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Research Article

Formulation, Characterization and Evaluation of Nanoparticles Containing Anti-Retroviral Drug

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Abstract

Nanoparticles render a promising drug delivery system of controlled and targeted drug release. These are specially designed to release the drug in the vicinity of target tissue. The aim of this present study was to develop and evaluate eudragit RS100 nanoparticles containing nanoparticles zidovudine in different drug to polymer ratio by nanoprecipitation method. SEM indicates that nanoparticles have a discrete spherical structure without aggregation. The average particle size was accurately found to be 720.1nm. The particle size of the nanoparticles was gradually increased with increase in the proportion of eudragit RS100. The drug containing nanoparticles was increasing on increasing polymer concentration up to a particular concentration ratio. No difference was observed in the extent of degradation of product during sixty days in which, nanoparticles were stored at various temperatures. FT-IR studies indicated that there were no chemical interaction between drug and polymer and stability of drug. The in-vitro release character from all the drug loaded batches was found to be zero order and rendered sustained release over a period of 24 h. The prepared formulations overcome and breakup the drawbacks and limitations of zidovudine sustained release formulations and could possibility be advantageous in terms of increased bioavailability and efficacy of zidovudine.

Key Words: Nanoparticles, Nanoprecipitation Method, Eudragit RS100, Zidovudine.

Introduction

During last two decades, considerable attention was given to the development of novel drug delivery system (NDDS)[1]. The rational for control drug delivery is to be alter the pharmacokinetics and pharmacodynamics of drug substance in order to develop the therapeutic efficacy and safety through the use of drug delivery system. Besides more traditional matrix or reservoir drug delivery system, colloidal drug delivery system has profited in popularity. The major colloidal drug delivery system included liposome and polymeric nanoparticles. These systems has been investigated primarily for site specific drug delivery, for controlled drug delivery, and also for the enhancement of dissolution rate as well as bioavailability of poorly water-soluble drugs.

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The foremost route of administration under investigation are parenteral route, however, other routes such as the oral, ocular, or topical routes are also being investigated frequently. In view of oral drug delivery system microsphere[2], microcapsule, nanoparticles, liposomes, and niosomes are best options to develop conventional dosage form. Nanoparticles are colloidal polymer particles of a size below the range 1mm[3-4] and hold promise as drug delivery for parenteral, peroral and vaccines. Due to their wider stability and due to their easiest manufacturing they offer advantages over other colloidal carriers such as liposomes and cell ghosts. They offer advantages like increased and improved bioavailability, site specific drug delivery, sustained release of drug over long period of time, retention of dosage form in entire length of gastrointestinal tract and convenient to patient due to reduction in continuous dosing[5]. Eudragit polymers are series of well known acrylate and methacrylate polymer available in different ionic forms. Eudragit RS 100 is insoluble in aqueous media but it is permeable and has pH-independent release profile. The permeability of Eudragit RS 100 is due to presence of quaternary ammonium group present in their structure[6]. Abacavir is an a nucleoside analog reverse transcriptase inhibitor (NRTI) used to treat harmful HIV and AIDS. It is available under the trade name Ziagen (ViiV Healthcare) and in the combined formulations Trizivir (abacavir, zidovudine and lamivudine) and Kivexa/Epzicom (abacavir and lamivudine). It has been well tolerated, the main side effect is hypersensitivity, this can be severe, and in rare cases, possibility for fatal. Genetic testing can indicating whether an individual will be hypersensitive; over 90% of patients can safely take zidovudine. However, in separate study, the risk of heart failure increased by 90%.Viral strains are resistant to lamivudine (3TC) are generally sensitive to zidovudine, whereas some strains are resistant to lamivudine are not as sensitive to zidovudine[7].

MATERIAL AND METHOD

Zidovudine was obtained as gift sample from Micro Labs bangalore. Eudragit RS 100 was obtained from Yarrow Chem Products.Mumbai. Tween80 was procured from Rolex Laboratory Reagent. Bombay and Acetone obtained from Yarrow chemicals.Mumbai. All other chemicals used were of analytical grade.

Preparation of nanoparticles

Nanoparticles, loaded with Zidovudine were prepared by Co-precipitation method. Briefly a 20mg zidovudine and various proportions of eudragit RS 100 were dissolved in acetone (5ml). The organic phase was poured drop wise into 10ml of aqueous phase containing 1% of tween 80 under magnetic stirring at room temperature. Nanoparticles were spontaneously formed and turned the solution in to milky colloidal suspension. Then acetone was removed by continuing stirring for overnight at room temperature. Formulation optimization was pursued to obtain nanoparticles of desired physical properties. Effect of various polymer drug rations from 1:1, 1:2 ,1:3 ,1:4 and 1:5 and the stabilizer concentration 1%w/v were assessed on drug encapsulation efficiency and particle size.

By follow the above mentioned procedure five other batches of nanoparticles in the ratio of 1:1, 1:2, 1:3, 1:4 and 1:5 were prepared and named F1, F2, F3, F4 and F5 respectively. Particle size, surface morphology and zeta potential. The surface morphology (roundness, smoothness, and formation of aggregates) and particle size was studied by scanning electron microscopy (SEM)[10-11]Zeta potential of the best formulation (F1) was determined by zeta potential probe model DT- 300. Drug content was determined by known centrifugation method. The redispersed nanoparticles suspension was centrifuged at 15,000 rpm for 40 min at 25° to separate the free drug in the supernatant. The concentration of zidovudine in the supernatant was determined by UV-Visible spectrophotometrical system at 266 nm after using suitable dilution. Fourier Transform Infra-red Spectroscopy (FT-IR) analysis The FT - IR spectra of pure zidovudine and Eudragit RS 100 nanoparticles loaded with zidovudine was recorded to check drug polymer interaction and stability of drug. In vitro release studies were carried out by dialysis tubes with an artificial membrane. The prepared zidovudine nanoparticles and 10 ml of phosphate buffer ph 7.4 added to the dialysis tube and subjected to dialysis by immerse the dialysis tube to the receptor compartment consist of 250 ml of phosphate buffer pH 6.8. The medium in the receptor was agitated continuously utilize a magnetic stirrer at 37±1°.5ml of sample of receptor compartment has been taken at various intervals of time over a period of 24 h and each and every time fresh buffer was replaced. The amount of drug releasing was determined spectrometrically at 266 nm. Kinetic modeling used in order to understand the kinetic mechanism of drug release, the result of in vitro drug release study of nanoparticles were fitted with various kinetic equation such as zero order[12] (cumulative % release vs. time), first order[13] (log % drug remaining vs. time), Higuchi's model[14] (cumulative % drug release vs square root of time). r^2 and k values were calculated for the linear curve obtained by regression analysis of the above plots.

Stability Studies

Zidovudine containing nanoparticles were stored at elevated temperature and relative humidity (25±2^{0}C/60%±5% RH, 40±2^{0}C/75%±5% RH) in a stability analysis chamber over a period of 2 months. Freshly prepared nanoparticles were stored at 5±3^{0}C used as control. Samples were kept for 90 days for stability analysis and after 90 days, drug loading of nanoparticles were compared with those of the control formulations.[15]

Result and Conclusion

Interaction between the drug and polymers commonly lead to identifiable change in the FT -IR pattern. zidovudine, Eudragit RS100 and physical mixture of zidovudine and Eudragit S 100 are demonstrated in Figures 1-3. Matching up to FT-IR spectrum of Zidovudine with physical mixture revealed no distinctive changes in the pattern of FTIR spectrum. Hence the polymer was compatible with drug.

Colloidal drug delivery system offers a number of advantages over conventional dosage form, due to their particle size[12]. Instantaneous formation of a colloidal suspension occurred as a result of the polymer deposition on the interface between the organic phase and water when partially water miscible organic solvent (acetone) diffused out quickly into the aqueous phase from each transient particle intermediate. According to the marangoni effect, the transient particle intermediate causes a size reduction to the nano range. Eudragit RS100 Nanoparticles were successfully prepared by the nanoprecipitation technique. The method is simple, reproducible, fast, economic and one of the easiest procedures for the preparation of nanoparticles.

Nanoparticles were spontaneously formed when the organic phase (acetone) was added drop wise into stirred aqueous surfactant solution (1%w/v tween 80). [13]. Nanoparticle size is affected by processing parameter such as drug polymer ratio, concentration of surfactant and phase ratio.

Particle Size Analysis

Particle size analysis of the zidovudine nanoaprticles was done by the Malvern system and the mean particle size of the nanoparticles was found to be 720.1 nm. Figure 4 shows the particle size distribution of the Zidovudine loaded Eudragit RS100 nanoparticles.

Surface Charge

Surface charge analysis of the zidovudine loaded eudragit RS100 nanoparticles was done by the Malvern Zetasizer and the zeta potential was found to be -28.5 mV. The result of Zeta potential distribution is shown in figure 5.

Surface Morphology

The surface morphology of the prepared nanoaprticles was characterized by SEM studies. Figure 6 shows the

SEM images of Eudragit RS100 nanoparticles containing the drug Zidovudine.

Determination Of Process Yield, E.E And Drug Loading Capacity (%)

The practical yield and drug loading (%) of different batches are shown in Table 1. The process yield ranged between 82.32 to 91.28% w/w depends on the drug polymer ratio. E.E was found to be 55.82% to 68.42%. The drug loading capacity ranged between 8.36 to 26.25% w/w.

***In Vitro* Drug Release Studies**

The drug releases from the nanoparticles were studied by dialysis method. The in vitro release profiles of zidovudine from eudragit RS100 nanoparticles are shown in Table 2 and Figure 7. The cumulative percentage release of zidovudine from eudragit RS100 nanoparticles varied from 77.60% to 96.59% depends on the drug polymer ratio for 24 hr.

Conclusion:

The method of preparation of nanoparticles of zidovudine was found to be simple and reproducible. The slow and constant release of zidovudine from nanoparticles maintain constant drug plasma concentration thereby increasing therapeutic efficacy. This study shows that polymethacrylic acid nanoparticles could be a useful carrier for zidovudine. The developed formulation overcome and alleviates the drawbacks and limitations of a zidovudine sustained release formulations.

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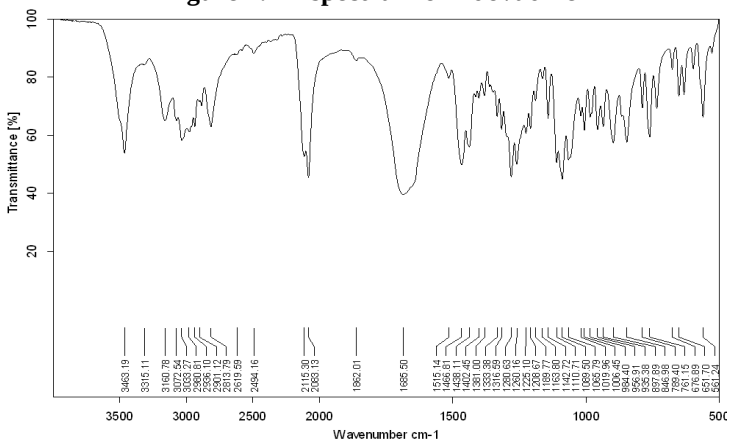
Figure 1: IR spectrum of zidovudine



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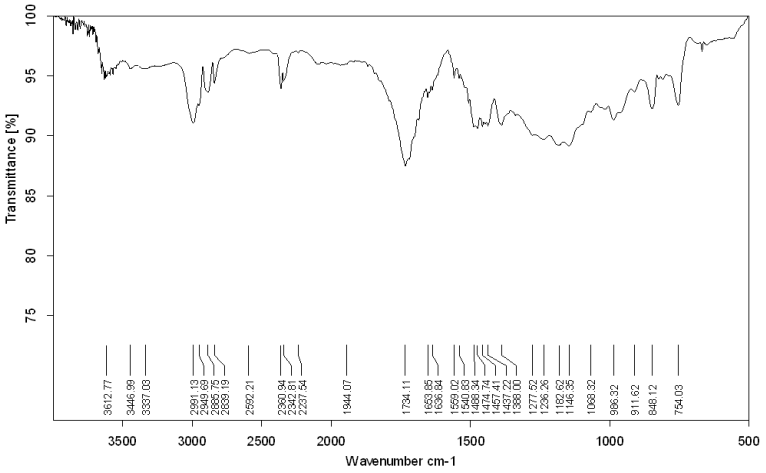

Figure 2: IR spectrum of Eudragit RS100

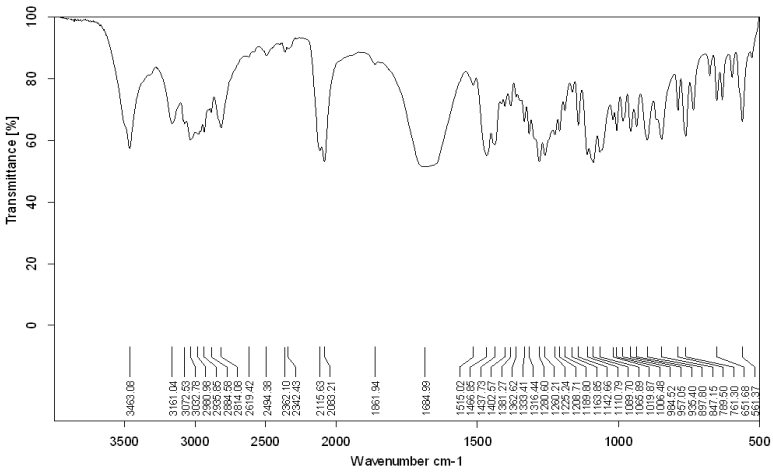

Figure 3: IR spectrum of zidovudine + Eudragit R

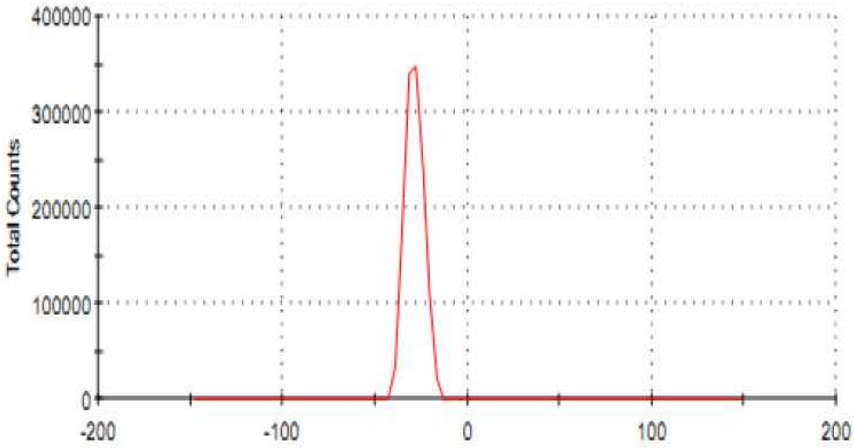

Figure 5: Zeta potential distributions of Zidovudine nanoparticles (F1).

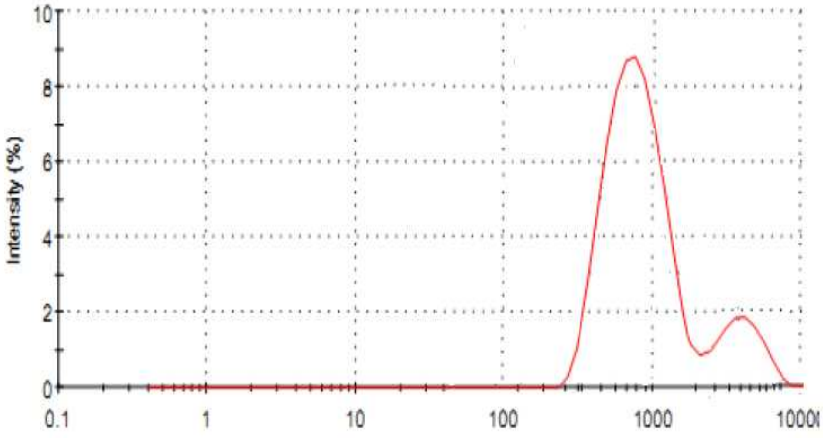

Figure 4: Particle size distributions of Zidovudine nanoparticles (F1).

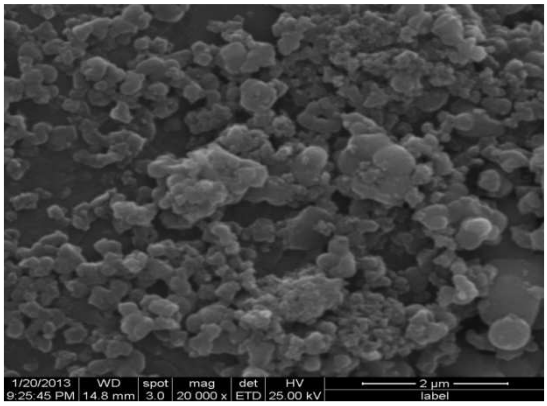

Figure 6: Scanning electron microscopy (SEM) images of Zidovudine nanoparticles (F1).

Table 1: Data of Process yield and drug loading capacity (%) of Zidovudine loaded Eudragit RS100 nanoparticles for F1-F5

Batch code	Entrapment efficacy	Process Yield (%)	Drug loading (%)
F1	55.82	82.32	8.36
F2	61.51	84.23	13.78
F3	62.24	88.99	17.28
F4	64.19	90.64	23.82
F5	68.42	91.28	26.25

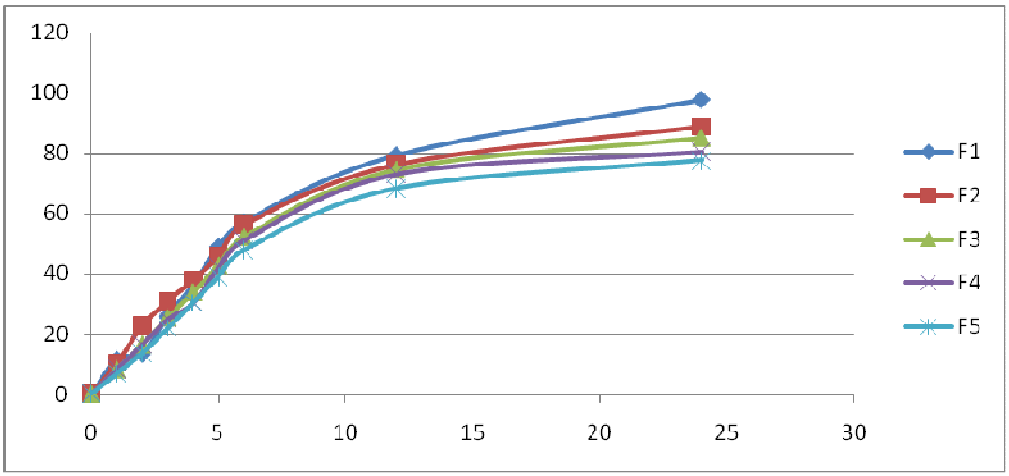

Figure 7: In vitro drug release profile for F1 to F5 formulations

Table 2: In vitro release profile of Eudragit RS100 nanoparticles of drug zidovudine with different drug polymer ratio

Time (hrs)	Batch code				
	F1	F2	F3	F4	F5
1	11.79	10.28	8.17	8.22	6.84
2	13.75	22.73	16.41	16.39	13.53
3	26.56	30.88	25.34	24.76	21.80
4	37.78	37.93	33.87	30.14	30.34
5	44.53	45.85	42.67	42.13	39.09
6	53.55	56.25	52.17	50.96	47.84
12	76.73	76.25	74.54	72.93	68.26
24	96.59	88.99	85.08	80.38	77.60