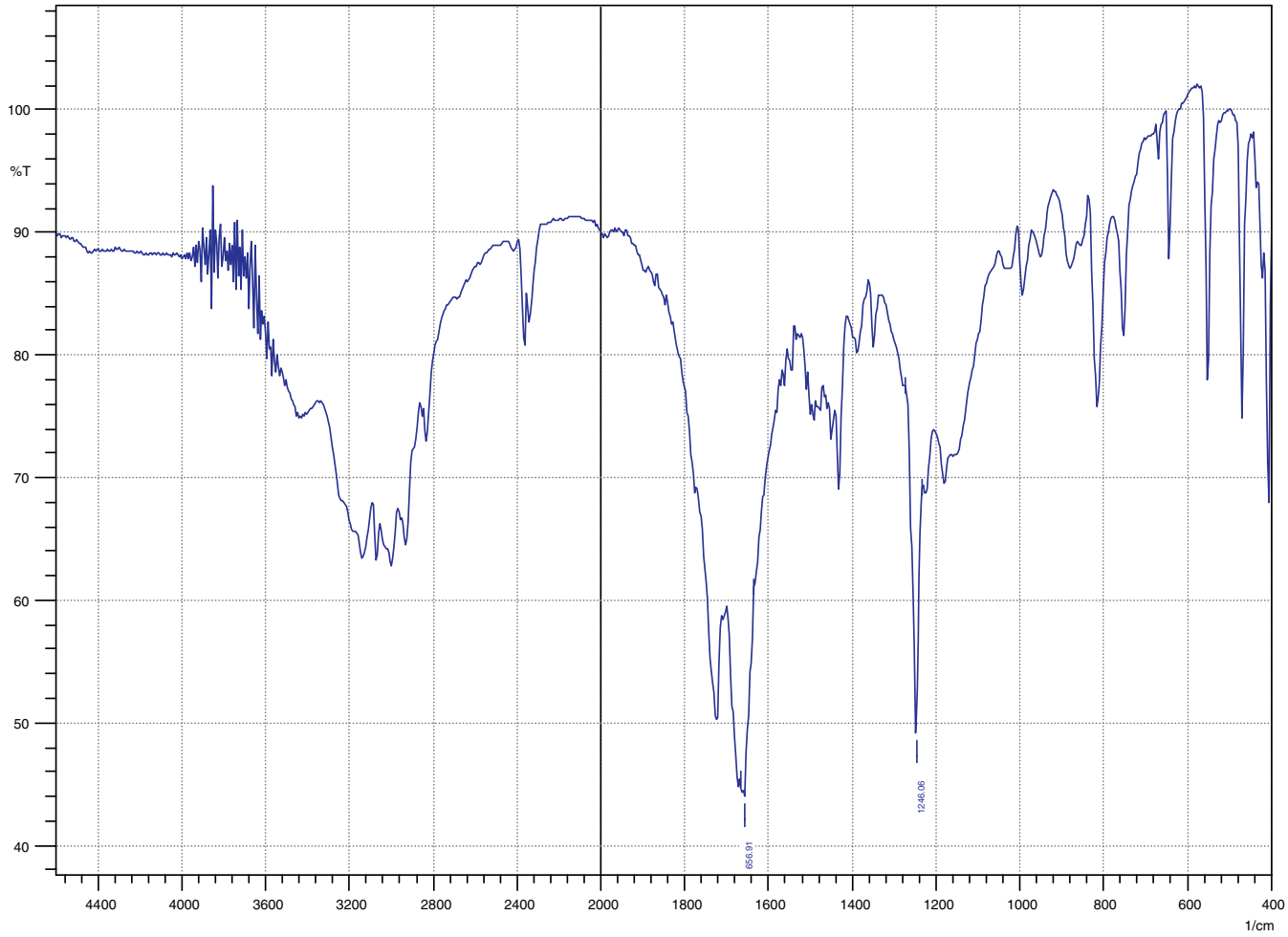

Fig. 10. FTIR spectra of formulation L6.

61.24 ± 3.273% to 82.75 ± 2.638% and for Eudragit RS 100 and RL 100 combination, the range was 81.98 ± 10.906% to78.26 ± 2.632%. The % yield was found to be increased with the concentration of polymer. The formulations of combinations of Eudragit RS and Eudragit RL (SL1-SL3) did not show any influence on % yield of the formulation.

3.3. *Entrapment efficiency*

As shown in Table 2 and Figures 1, 2 and 3, high entrapment efficiency of the drug was obtained for all Eudragit formulations. The % entrapment efficiency of the formulations of Eudragit RS (S1-S6) found in the range of 73.02 ± 2.869% to 95.53 ± 1.286%, for Eudragit RL, it was in the range of 70.42 ± 1.940% to 91.47 ± 0.997%, for Eudragit RSPO, it was in the range of 62.91 ± 2.516% to 90.12 ± 3.350% and for Eudragit RS and RL combination, the range was 66.44 ± 19.596% to 85.00 ± 7.618%.

The data revealed that entrapment efficiency was highly influenced by the type of polymer, solvent used to dissolve the drug and polymer, polymer concentration, and method use to prepare the microspheres (3,8,9,10,11).

3.4. *In vitro release study*

In vitro release studies of the formulations of Eudragit were carried out in the PBS (pH 7.4) at 37 ± 0.5°C. As shown in Figures 4, 5, 6 and 7, the initial higher release of 5-FU from all the formulations might have resulted from the dissolution of the drug crystals presented on the surface of the microspheres (11).

The formulations of Eudragit RS, S1, S2 and S3 showed the complete drug release after 8, 9 and 11 h, respectively. Formulation S4 and S5 showed the complete release in 12 h, while formulation S6 failed to release completely in 12 h, though both the formulations S4 and S5 showed complete and sustained release in 12 h. S5 was considered as the optimized formulation for Eudragit RS 100 because of higher entrapment and a higher yield as compared to S4. The formulations of Eudragit RL, L1, L2, L3, L4 and L5 were not able to sustain the drug release for 12 h and completely released after 5, 5, 8, 10 and 11 h, respectively. Formulation L6 was the only formulation able to sustain the drug for 12 h which is desired. So L6 was considered as the optimized formulation for Eudragit RL 100. Release rates of 5-FU from Eudragit RL were faster than that from Eudragit RS

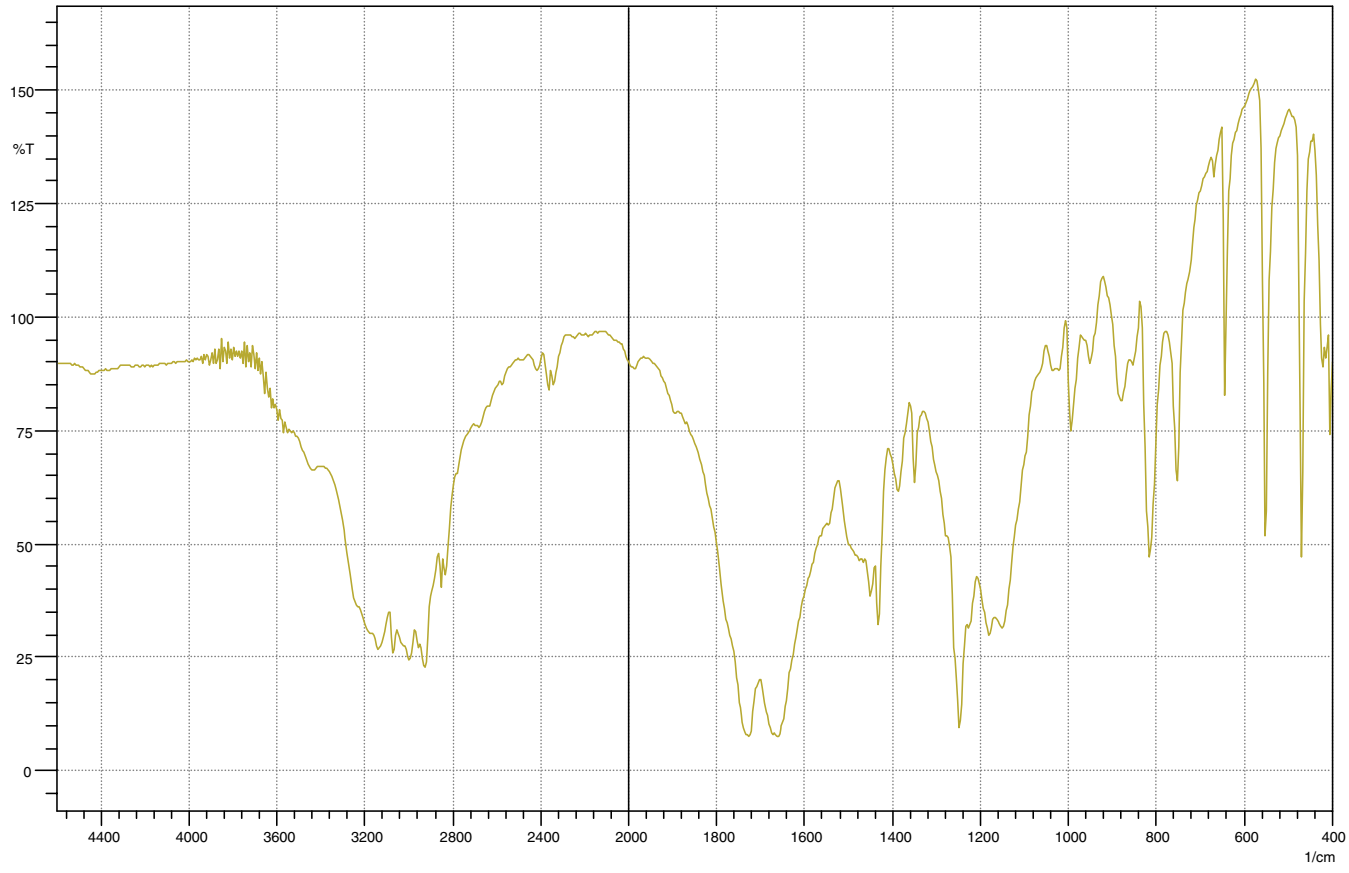

Fig. 11. FTIR spectra of formulation P5.

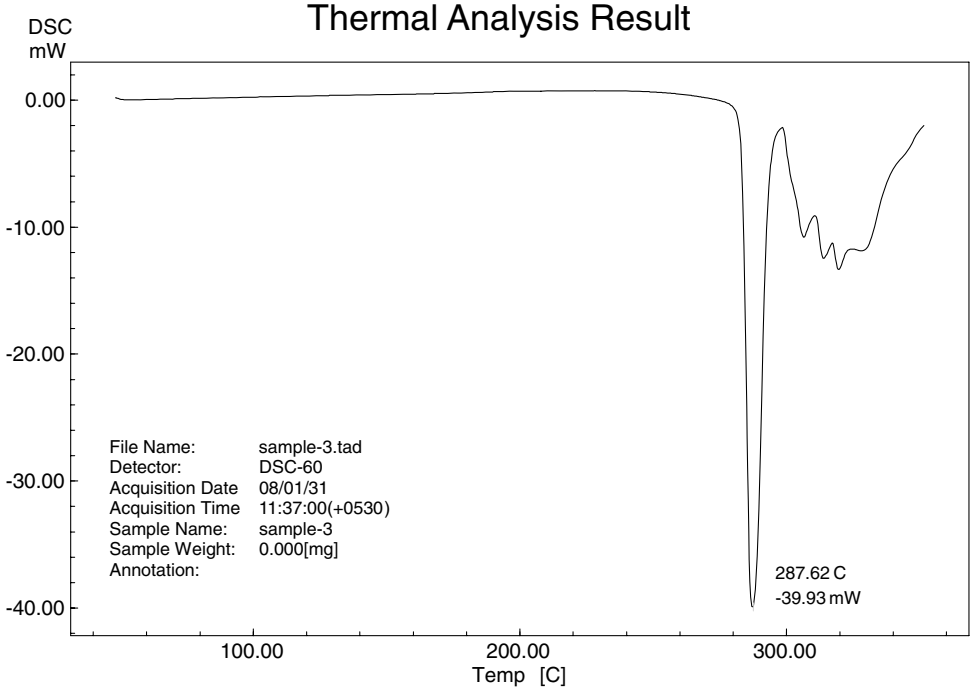

Fig. 12. DSC thermogram of pure 5-FU.

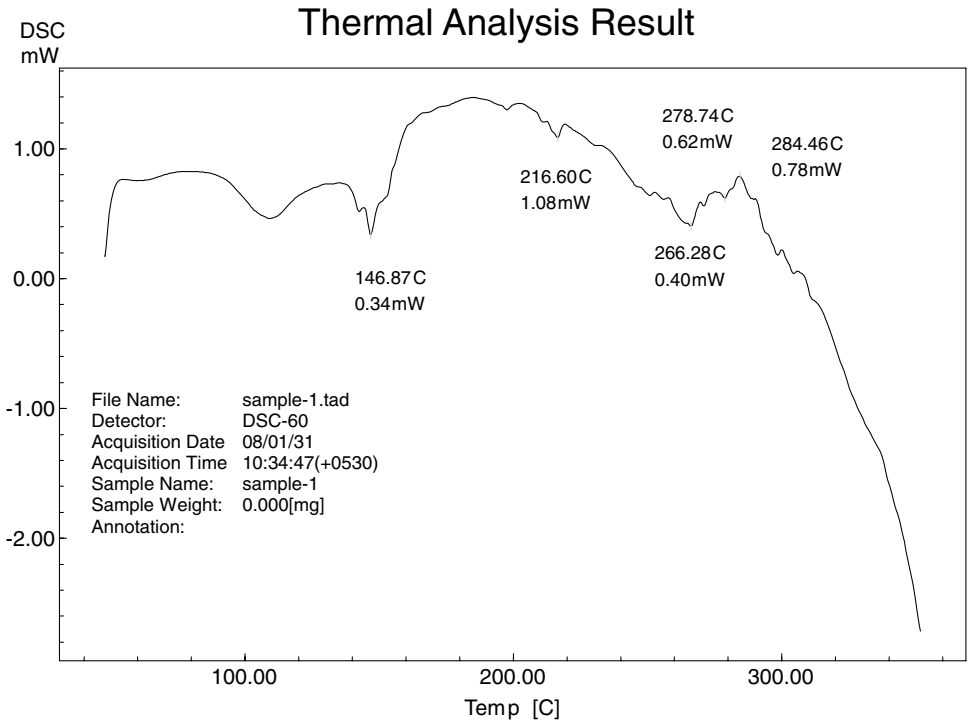

Fig. 13. DSC thermogram of formulation S5.

due to the fact that the amount of quarternary ammonium groups of Eudragit RS is lower than that of Eudragit RL. Therefore, Eudragit RL is more permeable to water, so that release was less retarded (3). The formulations of Eudragit RSPO, P1, P2 and P3 were not able to sustain the drug release for 12 h and completely released after 9, 9 and 10 h, respectively. Formulation P4 showed the complete release after 12 h, while formulation P5 showed $97.62 \pm 1.434\%$ release and formulation P6 failed to release the drug completely at 12 h, and the drug released only was about 82%.

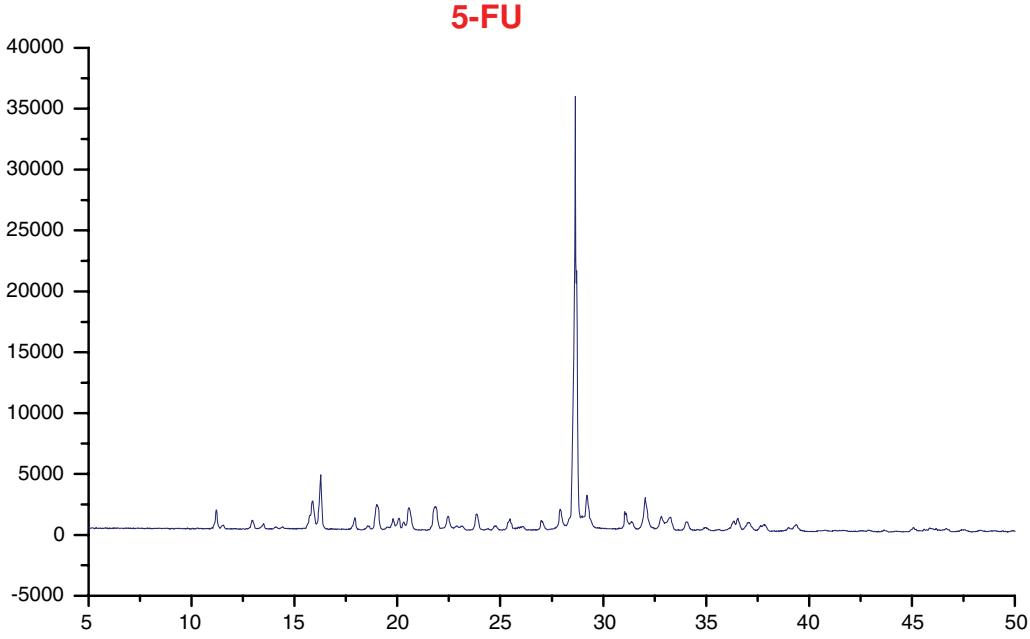

Fig. 14. X-ray powder diffraction pattern of pure 5-FU.

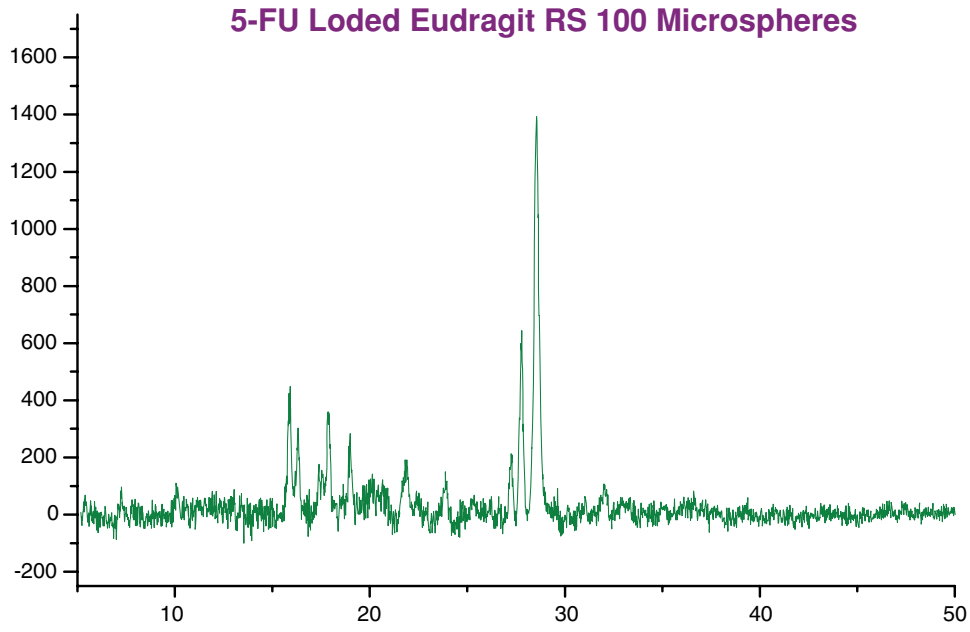

Fig. 15. X-ray powder diffraction pattern of formulation S5.

The release of Eudragit RSPO microspheres was nearly the same as that of Eudragit RS due to the same characteristics of both polymers. As formulation P5 showed, there is a somewhat smaller release after 12 h, as compared to P4 it was selected as an optimized formulation for Eudragit RSPO due to high entrapment and yield. For the formulations of Eudragit RS and Eudragit RL, both the polymers were used, SL1 having Drug:Eudragit RS:Eudragit RL ratio 1:2.85:0.15 showed complete drug release after 10 h, as shown in Table 7 the release was increased as the amount of Eudragit RL was increased in the formulation SL2 having Drug:Eudragit RS 100:Eudragit RL 100 ratio 1:2.7:0.3 showed the complete release after 9 h, for the formulation SL3 (Drug:Eudragit RS:Eudragit RL ratio 1:2.55:0.45) the drug was completely released after 9 h, the release was always higher than the formulation SL2 for every hour.

It revealed that while increasing the amount of Eudragit RL in combination, the release rate was increased due to the same result as described above.

The dissolution data revealed that for all the formulations as the polymer concentration increased, the drug release rate decreased dramatically, depending on the drug-polymer ratio (9).

Table 4. IR Spectral Assignments for 5-Fluorouracil

Characteristic of	*Frequency (cm^{-1})*
NH stretch	3124
C=O stretch	1716 and 1657
CH in plane deformation	1245
CH out of plane deformation	813

3.5. *Release kinetics*

The release kinetics of all the formulations were checked by fitting the release data to various kinetic models, and the release was best fitted to the Higuchi model. It was further confirmed by fitting the data to the Korsmeyer-Peppas equation and the n value for all the formulations obtained between 0.2776 and 0.5082, and this revealed that the release followed the square root of time mechanism (1). The R^2 values for all the models are shown in Table 3.

3.6. *FTIR spectroscopy*

Drug polymer interaction was checked by the IR spectrum of the optimized formulations with the IR spectrum of pure drug.

The IR spectrum of pure drug shows the characteristic peaks at 3124 cm^{-1} for NH stretching, 1716 cm^{-1} and 1657 cm^{-1} for C=O stretching, 1245 cm^{-1} for CH in-plane deformation and 813 cm^{-1} for CH out-of-plane deformation. They were checked in the IR spectrum of optimized

Table 5. Thin layer chromatography of 5-FU, formulations S5, L6 and P5

	R_f Values			
Sample	*5-FU*	*S5*	*L6*	*P5*
1	0.8	0.79	0.78	0.79
2	0.8	0.78	0.79	0.77
3	0.79	0.8	0.81	0.8
Mean	0.7967	0.79	0.7933	0.7867
SD	0.0058	0.01	0.0153	0.0153

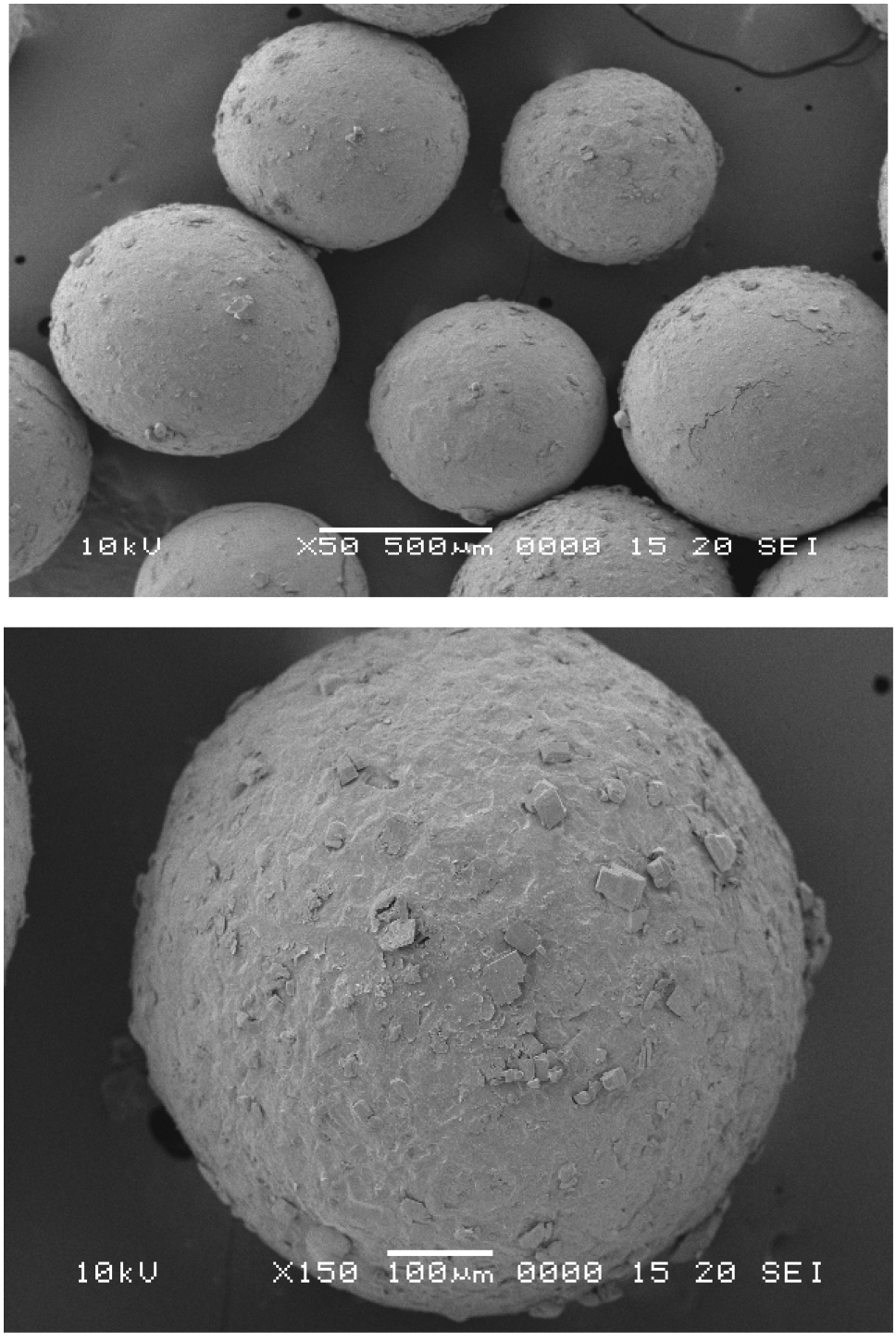

Fig. 16. Scanning Electron Microscopy of formulation S5.

formulations. As shown in Figures 8, 9, 10, and 11, there was no significant difference in the IR spectra of pure 5-FU and drug loaded Formulation S5, L6, and P5.

The results suggested drug stability during the encapsulation process. This was further supported by DSC results (4).

3.7. *DSC study*

DSC is very useful in the investigation of thermal properties of the microspheres, providing both qualitative and quantitative information about the physicochemical state of drug inside the microspheres (1). Drug may have been dispersed in the crystalline or amorphous form or

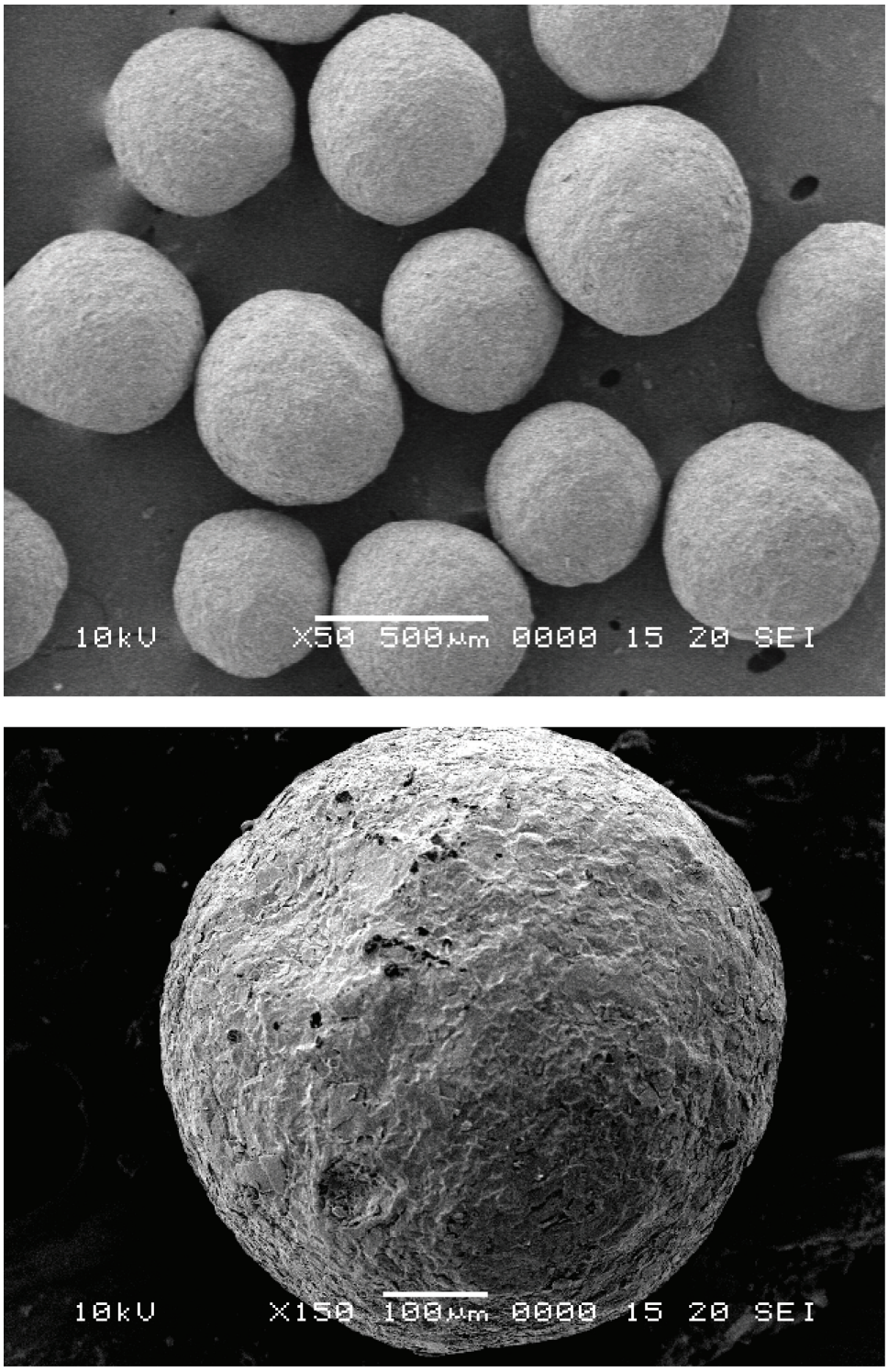

Fig. 17. Scanning Electron Microscopy of formulation L6.

dissolved in the polymer matrix during formation of the microspheres. There is no detectable endotherm if the drug is present in a molecular dispersion or solid solution state in the polymeric microspheres loaded with drug (1).

In the present investigation, DSC thermograms of pure drug, drug loaded microspheres of formulations S5 were taken. As shown in Figure 12, the thermogram of pure 5-FU shows melting endotherm at 287.62°C, which corresponds to its melting point.

Drug loaded Eudragit RS 100 microspheres (Formulation S5) showed a broad small peak at 278.74°C as shown in Figure 13, indicating the presence of drug in crystalline form.

The reduction of height and sharpness of the endotherm peak is due to the presence of polymer in the microspheres.

3.8. *X-ray powder diffractometry (X-RPD)*

The X-ray powder diffraction patterns of pure 5-FU (Fig. 14), 5-FU loaded Eudragit RS 100 microspheres (Fig. 15) were taken. The sharp peaks of drug were also present in the microspheres. The sharpness of the peaks in the formulations also revealed the presence of the drug in crystalline form (12).

3.9. *SEM*

Scanning electron microscopy of the formulations S5 and L6 were carried out. For the formulation S5 (Fig. 16) and formulation L6 (Fig. 17), it showed the spherical shape of the microspheres with a rough surface. The rough surface was due to the presence of the drug crystals on the surface (1).

3.10. *TLC study*

TLC of pure drug and that of formulations were carried out using methanol as solvent system on precoated silica gel plate. Iodine vapor was used for detection of spots. The R_f values for pure drug and the formulations are reported in Table 5. The results showed there was no detectable change in R_f values of formulations compared to pure drug which revealed no drug-polymer interaction.

4. Conclusions

5-FU microspheres were prepared easily and successfully using the solvent evaporation method. The yield and entrapment efficiency was high for all the formulations prepared. Particle size, entrapment efficiency and production yield were highly influenced by the type of polymer and polymer concentration. *In vitro* dissolution of optimized formulations of various Eudragit, S5, L6 and P5 in PBS (pH 7.4) they have the potential to target 5-FU in the colon. The drug targeting to colon can further be increased by coating the microspheres with pH dependent Eudrgit P-4135 F. According to the results of FTIR, TLC, DSC and XRPD analysis, no drug interaction occurred with polymer and 5-FU was recrystallized upon solvent evaporation and was found to be in crystal form in the microspheres.

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