ISSN: 0976-4607
Research Article

International Journal of Innovative Pharmaceutical Research

Journal homepage: www.ijipr.com

Formulation and Evaluation of Cytarabine Nanoparticles

Umasankar. K[1*] and Uma Maheswara Reddy. C[2]

[1*]Maharaji College of Pharmacy, Besant Nagar, Chennai, Tamil Nadu, India- 600 090.
[2] Sri Ramachandra College of Pharmacy, Sri Ramachandra University,
Porur, Chennai, Tamil Nadu, India – 600 116.

ABSTRACT

The present study deals with the formulation and evaluation of cytarabine nanoparticles. Cytarabine is a synthetic pyrimidine nucleoside. Cytarabine is most commonly used to treat acute myeloid leukaemia. The purpose of this research is to minimize the frequency of doses and toxicity and to improve the therapeutic efficacy by formulating cytarabine nanoparticle. Cytarabine nanoparticles were formulating by ionic gelation method using polymer chitosan with three different ratios. Nanparticles 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 invitro release of cytarabine nanoparticles were carried out which exhibited a sustained release of cytarabine from nanoparticles upto 16 hrs. The results showed that nanoparticles were more beneficial in providing drug delivery system.

KEY WORDS: Cytarabine, Nanoparticles, Chitosan, Ionic Gelation.

INTRODUCTION

In recent decades there been increased interest in the use of nanoparticles for drug delivery applications. [1]Nanoparticles are colloidal - sized particles, possessing diameters ranging between 1 and 1000 nm, and drugs may be encapsulated, adsorbed or dispersed in them. A wide varity of nanoparticles composed of a range of materials including lipids, polymers and inorganic materials have been developed, resulting in delivery systems that vary in their physicochemical properties and thus their applications.

The purpose of this study is to reduce the frequency of doses and toxicity and to improve the therapeutic efficacy by formulating cytarabine nanoparticles and to evaluate their particle size, entrapment efficiency, drug release and stability studies.

The drug (cytarabine) was gift sample obtained from Biochem Labs Bangalore and polymer chitosan is from Central Institute of Fisheries Technology,Cochin). Remaining all other chemicals and solvents were used in this formulation were of analytical grade.

***Corresponding author**
Umasankar. K
Email id: sankarpharm@yahoo.co.in

Preparation of Cytarabine Nanoparticles by Ionic Gelation Method

The polymer chitosan (Rawat S *et al*., 2008) was dispersed in 50 ml of 5% glacial acetic acid solution and stirred for 4 hours continuously then it was stabilized for overnight to obtain clear 0.4% chitosan gel. In ionotropic gelation method (EricAllemann *et al*., 1993) 0.4% chitosan gel and 0.5% of Tripolyphosphate solution (cross linking agent) were useds. Chitosan nanoparticles formed spontaneously upon addition of 1.2 ml of an aqueous Tripolyphosphate solution to 3 ml of chitosan solution under high speed stirring (3000 rpm) using high speed stirrer. The resulting chitosan particle suspension were centrifuged at 10,000 rpm for15 minutes. The particles were washed with distilled water and freeze dried, same method used for three different formulations with various proportion of polymer concentration (Table.1).

Characterization of cytarabine Nanoparticles

Particle Size Analysis (Krishna RSM *et al*., 2006, Joseph NM *et al*., 2007)

The particle size of the Cytarabine Nanoparticles were evaluated by Scanning Electron Microscope were ranging from 350 nm to 600 nm, particle size varies depending on the polymer load (Table.2)

Determination of percentage of drug entrapment efficiency (Gomez BC *et al*., 1997)

The Cytarabine Nanoparticle suspension were centrifuged at 12000 rpm in cooling centrifuge at 15^{o}C for 10 min. The supernatant fluid was analysed spectrophotometrically at 254 nm (Table.2).

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

***In vitro* release of Cytarabine from Nanoparticles**

The *in vitro* Lifeng Qi *et al*., 2006 and Maitra A *et al*., 2002) release of Cytarabine from nanoparticles was studied by using simple diffusion cell apparatus which is opened 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 soaked overnight in the dissolution medium. The medium was stirred by using the magnetic stirrer and the temperature was maintained at 37^{o}C ± 0.5^{o}C. Periodically 5 ml of sample was withdrawn and analysed spectrophotometrically at 254nm (Table.3).

Stability Studies

The Formulated Nanoparticles (Kim YH *et al*., 2008) were kept in small air tight glass containers and stored at different temperature such as 4^{o}C, room temperature and 45^{o}C. The Drug content was observed in different time interval of Ist week, IInd, IIIrd and IVth week. There was no appreciable changes in drug content was observed in room temperature and 4^{o}C. Table.4 showed the stability of Cytarabine nanoparticles.

Table.1 Formulation of Cytarabine Nanoparticles

Sr.No	Batch Code	Drug (mg)	Polymer (mg)	Drug:Polymer Ratio
1	CN-I	50	50	1:1
2	CN-II	50	100	1:2
3	CN-III	50	150	1:3

Table.2 Particle Size and Percentage of Entrapment Efficiency

Sr.No	Batch Code	Drug:Polymer Ratios	Particle Size(nm)	Entrapment Efficiency (%)
1	CN-I	1:1	350	90.6 ± 0.5
2	CN-II	1:2	460	86.2 ± 0.7
3	CN-III	1:3	600	85.4 ± 0.5

Table.3 *Invitro* Release of Cytarabine from Cytarabine Nanoparticles

Sr.No	Time in Hours	CN-I (%)	CN-II (%)	CN-III (%)
1	0	0	0	0
2	0.5	12.46	11.12	9.31
3	1	24.17	22.12	19.55
5	2	36.39	33.14	30.31
7	4	46.17	44.17	38.31
9	6	55.62	55.25	42.23
10	8	63.32	62.14	50.32
11	10	68.40	64.21	57.51
12	12	72.31	68.09	61.73
13	14	84.14	82.21	67.29
14	16	90.06	88.1	78.61

Table.4 Stability Studies

% of Drug Remaining									
Batch	**CN-I**			**CN-II**			**CN-III**		
Time	**4^{O}C**	**Room Temp**	**45^{O}C**	**4^{O}C**	**Room Temp**	**45^{O}C**	**4^{O}C**	**Room Temp**	**45^{O}C**
Initial	100	100	100	100	100	100	100	100	100
Ist Week	98.2	97.2	96.4	98.4	98.5	96.4	99.2	98.8	97.4
IInd Week	95.2	95.6	91.4	96.2	97.1	93.6	96.6	98.2	95.4
IIIrd Week	91.4	92.2	88.2	92.5	94.6	85.4	94.2	96.4	91.4
IVth Week	89.2	91.4	85.2	91.9	92.8	86.2	93.5	94.2	87.8

Fig.1 INVITRO DRUG RELEASE FROM CYTARABINE NANOPARTICLES

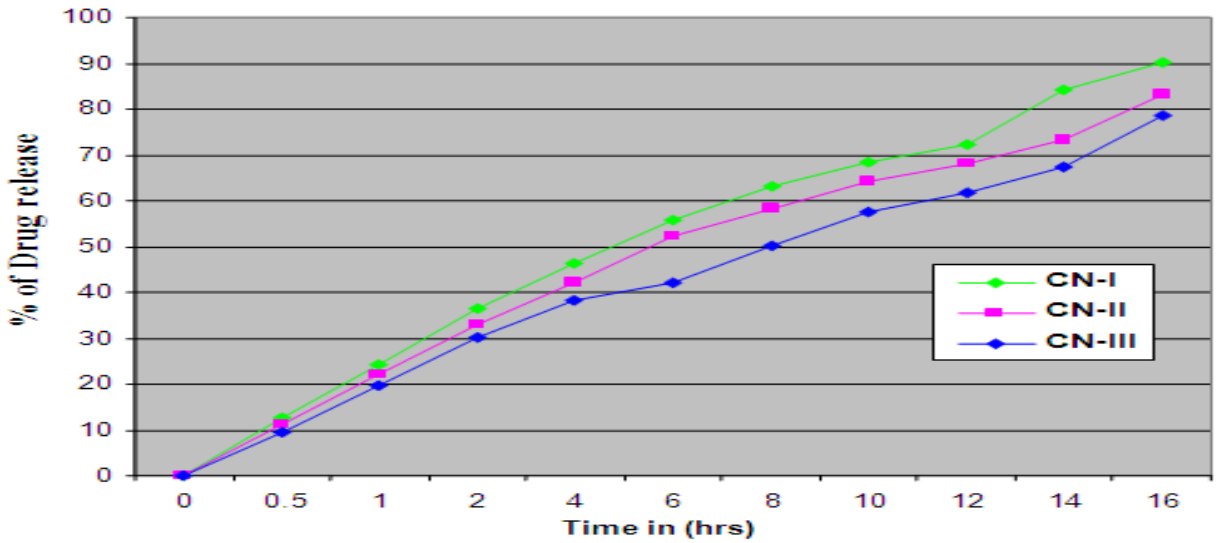


Fig.2 STABILITY STUDIES OF CYTARABINE NANOPARTICLES (CN-I)

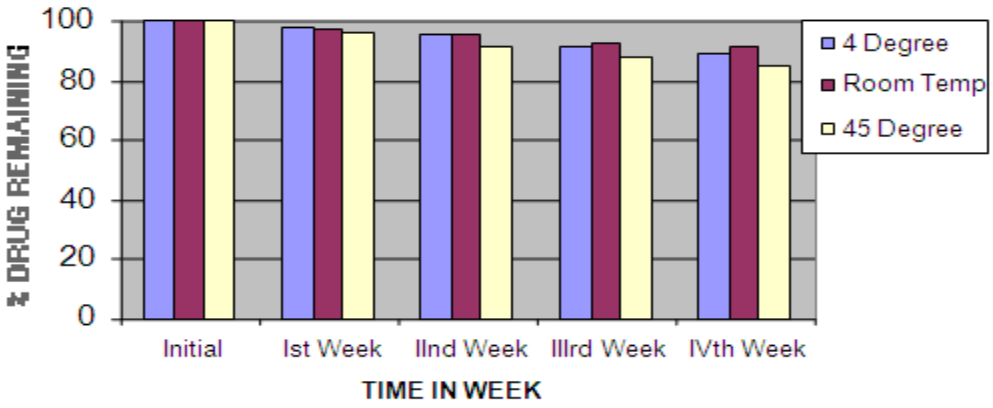


Fig.3 STABILITY STUDIES OF CYTARABINE NANOPARTICLES (CN-II)

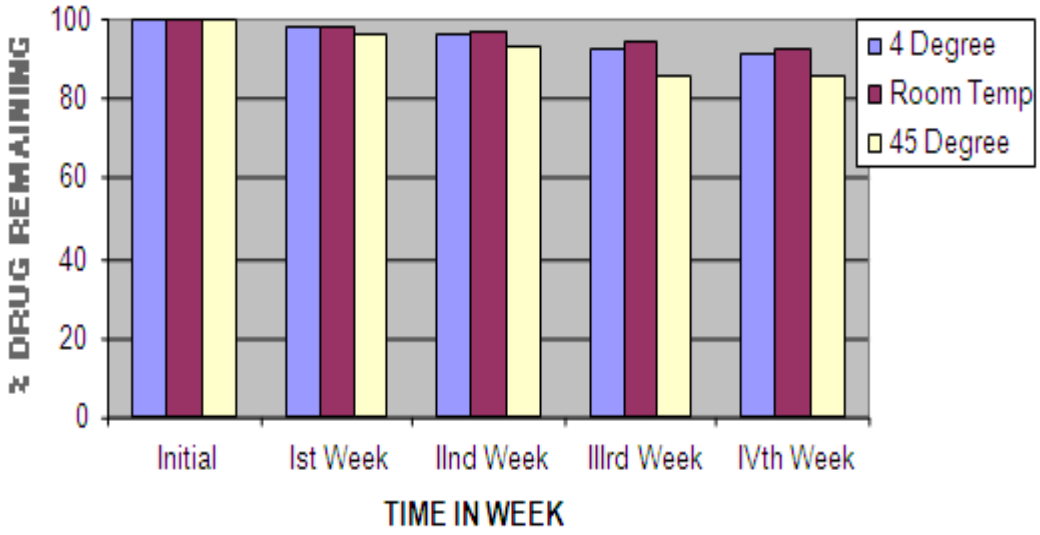
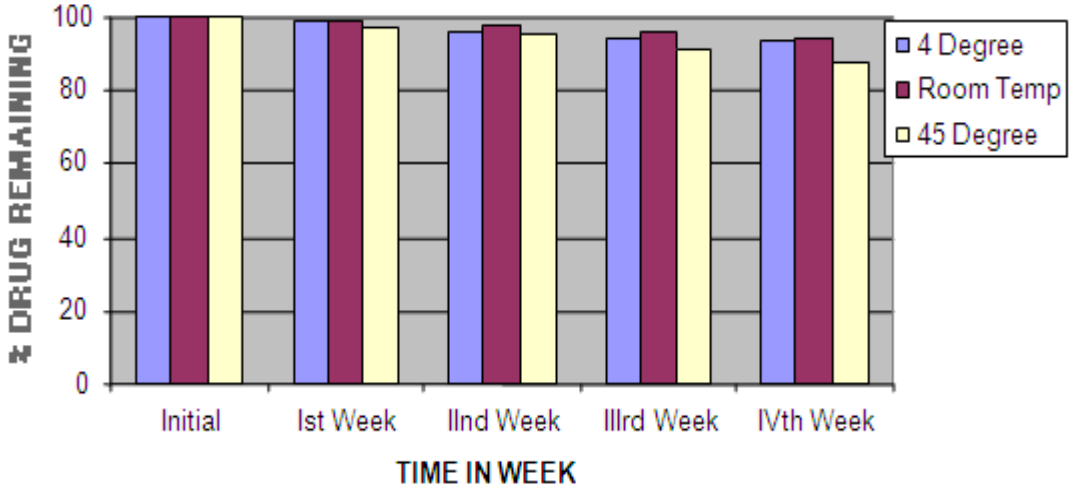


Fig.4 STABILITY STUDIES OF CYTARABINE NANOPARTICLES (CN-III)



RESULTS AND DISCUSSION

The Nanoparticles were prepared by Ionic Gelation method by using Chitosan polymer. The particle size were evaluatd by SEM were manging from 350 nm to 600 nm. The entrapment efficiency of the drug was enhanced by increasing the load of polymer. Batch no CN-III 1:3 ratio of drug and polymer has highest percentage of entrapment efficiency. The percentages of drug release were observed in three different formulations. The cumulative percentage of drug release from Cytarabine nanoparticles after 16th hour was 90.06, 88.1, 78.61 respectively for CN-I, CN-II, CN-III. Sustained release was observed in 1:3 drug polymer ratio when compared with other two formulations. In stability studies there were no Changes in the drug content in room temperature and 4^{o}C which was suitable for the storage condition. From all the above results the cytarabine nanoparticles with 1:3 ratio of drug polymer showed significant sustained release with efficient drug delivery.

REFERENCES

EricAllemann, Robert Gurny and Eric Doelker, Drug-Loaded Nanoparticles-Preparation Methods and Drug Targeting Issues. *Eur.J.Pharm.Biopharm*, 1993;39(5):173-191.

Gomez BC and Duncan R Evaluation of the biological properties of soluble chitosan and chitosan microspheres. *Int. J of pharm*. 1997;148:231-240.

Joseph NM, Sharma PK and Irchhaiya R, Preparation and characterization of Modified Gelation Nanoparticles as Carriers of Cytarabine. *Asian Journel of Pharmaceutis*. 2007;1:179.

Kim YH, Hwang HY, Kim I and Kwon IC, Tumor targetability and antitumor effect of docetaxel loaded hydrophobically modified glycol chitosan nanoparticles. *J. Control. Rel*. 2008;74:317-323.

Krishna RSM, HG Shivakumar, DV Gowda and Banerjee, Nanoparticles: A Novel Colloidal Drug Delivery System. *Indian J.Pharm.Educ.Res*. 2006;40(1):15-19.

Lifeng Qi and Xu Z, Invivo antitumar activity of chitosan nanoparticles. *Bioorganic and Med. Chemistry Letters*. 2006;16:4243-4245.

Maitra A, Banarje T, Mitra S, Sing AK and Sharma RK, Preparation, characterization and biodistribution of ultrafine chitosan nanoparticles. *Int. J. Pharm*s. 2002;243:93-105.

Rawat S, Malviya N and Motwani S, Smart Biodegratable polymeric Nanoparticles and their applications: A Review, *Indian Drugs*, 2008;45(8):601-605.

Vyas SP and Khar RK, Targeted and controlled Drug Delivery-Novel carrier systems.