ABSTRACT

Objective: The attempt of the present study was to improve bioavailability and dissolution rate along with reduction in dosing frequency of Zidovudine from microspheres.

Methods: In this study an effort was taken to devise and evaluate Zidovudine sustained release microspheres using different polymers such as Ethyl cellulose (EC), Eudragit RS100, Hydroxypropyl methylcellulose (Methocel K4M and Methocel K15M) by emulsion solvent evaporation method. UV-Spectrophotometric method was applied to calculate the drug content and in vitro dissolution studied according to USP paddle method were carried out in Phosphate Buffer (pH 7.4) for 8 hours. Scanning electron microscopic (SEM) technique was performed to obtain the particle size and morphological changes due to different polymers. Drug polymer compatibility studies were performed by Fourier Transform Infrared (FTIR) spectroscopy, Differential Scanning Calorimetry (DSC) and X-ray Powder Diffractometry (XRD).

Results: The maximum and minimum releases of microspheres were observed 93.12% and 75.07% respectively after 8 hours. Drug entrapment efficiency for formulations varied from 56.21% to 94.14%. The release kinetics were studied in different mathematical release models following the zero order, first order, Higuchi, Hixon-Crowel and Korsemeyer to find out the linear relationship and release rate of drug. In this experiment, it is difficult to explain the exact mechanism of drug release. The drug might be released by both diffusion and erosion as the correlation coefficient (R²) best fitted with Korsemeyer model. No interaction between drug and polymers were observed from FTIR, DSC and XRD studies.

Conclusion: In vitro study and different compatibility evaluation of Zidovudine from microspheres was showed that optimum release profiles may be obtained compared to pure drug.

Keywords: Zidovudine, Microspheres, Emulsion solvent evaporation method, Korsemeyer model.

INTRODUCTION

Zidovudine (Zidovudine, AZT) is extensively used for the management of Acquired Immuno Deficiency Syndromes (AIDS) and related conditions, either alone or in combination with other antiviral agents. The azido group increases the lipophilic nature of AZT, allowing it to cross infected cell membranes easily by diffusion and thereby also to cross the blood brain barrier. Cellular enzymes alter AZT into the effective 5'-triphosphate form. Studies have proven that the termination of HIV's forming DNA chains is the specific factor in the inhibitory effect. This virustatic drug has low oral bioavailability (60%) due to substantial first-pass metabolism, thus requiring frequent administration of large doses (200 mg every 4-6 h) to continue therapeutic drug level. Thus the short half-life of 1 h and frequent dosing of large doses due to low oral bioavailability makes AZT a good candidate for microencapsulation. Microencapsulation of AZT provides the prolonged release of a single dose, thereby minimizing the frequent administration and hence total dose required to elicit pharmacological activity, thereby reducing the side effects [1]. Microspheres are defined as homogeneous, monolithic particles in the size range of about 0.1-1000 μm and are generally used as drug carriers for sustained release. These systems have considerable importance in biomedical applications. Microspheres can be produced for protection of core material, reduction of gastric irritation, and decrease in volatility, conversion of liquid to pseudo-solid, cell microencapsulation, and designing of pulsatile drug delivery systems. Administration of the drug in the form of microspheres usually improves the treatment by providing the localization of the active substances at the site of action and by prolonging release of drugs. This technology is generally used for the reason of protection, controlled release, and incompatibility of the core materials [2].
Acrylic polymers are widely used as tablet coatings and as retardants of drug release in sustained release formulations. Methacrylate copolymers (Eudragits) have recently received increased attention for modified dosage forms because of their inertness, solubility in relatively non-toxic solvents and availability of resins with different properties. Eudragits are insoluble in water and digestive juices, but they are permeable and both have pH-independent release profiles. The permeability of Eudragit RS and RL in aqueous media is due to the presence of quaternary ammonium groups in their structure; Eudragit RL has a greater proportion of these groups and as such is more permeable than Eudragit RS [8-9]. The main goal of drug delivery systems is to achieve desired concentration of the drug in blood or tissue, which is therapeutically effective and non toxic for a prolonged period. The oral controlled release micro particulate drug delivery system of AZT underlying principle of the present work was to prepare and evaluate the proportion of these groups and as such is more permeable than RL in aqueous media is due to the presence of quaternary and digestive juices, but they are permeable and both have pH - of resins with different properties. Eudragits are insoluble in water using different polymers by water-in-oil emulsion solvent diffusion method with high entrapment capacity and extended release. Drug polymer interactions in the solid state were studied by differential scanning calorimetry (DSC) and Fourier Transform Infrared (FTIR) spectroscopy was performed to detect the functional group of pure drug and polymer. The surface characteristics were evaluated by scanning electron microscopy (SEM).

**MATERIALS AND METHODS**

**Materials:** Zidovudine as an endowment sample from Beximco Pharmaceutical limited, Bangladesh, Ethyl Cellulose (Colorcon Asia Pvt. Limited, India), Eudragit RS100 (Evonik, Germany), Methocel K4M (Colorcon Asia Pte. Limited, India), Methocel K15M (Colorcon Asia Pte. Limited, India), Acetonitrile (Merck, Germany), Acetone (Merck, Germany), Light liquid paraffin (Merck, Germany), cyclohexane (Merck, Germany), Span 80 (Merck, Germany), Sodium hydroxide (Merck, Germany), Potassium dihydrogen phosphate (Merck, Germany), distilled water etc.

**Methods**

**Preparation of Zidovudine microspheres by emulsion solvent evaporation technique**

The preparation of microspheres by solvent evaporation method was initiated from dispersion of Zidovudine in 70 ml of light liquid paraffin (LLP) using 1% span 80. At first, LLP was emulsified in a plastic beaker with Span 80 for few minutes with the help of stirrer at 500-1500 rpm. By this time the polymer solution (internal phase) was prepared by dissolving properly weighed polymer(s) in combination of acetonitrile and acetone at a ratio of 5:5 in a volumetric flask. Then appropriately weighed Zidovudine was added in the internal phase slowly and stirrer for 20-30 minutes. After proper mixing prepared polymeric phase was added drop wise to the external phase. Stirring was performed for 2.5 hours. After stirring, the microspheres were decanted and washed by n-haxen and allowed for drying in natural air. The microspheres transferred to glass vials and placed in the desicators for further analysis.

**Table 1: Formulation of designed sustained release microspheres of Zidovudine with different polymers by emulsion solvent evaporation method**

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Polymer concentration (gm)</th>
<th>D: P Ratio</th>
<th>Actual drug loading (%)</th>
<th>Drug entrapment efficiency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ethyl cellulose</td>
<td>Eudragit RS100</td>
<td>Methocel K4M</td>
<td>Methocel K15M</td>
</tr>
<tr>
<td>A1</td>
<td>-</td>
<td>0.5</td>
<td>0.5</td>
<td>-</td>
</tr>
<tr>
<td>A2</td>
<td>-</td>
<td>2</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>A3</td>
<td>-</td>
<td>4</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>B1</td>
<td>0.5</td>
<td>-</td>
<td>0.5</td>
<td>-</td>
</tr>
<tr>
<td>B2</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>B3</td>
<td>2</td>
<td>4</td>
<td>-</td>
<td>0.5</td>
</tr>
<tr>
<td>C1</td>
<td>-</td>
<td>0.5</td>
<td>-</td>
<td>0.5</td>
</tr>
<tr>
<td>C2</td>
<td>-</td>
<td>2</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>C3</td>
<td>-</td>
<td>4</td>
<td>-</td>
<td>2</td>
</tr>
</tbody>
</table>

**Solubility study:** Solubility of Zidovudine was studied in various pH media which is shown in table 3.

**Estimation of Actual drug loaded and drug entrapment efficiency (DEE)**

At first, approximately 20 mg equivalent amount of zidovudine microspheres was taken in a 100 ml volumetric flask and dissolved and then was sonicated for 20 minutes to make a clear solution. Few ml of phosphate buffer (pH 7.4) was then added to it and again sonicated for 10 minutes. The volume was made up to 100 ml with phosphate buffer. The solution was finally filtered. 10 ml of the above solution was taken (If further dilution is necessary) in another volumetric flask and was made it 100 ml with phosphate buffer. Absorbance value was determined using UV spectrophotometer at a wavelength of 266 nm. Using the absorbance value, the amount of zidovudine entrapped was determined with the help of Standard curve. Using the absorbance value, the amount of zidovudine entrapped was determined with the help of Standard curve that is shown in table 1. % drug entrapment efficiency (DEE) was calculated by using the following equations –

\[
\text{In vitro drug release studies of zidovudine microspheres}
\]

The in vitro dissolution studies were performed up to 8 hours using USP type II dissolution apparatus (VDA-8DR, VEEGO Instruments Corporation, India) at 50 rpm. The dissolution medium consisted of phosphate buffer pH 7.4 (900 mL), maintained at 37 ±0.5°C. An aliquot (10 mL) was withdrawn at specific time intervals and filtered through 0.45 μ (Millipore) filter. After that the samples were analyzed in UV-VIS spectrophotometer at a wavelength of 266 nm and cumulative percentage of the drug released was calculated.

**Kinetic analysis of Drug Release**

To study the mechanism of drug release from the microcapsules, the release data were fitted to zero order, first order and Higuchi equation. Therefore, the dissolution data was fitted to the well known exponential equation (Korsmeyer equation), which was often used to describe the drug release behavior from polymeric system [10-11].

\[
\log(M_t/m_0) = \log K + K \cdot \log t
\]

Where, \( M_t \) is the amount of drug release after infinite time, \( K \) is a release rate constant incorporating structural and geometric characteristics of the mechanism of drug release. To clarify the release exponent batches of microspheres, the log value of percentage drug dissolved was plotted against log time for each batch according to the above equation. A value of \( n > 0.45 \) indicates Fickian (case I) release, \( n > 0.45 \) but \( < 0.89 \) indicates anomalous release and \( n < 0.45 \) indicates super case II type of release.

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release. Case II generally refers to the erosion of the polymeric chain and anomalous transport (non Fickian) refers to a combination of both diffusion and erosion controlled drug release.

**Successive fractional dissolution time**

To characterize the drug release rate in different experimental conditions like \( T_{25ab} \), \( T_{50ab} \) and \( T_{80ab} \) were calculated from dissolution data according to the following equations:

\[
T_{25ab} = \left( \frac{0.25}{k} \right)^\frac{1}{n}
\]

\[
T_{50ab} = \left( \frac{0.50}{k} \right)^\frac{1}{n}
\]

\[
T_{80ab} = \left( \frac{0.80}{k} \right)^\frac{1}{n}
\]

Another fractional tool MDT (Mean dissolution time) can be calculated by the following equation:

\[
MDT = \left( \frac{n}{n + 1} \right)^{\frac{1}{n}}
\]

MDT value is used to characterize the drug release rate from the microspheres and the retarding efficiency of the polymer. A higher value of MDT indicates a higher drug retarding ability of the polymer and vice versa. The MDT value is also considered to be a function of polymer loading, polymer nature and physico-chemical properties of the drug molecule [12].

**Drug-polymer compatibility study by Fourier transforms infrared (FTIR) spectroscopic analysis**

To study the interaction between drug and polymers used in the preparation of formulation, FTIR spectroscopic study was carried out for the test samples. FTIR can provide very useful information about functional group. The FTIR technique is to measure the absorption of various infrared radiations by the target material, to produces an IR spectrum that can be used to identify functional groups and molecular structure in the sample shown in fig 5. FTIR spectrum of pure zidovudine and formulated microspheres were recorded by using FTIR 8400S (SHIMADZU, Japan). Appropriate quantity of KBr and microspheres (in the ratio 100:2) were mixed by grinding in an agate mortar. Disk was made with about 100mg mixture under hydraulic pressure of 600 Kg. Then the FTIR spectra were recorded between 4000 to 400 cm\(^{-1}\). The resolution was 2 cm\(^{-1}\).

**Table 2: Mechanism of transport from interpretation of diffusion exponent**

<table>
<thead>
<tr>
<th>Cylinder</th>
<th>Sphere</th>
<th>Slab</th>
<th>Mechanism of transport</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.45 or 0.45</td>
<td>&lt; 0.43 or 0.43</td>
<td>&lt; 0.5 or 0.5</td>
<td>Fickian (Case I) diffusion</td>
</tr>
<tr>
<td>&gt; 0.45 or &lt; 0.89</td>
<td>&gt; 0.43 and &lt; 0.85</td>
<td>&gt; 0.5 and &lt; 1.0</td>
<td>Anomalous/ non Fickian transport (Erosion and diffusion)</td>
</tr>
<tr>
<td>0.89</td>
<td>0.85</td>
<td>1.0</td>
<td>Case II/Zero order transport</td>
</tr>
<tr>
<td>&gt; 0.89</td>
<td>&gt; 0.85</td>
<td>&gt; 1.0</td>
<td>Super case II transport</td>
</tr>
</tbody>
</table>

**Surface morphology study with the help of scanning electron microscope (SEM)**

Surface nature of microspheres was examined with the help of Scanning Electron Microscope (JEOL, JSM-6490 LA, Japan). The microspheres were dried completely before examination SEM was done at different magnifications of 20 kV X 40, 20 kV X 100, 20 kV X 200, 20 kV X 500 to examine the surface picture and size of the microcapsules that changed from formula to formula shown in fig.6. The working distances were 10 and 11 inches.

**Drug-polymer compatibility study by Differentiate scanning calorimetry (DSC) study of microsphere**

The thermal behavior of the microspheres was investigated using differential scanning calorimeter (DSC 60, Shimadzu, Japan). Samples of about 5 mg were placed in 50 µm perforated aluminium pans and sealed. All samples were run at a heating rate of 10\(^{\circ}\)min over a temperature range of 5–300\(^{\circ}\)C in atmosphere of nitrogen as purging gas at a flow rate of 25 ml/min.

**Particle size measurement**

The size of the microspheres was analyzed by laser particle size analyzer (Malvern Instruments, Mastersizer 2000, Malvern, UK) using distilled water.

The sample was vortexed for 1 minute before sampling. The samples were then sonicated in a sonicator attached to the instrument throughout the process, and the duration of sonication was kept constant for all samples. The obscuration ranged from 0.08% to 3.62%.

**X-ray powder Diffraactometry (XRD)**

X-ray powder diffraction was carried out to investigate the effect of microencapsulation process on crystallinity of drug. Powder XRD patterns were recorded on X -RD (Model no- PW3040 Xpert MPD system) using Philips Analytical X-Ray B. V. The scanning rate employed was 20 min \(^{-1}\), over the 14 to 88 diffraction angle (02θ) range. The XRD patterns of drug, polymer, blank microspheres and the retarding efficiency of the polymer. A higher MDT value is also considered to be a function of polymer loading, polymer nature and physico-chemical properties of the drug molecule [12].

**RESULTS AND DISCUSSION**

**Solubility study in different media**

The solubility of zidovudine in water, 0.1 N HCl, phosphate buffer pH 6.8 and 7.4 was found to be 28.90 mg/ml, 27.36 mg/ml, 21.36 mg/ml and 20.1 mg/ml respectively shown in fig.1. It implies that drug will be better absorbed from the alkaline environment of the intestine. Hence, the dissolution study was carried out in phosphate buffer at pH 7.4.

**Table 3: Solubility of Zidovudine in various pH media**

<table>
<thead>
<tr>
<th>Media</th>
<th>Solubility (mg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Water</td>
<td>28.90</td>
</tr>
<tr>
<td>0.1 N HCl</td>
<td>27.36</td>
</tr>
<tr>
<td>pH 6.8 phosphate buffer</td>
<td>21.36</td>
</tr>
<tr>
<td>pH 7.4 phosphate buffer</td>
<td>20.1</td>
</tr>
</tbody>
</table>

**Actual drug loaded and drug entrapment efficiency (DEE) of prepared microspheres**

Drug loading and the drug entrapment efficiency (DEE) of the prepared microspheres were carried and the results are summarized in table 1 and graphical presentation are given bellow in fig.2. The actual drug loaded and the drug entrapment efficiency were found to be in the range of 10.75% to 1891% and 67.15% to 96.73% respectively.
In vitro drug release study of prepared microspheres

The analysis of the mechanism of drug release from pharmaceutical device is important but complicated. Therefore, several equations have suggested for this purpose. As far as the release from microcapsules is concerned, this problem is practically evident. In fact, it should be kept in mind that cumulative drug kinetics can be altered and only release from an individual microcapsule can provide a valid example of true mechanism. Many describe the release rate process by simply comparing the correlation coefficient values of lines collected from graphical presentation of different mathematical model. The model with highest correlation coefficient is selected.

The in vitro drug release study was performed using paddle type (USP type 2) dissolution apparatus in phosphate buffer (pH 7.4) at 37°C up to 8 hours depending upon the formulation variables. To find out the mechanism of drug release, the controlled release Zidovudine microspheres were treated in different mathematical models like Zero order (cumulative percentage of drug release versus time), First order (log percentage of drug remaining versus time), Higuchi model (cumulative percentage of drug release versus square root of time), Hixon-crowell model (cubic root percentage release versus time), Korsemeyer model (log cumulative percentage of drug release versus log time). The release data was plotted. From the linear portions of the curve slope correlation coefficients (R²) were calculated.

With the Korsemeyer plot, linearity was noted highest in all formulations using all data points. The data yielded apparently straight line with Korsemeyer plot (R² > 0.99) while a bit with Zero order, First order kinetics and Higuchi plot. No linearity was noted with Hixon-crowell kinetics. It is observed that zidovudine released from sustained release microsphere followed Korsemeyer release log cumulative percentage of drug release versus log time. The mechanism of drug release was calculated according to Peppas equation. The calculated "n" values along with the correlation coefficients (R²) have been shown in table 4. The values of n depend upon the polymer concentration. The calculated "n" values suggest that the mechanism of drug release followed non-Fickian transport.

![Fig. 1: Histogram representing solubility of Zidovudine in various pH media](image1)

![Fig. 2: Comparative percent release study of Actual drug loading and drug entrapment efficiency of formulations A1, A2, A3, B1, B2, B3, C1, C2 and C3 respectively](image2)

**Table 4: Rate constant (K) and correlation coefficient (R²) of formulations of prepared microspheres**

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Zero Order</th>
<th>First Order</th>
<th>Higuchi</th>
<th>Hixon-Crowell</th>
<th>Korsemeyer-peppas</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>K₀</td>
<td>R²</td>
<td>K₁</td>
<td>R²</td>
<td>K₉</td>
</tr>
<tr>
<td>A1</td>
<td>9.82</td>
<td>0.951</td>
<td>-0.124</td>
<td>0.991</td>
<td>30.47</td>
</tr>
<tr>
<td>A2</td>
<td>9.68</td>
<td>0.969</td>
<td>-0.118</td>
<td>0.985</td>
<td>28.55</td>
</tr>
<tr>
<td>A3</td>
<td>9.04</td>
<td>0.981</td>
<td>-0.12</td>
<td>0.991</td>
<td>27.62</td>
</tr>
<tr>
<td>B1</td>
<td>8.47</td>
<td>0.966</td>
<td>-0.109</td>
<td>0.929</td>
<td>25.76</td>
</tr>
<tr>
<td>B2</td>
<td>8.65</td>
<td>0.968</td>
<td>-0.103</td>
<td>0.756</td>
<td>25.55</td>
</tr>
<tr>
<td>B3</td>
<td>9.79</td>
<td>0.976</td>
<td>-0.11</td>
<td>0.95</td>
<td>29.77</td>
</tr>
<tr>
<td>C1</td>
<td>10.78</td>
<td>0.974</td>
<td>-0.11</td>
<td>0.976</td>
<td>32.74</td>
</tr>
<tr>
<td>C2</td>
<td>9.28</td>
<td>0.979</td>
<td>-0.119</td>
<td>0.935</td>
<td>25.55</td>
</tr>
<tr>
<td>C3</td>
<td>8.95</td>
<td>0.976</td>
<td>-0.115</td>
<td>0.926</td>
<td>26.66</td>
</tr>
</tbody>
</table>
Formulations A1 to A3 were prepared by using Eudragit RS100. Zidovudine microspheres were prepared by using different polymers. Effect of different polymers on the release of zidovudine from microspheres was evaluated. After the end of 8 hours of dissolution, the release of drug from microspheres was 84.13%, 77.70%, and 75.06% respectively.

Formulations C1 to C3 were prepared by using Eudragit RS100 and Methocel K15M. Hydrophobic nature of these polymers resulted in less permeation of dissolution medium, thereby releasing the drug more slowly. The addition of ethyl cellulose retards the rate of drug release. Good polymer/drug compatibility was observed.

Methocel K4M was used to control the release of drug due to its high water content. The IR Spectra of Zidovudine was recorded, and characteristic peaks of zidovudine were observed in the spectra indicating successful drug incorporation. The mechanism of drug release was diffusion controlled and erosion. Comparative drug percent release of Zidovudine microspheres consisting of different polymers after 8 hours is shown in fig. 3c.

**Successive fractional dissolution time**

To characterize the drug release rate in different experimental conditions, formulations were studied. MDT of formulations A1, A2, and A3 were found to be 4.60 hours, 5.16 hours, and 5.23 hours respectively. MDT of formulations B1, B2, and B3 were found to be 4.78 hours, 4.83 hours, and 4.00 hours respectively. MDT of formulations C1, C2, and C3 were found to be 3.59 hours, 4.39 hours, and 4.75 hours respectively. The n value of formulations was determined, and it was found to be between 0.45-0.83, indicating that the mechanism of the drug release was diffusion controlled.

**Drug polymer compatibility study by Fourier transform infrared (FTIR) spectroscopy**

The drug polymer interaction was studied by FTIR analysis. The FTIR spectrum of zidovudine alone and its combination with polymers showed characteristic peaks. The IR Spectra of Zidovudine was recorded, and characteristic peaks of zidovudine were observed in the spectra indicating successful drug incorporation.

**Effect of polymer concentration on surface morphology of prepared microspheres**

The surface topography of the microspheres was investigated by SEM. As seen in fig. 6, they were spherical in shape and exhibited a porous surface. The SEM of drug-loaded microspheres in fig. 6b had a rough surface due to higher concentrations of drug in the microspheres compared to the blank microspheres in fig. 2a. Surface study of the microspheres after release study showed bigger pores (fig. 2c) suggesting that the drug was released through pores and the mechanism of drug release was diffusion controlled.
Fig. 5: FTIR of A) Pure zidovudine B) formulation A1 C) formulation B2 and D) formulation C3 respectively.
Differentiate scanning calorimetry (DSC) study of microsphere

DSC study of drug loaded microspheres was performed to determine the drug polymers compatibility.

The DSC curves of pure zidovudine, zidovudine loaded different polymers containing microspheres are presented in fig. 7. It was evident from the DSC profile (fig.7a) that zidovudine exhibited a sharp endothermic peak at 124°C, which corresponds to the reported melting temperature of the drug. The same DSC profile (fig. 7b and fig. 7c) of the drug appeared at the temperature corresponding to its melting point in the zidovudine loaded formulation A1 and B3 microspheres but with the loss of its sharp appearance. It appears that there is a significant reduction of drug crystallinity in the microspheres.
Particle size analysis

In the present study, the particle size of selected formulations was determined using a Malvern Mastersizer. It is observed from the Figure 8 that increasing the polymer ratio the mean particle size was increased. When the drug polymer ratio was increased form 1:1 to 1:6, larger particles were formed, because the viscosity of the emulsion medium was increased with increasing amount of polymer. Due to increase in viscosity, larger emulsion droplets were formed which were difficult to break and hence they are precipitated as such leading to increase in mean particle size. It was observed from the investigation that when stirring speed was low (500 rpm), larger spherical microspheres were formed. This may be due to inadequate stirring speed which was not able to break the emulsion droplets. Stirring speed above 1500 rpm resulted in formation of spherical small microspheres, which may be due to higher degree of emulsification of the polymeric phase at a higher speed. Hence it confirms that effective drug loading has been taken place in microspheres which increased the particle size of the microspheres.

X-ray powder Diffactometry (XRD)

The X-ray powder diffraction patterns of pure drug, polymer and drug loaded microspheres as stated in fig. 9a reveals that the intensity of the peaks for the pure drug was sharp. But when it was incorporated into the polymer matrix, the drug peaks showed a loss of sharpness probably due to decreased crystallinity of the drug shown in fig. 9b.

CONCLUSION

In the present study, an attempt was made to prepare and evaluate Zidovudine microspheres employing different polymer in single and in blend by emulsion solvent evaporation method. The obtained microspheres were spherical in shape and freely flowing. The in-vitro drug release study indicated that the prepared zidovudine microspheres released drug for 8 hours or longer and would be capable of reducing the frequency of administration depending upon the formulation variables. As the concentration of polymers was increased, the release rate decreased gradually and the release studies showed that formulations containing highest concentration of Ethyl cellulose and Eudragit RS 100 gave the best sustained effect. The drug release data was plotted in Zero order, First order, Higuchi, Hixon-Crowell, Korsemeyer equations. All the formulations prepared by emulsion solvent evaporation were found to follow the Korsemeyer release mechanism. The release exponents were also studied from Korsemeyer equation to get the fickian and non fickian release behavior. The calculated n values suggest that the mechanism of drug release followed non Fickian (anomalous) transport.

CONFLICT OF INTERESTS

The authors declare that they have no competing interests.

AUTHOR’S CONTRIBUTIONS

TM performed the experiment and prepared the manuscript; ID supervised the work and helped in study design; SR and AI gave consultation on different statistical analysis and AH helped by providing different polymers and preparation of the manuscript. All authors read and approved the final manuscript.

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