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Formulation and Evaluation of Nano Particles of an Anti-Viral Drug

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Research Article

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ABSTRACT

In the present study nanoparticles of Zidovudine which is used for treatment of anti-retro viral therapy were prepared and characterized. The Zidovudine nanoparticles were prepared by Ionic gelation method by using different concentration of Chitosan and SodiumTripoly phosphate. Acetic acid was used to dissolve the chitosan and the 10 mg of Zidovudine drugs is added to each of the formulation. The nanoparticles of Zidovudine were evaluated for practical yield, entrapment efficiency, particles size, Charge determination, drug release and stability studies.

Nanoparticles have large (functional) surface which are able to bind, adsorb and carry other compounds such as drugs, probes, protein and has a surface that might be chemically more reactive compared to their fine analogues

INTRODUCTION

Antiviral are a class of medication specifically used for treating viral infection like antibiotic for bacteria, specific antivirals are used for specific viruses. Unlike most antibiotics, most antivirals drugs do not destroy their target pathogen; instead they inhibit their development [1]. Using nanoparticles as a drugs carrier system could improve the delivery of antiviral to the mononuclear phagocyte system in the in vivo, overcoming pharmacokinetic problems and enhancing the activities of drugs for the treatment of HIV infection and AIDS [2].

The nanoparticuate drugs delivery system have the potential power to improve the drugs stability, increase the duration of therapeutic action and permits administration through enteral or parenteral administration, which may prevent drugs degradation and metabolism as well as cellular efflux [3]. Nanoparticles was evolved as a promising drug delivery because of their sustained and controlled release, subcellular size, biocompatibility with the tissue and cells [4].

Zidovudine is a thymidine analogue. It is phosphorylated in the body to its active form Zidovudine triphosphate which interferes in DNA synthesis of retroviruses by inhibiting DNA replication. Zidovudine inhibits the key enzyme reverse transcriptase. Human DNA polymerase is inhibited only at a conc. 100 times more than that required to inhibit viral reverse transcriptase. The oral bioavailability of Zidovudine is 65% due to first pass metabolism.

MATERIALS AND METHODS

Zidovudine was obtained as gift sample from Micro labs; Chitosan was procured from Indian sea food ltd, Kerala, Sodium tri polyphosphate was from Quest international, Bangalore & Sodium hydroxide& Acetic acid are from Ranbaxy.

Preformulation studies

Standard graph of Zidovudine in distilled water

A spectrophotometric method is developed at λmax 266 nm.

Stock-1 solution: 100 mg of Zidovudine was weighed accurately & transferred in 100 ml volumetric flask and dissolved in water and the volume is made up to the mark with distilled water . (1000 µg/ml).

Stock-2 solution: 10 ml from stock-1 solution was diluted to 100 ml with water (100 µg/ml). From this solution 0.2, 0.4, 0.6, 0.8 and 1 ml was pipetted out and diluted to get 2, 4, 6, 8 and 10 µg/ml by using distilled water. Distilled water is used as a Blank solution. Standard curve was prepared by plotting concentration vs. absorbance at 266.0 nm. The mean ±S.D of three determinations were reported [4].

Determination of melting point

Melting point of Zidovudine was determined by capillary method. Fine powder of Zidovudine was filled in glass capillary tube (previously sealed on one end). The capillary tube is tied to thermometer and the thermometer was placed in tube containing liquid paraffin [5]. The assembly was kept on heating and temperature was allowed to increase gradually. Temperature at which the powder melted was noticed.

Drug-excipients Compatibility study

A successful formulation of a stable and effective solid dosage form depends on careful selection of the excipients that are added to facilitate administration, promote the consistent release and bioavailability of the drug and protect it from degradation [6-10].

The compatibility of the drugs with the excipients was determined by subjecting the physical mixture of the drugs and the polymer of the formulation to infrared absorption spectral analysis (FTIR). Any change in the chemical composition of the drugs after combining it with the polymer was investigated with I.R spectral analysis.

Weighed amount of the drugs or physical mixtures of the drugs with the other excipients was mixed with 100 mg of Potassium bromide (dried at 40-50°C). The mixture was taken and compressed under 10-ton pressure in a hydraulic press to form a transparent pellet. The pellet was scanned by IR spectrophotometer [11-15].

Formulation of Zidovudine Nanoparticles

Zidovudine is a thymidine analogue. It is phosphorylated in the body to its active form Zidovudine triphosphate which interferes in DNA synthesis of retroviruses by inhibiting DNA replication. Zidovudine inhibits the key enzyme reverse transcriptase. Human DNA polymerase is inhibited only at a concentration 100 times more than that required to inhibit viral reverse transcriptase. The bioavailability of Zidovudine is 60-70%.

Preparation of Nanoparticles

Chitosan nanoparticles were prepared by ionic cross linking of chitosan solution with TPP anions. Chitosan was dissolved in aqueous solution of acetic acid (0.25, v/v) at various concentrations such as 1.0, 2.0, 3.0 and 4.0 mg/ml. Under magnetic stirring at room temperature, 5 ml of 0.4 % (w/v) TPP aqueous solution was added drop wise using syringe needle into 10 ml chitosan solution containing 10 mg of Zidovudine. PH was adjusted to 6.0 by adding 0.1 M NaOH. The stirring was continued for about 30 min. The resultant nanoparticles suspensions were centrifuged at 12000 × g for 30 min using C24 centrifuge. The formation of the particles was a result of the interaction between the negative groups of the TPP and the positively charged amino groups of chitosan (ionic

gelation). The sediment is collected and re-dispersed in 10 ml of distilled water by vortexing in a vortex mixer for 5 min. The sediment is also collected and dried to get the practical yield. Similarly 0.6%, 0.8%, 1.0 % of TPP were also used to prepare the nanoparticles by using the above mention method.

RESULTS

Standard curve of Zidovudine by using distilled water (λmax=266.0 nm) (Table 1) (Figure 1).

Table 1. Standard curve of Zidovudine in distilled water.

Concentration (µg/ml)	Absorbance (MEAN±SD) n=3
0	0±.000
2	0.089±.002
4	0.150±.003
6	0.229±.005
8	0.302±.006

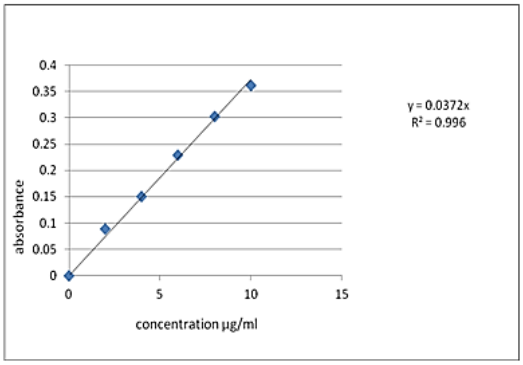

Figure 1. Standard curve of Zidovudine in water.

DISCUSSION

Preformulation Studies

Zidovudine nanoparticles were prepared using ionic gelation method by varying the concentration of chitosan and TPP. It is advised that the nanoparticles will be taken up directly into the systemic circulation bypassing the first pass metabolism.

Standard graph of Zidovudine in distilled water

The standard graph was found to be linear in the range of 2-10 µg/ml. The R2 and the slope were found to be 0.996 and 0.0372 respectively.

Determination of melting point

Melting point of Zidovudine was determined by capillary method. The melting point of Zidovudine was found to be 1220C-1250C, as in compliance with IP standards, indicating purity of the drug sample.

Drug-Excipient compatibility studies

IR spectra of Zidovudine alone and its combination with other polymers are shown in figure. An IR spectrum of pure Zidovudine showed the peaks at 3159.51, 1260.18, 3030.12, 3464.32, 1666.15 cm-1. These peaks can be considered as characteristic peaks of and were not affected and predominantly observed in IR spectra of Zidovudine along with the polymers as shown in the figure 5.1 indicated no interaction between Zidovudine, chitosan and TPP.

Formulation of nanoparticles

Nanoparticles were prepared by ionic gelation method by using different concentration of chitosan and TPP. Formulation F1-F4, with increasing concentration of chitosan and 0.4% TPP the drug entrapment efficiency was found to be 35.41% to 42.43% and the Drug release was found to be 88.21% to 84.11% at 6 hour. As the chitosan concentration is increasing Drug Entrapment efficiency and Percentage yield was found to be increased whereas the drug release was found to be decrease with increasing in the chitosan concentration. The influence of chitosan on particles size was not clear it ranged between 655.21 nm to 760.9 nm.

Formulation F5 to F8 when similar concentration of chitosan were formulated using 0.6% TPP the particles size was found to be in 458.6 to 593.4 nm. The influence of chitosan on TPP was found to be similar but when the concentration of TPP was increase to 0.6% the particles size was found to be decreased and the entrapment efficiency, drug content and percentage yield was found to be increased.

Drug release was observed up to 8 hr. and found to be 83.82 to 89.36%. Formulation F9 to F12 when similar concentration of chitosan were formulated using 0.8% TPP the particles size was found to be in the ranges of 398.92 to 300.1 nm and the Entrapment Efficiency, drug content and percentage yield was found to increase. Similar observation were found as chitosan concentration is increased from 1 mg/ml to 4 mg/ml, the yield and entrapment efficiency were found to be increased.

When TPP concentration was increased from 0.4 % to 0.8 % particles size was found to be decreased and Entrapment efficiency and yield were also increased. Drug release was found to be decreased. Drug released was observed up to 6 hr when TPP concentration was less, when TPP concentration was increased up to 1 % drug released extended up to 8 hr. Dissolution profile were shown in the fig no 5.26, 5.27, 5.28 and 5.29 There was no significant different between the trials using 0.8% TPP and 1% TPP solution.

Surface Morphology

The surface morphology of the nanoparticles is done by Scanning electron microscopy and was found that the particles are spherical in shape and without any agglomeration.

Gel electrophoresis

During Gel Electrophoresis study the nanoparticles moved toward the negatively charged electrode which indicates the nanoparticles are positively charged so that the nanoparticles can easily interact with the cell membrane for the maximum adsorption of the nanoparticles.

Stability study

The nanoparticles were found to be stable in terms of particle size and drug release even after a period of 45 days when stored at 4 °C and at room temperature.

CONCLUSION

The nanoparticles of Zidovudine are successfully prepared using different concentration of chitosan and TPP by ionic gelation method. The nanoparticles were further evaluated for different parameters. Pre-formulation studies were carried out to check the purity of the drug. The standard graph was performed and concluded that the standard graph was found to be linear in the range 2 to 10 µg/ml. FTIR technology was used to study the physical and chemical interaction between the drugs and the excipients used and were observed that there were no interaction between the Zidovudine and with the polymer used and TPP. F1 to F16 Nanoparticles formulation were prepared by varying the concentration of Chitosan and TPP. Based on the drug content, drug entrapment efficiency, particle size, morphology and in vitro release, formulation with 0.8 % of TPP was selected to be optimum

formulation. The stability studies were also carried out by using the formulation F11 As it is having minimum particle size observed. The stability studies showed closeness in data of in vitro release and particle size when compared to previous data at room temperature and at 4ºC.Thus nanoparticles of Zidovudine with 0.8% TPP was found to be the best formulation and the nanoparticles was found to be spherical, discrete, and free flowing and able to sustain the drugs release effectively.

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