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RESEARCH ARTICLE

Formulation and Evaluation of Stavudine Nanoparticles

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Manuscript Info *Abstract*

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The present study deals with the formulation and evaluation of Stavudine nanoparticles. Stavudine is one of the most essential nucleoside reverse transcriptase inhibitors for AIDS treatment with its oral bioavailability over 80%. Stavudine is most commonly used to treat HIV. The purpose of this research is to minimize the frequency of doses and toxicity and to improve the therapeutic efficacy by formulating stavudine nanoparticle. Stavudine nanoparticles were formulating by ionic gelation method using polymer chitosan with three different ratios. Nanoparticles were characterized by determining its particle size, drug entrapment efficiency, drug release and stability studies. The partical size ranged between 350nm to 600nm. Drug content was found of be supportive to the drug release pattern. The *in-vitro* release of stavudine nanoparticles were carried out which exhibited a sustained release of stavudine from nanoparticles upto 14 hrs. The results showed that nanoparticles were more beneficial in providing drug delivery system.

Introduction

In recent decades there been increased interest in the use of nanoparticles for drug delivery applications.Nanoparticles are colloidal - sized particles, possessingdiameters ranging between 1 and 1000 nm, and drugs maybe encapsulated, adsorbed or dispersed in them. A widevariety of nanoparticles composed of a range of materialsincluding lipids, polymers and inorganic materials havebeen developed, resulting in delivery systems that vary intheir physicochemical properties and thus their applications. The purpose of this study is to reduce the frequency of doses and toxicity and to improve thetherapeutic efficacy by formulating stavudine nanoparticlesand to evaluate their particle size, entrapment efficiency,drug release and stability studies.

Stavudine is one of the most essential nucleoside reverse transcriptase inhibitors for AIDS treatment with its oral bioavailability over 80%. In clinical study, Stavudine can appreciably increase CD4 cell counts and reduce mean serum P24 antigen levels and infectious HIV titres. However the duration of the above responses is inadequate Furthermore, D4T is slightly hydrophilic with its log *D*oct=-0.84, where *D*oct is the distribution coefficient between octanol and phosphate buffered saline.

Material and Methods

Stavudine was obtained as a gift sample from Cipla Ltd., Patalgangaand Mumbai. Chitosan(viscosity 100 cps) was purchased from Para's pharma Chem suppliers (Pune).Chitosan was procured from CIFT, Cochinand India.

Preparation of Stavudine Nanoparticles by IonicGelation Method

The polymer chitosan[1] wasdispersed in 50 ml of 5% glacial acetic acid solution andstirred for 4 hours continuously then it was stabilized forovernight to obtain clear 0.4% chitosan gel. In ionotropicgelation method[2] 0.4% chitosangel and 0.5% of Tripolyphosphate solution (cross linking agent) were used. Chitosan nanoparticles formedspontaneously upon addition of 1.2 ml of an aqueous Tripolyphosphate solution to 3 ml of chitosan solution underhigh speed stirring (3000 rpm) using high speed stirrer. Theresulting chitosan particle suspensionwere centrifuged at10,000 rpm for15 minutes. The particles were washed withdistilled

water and freeze dried, same method used for threedifferent formulations with various proportion of polymerconcentration (Table.1).

Table.1 Formulation of Stavudine Nanoparticles

SL. No	Batch Code	Drug (mg)	Polymer (mg)	Drug: Polymer Ratio
1	SN-1	50	50	1:1
2	SN-2	50	100	1:2
3	SN-3	50	150	1:3

Characterization of stavudine Nanoparticles
Particle Size Analysis[3,4]
The particle size of the Stavudine Nanoparticles were evaluated by Scanning Electron Microscope wereranging from 350 nm to 600 nm, particle size variesdepending on the polymer load (Table.2)

Determination of percentage of drug entrapment efficiency[5]
The Stavudine Nanoparticle suspension werecentrifuged at 12000 rpm in cooling centrifuge at 15^0C for10 min. The supernatant fluid was analysedspectrophotometrically at 266 nm (Table.2).

$$\text{Drug Entrapment (\%)} = \frac{\text{Amount of Drug in the Nanoparticles}}{\text{Amount of Drug fed in to system.}} \times 100$$

Table.2 Particle Size and Percentage of Entrapment Efficiency

SL. No.	Batch Code	Drug: Polymer Ratio	Particle Size (nm)	Entrapment Efficiency(%)
1	SN-1	1:1	350	88.6±0.4
2	SN-2	1:2	460	85.9±0.6
3	SN-3	1:3	600	82.3±0.4

***In vitro* release of Stavudine from Nanoparticles**
The *in vitro*[6,7] release of Stavudine from nanoparticles wasstudied by using simple diffusion cell apparatus which isopened at both ends, One end tied with sigma dialysis membrane which serves as a donor compartment. The dissolution medium used was freshly prepared phosphate buffer saline pH 7.4. Sigma membrane was soakedovernight in the dissolution medium. The medium wasstirred by using the magnetic stirrer and the temperature was maintained at $37^oC \pm 0.5^oC$. Periodically 5 ml of samplewas withdrawn and analysed spectrophotometrically at266nm (Table.3).

Table.3 In vitro Release of Stavudine from Stavudine Nanoparticles

SL. No	Time in (Hours)	SN-1 (%)	SN-2 (%)	SN-3 (%)
1	0	0	0	0
2	0.5	19.32	17.60	16.32
3	1	22.50	20.85	19.20
4	2	35.21	27.60	24.49
5	4	46.30	35.42	31.60
6	6	52.91	47.32	44.39
7	8	61.42	52.40	50.04
8	10	66.43	64.23	62.39
9	12	79.30	76.36	72.94
10	14	88.60	85.42	76.53

Stability Studies
The Formulated Nanoparticles[8] were kept in small air tight glass containers andstored at different temperature such as 4^oC,roomtemperature and 45^oC. The Drug content was observedindifferent time interval of I^{st} week, II^{nd}, $III^{rd}$and IV week.There was no appreciable changes in drug content wasobserved in room temperature and 4^oC. Table.4 showed the stability of stavudine nanoparticles.

Table.4 Stability Studies

% of Drug Remaining									
Batch	SN-1			SN-2			SN-3		
Time	4^0 C	Room Temp	45^0 C	4^0 C	Room Temp	45^0 C	4^0 C	Room Temp	45^0 C
Initial	100	100	100	100	100	100	100	100	100
I^{ST} Week	97.5	95.4	94.2	97.9	97.7	95.4	99.4	98.2	96.5
II^{nd}Week	95.2	95.7	92.3	95.4	96.3	93.1	98.9	98.0	94.3
III^{rd} Week	92.1	93.4	89.6	92.2	94.6	86.7	96.7	96.2	92.5
IV^{th}Week	89.2	91.2	86.3	90.3	91.8	87.2	93.4	94.0	88.6

Result and Discussion

The Nanoparticles were prepared by Ionic Gelationmethod by using Chitosan polymer. The particle size wereevaluated by SEM were managing from 350 nm to 600 nm.The entrapment efficiency of the drug was enhanced byincreasing the load of polymer. Batch no CN-III 1:3 ratio ofdrug and polymer has highest percentage of entrapment efficiency. The percentages of drug release were observed inthree different formulations. The cumulative percentage of
drug release from Cytarabine nanoparticles after 14th hourwas 88.6, 85.42, 76.53 respectively for SN-I, SN-II, SN-III.Sustained release was observed in 1:3 drug polymer ratiowhen compared with other two formulations. In stabilitystudies there were no Changes in the drug content in roomtemperature and 4^{o}C which was suitable for the storagecondition. From all the above results the Stavudine nanoparticles with 1:3 ratio of drug polymer showedsignificant sustained release with efficient drug delivery.

Fig.1 INVITRO DRUG RELEASE FROM STAVUDINE NANOPARTICLES

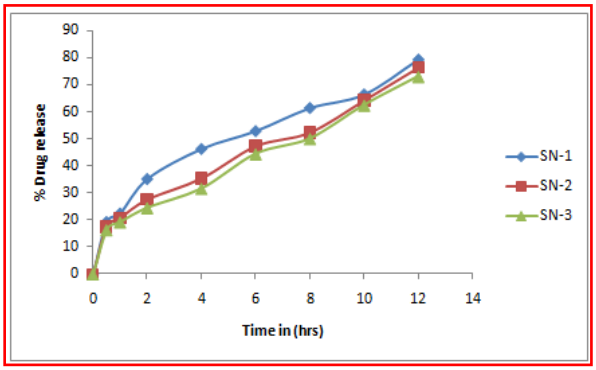


Fig.2 Stability studies of Stavudine Nanoparticles (SN-1)

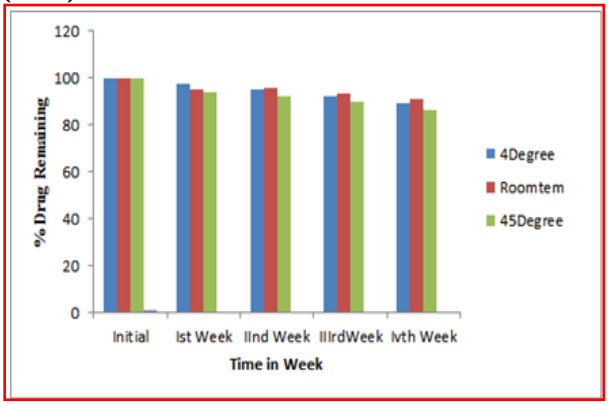


Fig.3 Stability studies of Stavudine Nanoparticles (SN-11)

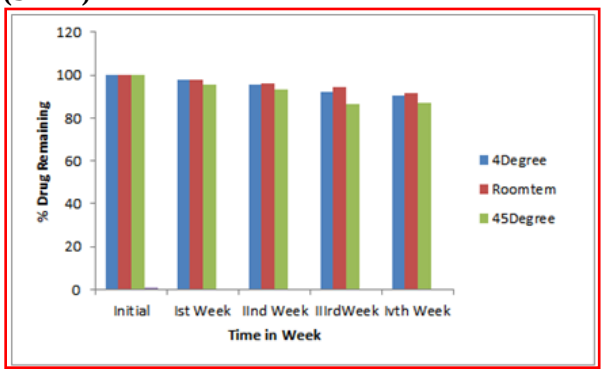
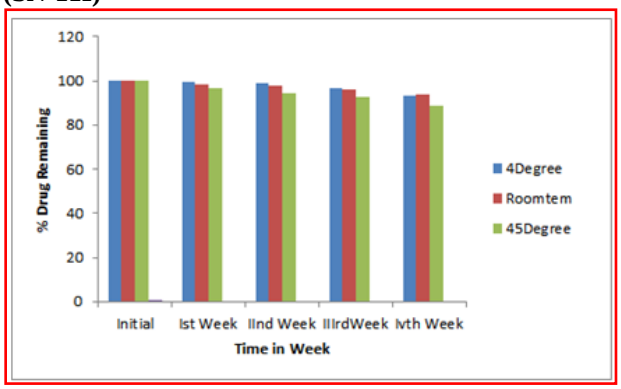


Fig.4 Stability studies of Stavudine Nanoparticles (SN-11I)



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