IJPSR (2015), Vol. 6, Issue 11 (Research Article)

INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES AND RESEARCH

Received on 15 May, 2015; received in revised form, 07 July, 2015; accepted, 14 September, 2015; published 01 November, 2015

FORMULATION AND COMPARATIVE STUDIES OF LOVASTATIN LOADED POLYMERIC NANOPARTICLES PREPARED BY IONIC GELATION AND SOLVENT EVAPORATION TECHNIQUE

Vinodh S. Mannur, Karishma K. Majik, Vinayak S. Mastiholimath and Dylan A. Furtado

Department of Quality Assurance KLES, College of Pharmacy, Belagavi, Karnataka, India.

Keywords:

Lovastatin, Ionic gelation, Solvent evaporation, Sodium Tripolyphosphate, Pleuronic F68

Correspondence to Author:
Dr. Vinodh S. Mannur

KLES College of Pharmacy, Belagavi-590010, Karnataka, India.

E-mail: vsmannur72@gmail.com

ABSTRACT: Nanotechnology mediated drug delivery has been reported to enhance the drug efficacy, bioavailability, reduced toxicity and improve patient compliance by targeting the cells and tissues to elicit the desired pharmacological action. Low oral bioavailability of poorly water-soluble drugs poses a great challenge during development of drug delivery systems. The purpose of the present work was to compare the characteristics of Lovastatin (LV) nanoparticles prepared by Ionic gelation (IG) and Solvent evaporation (SE) techniques using Sodium Tripolyphosphate and Pleuronic F68 as surfactants. In this study, an attempt was made to improve the solubility and dissolution characteristics of a poorly water-soluble drug LV using nanotechnology concept. The prepared nanoparticles were evaluated in terms of size, drug polymer compatibility by differential scanning calorimetry (DSC), polydispersity index (PDI), zeta potential, morphological characteristics by scanning electron microscopy (SEM), drug entrapment efficiency *in-vitro* release and stability studies. Nanoparticles prepared by IG and SE were in the range of (108nm to 486 nm) and (389nm to 521nm) with PDI of 0.447 and 0.557 having entrapment efficiency 68.2% and 62.8% with 15.3mV and 13.5mV zeta potential. *In-vitro* release studies showed that the nanoparticle formulations IG_2B and SE_4B were capable of releasing the drug in a sustained manner (68.58% and 84.81%) for about 10hours. Together, these results indicated that nanoparticulate formulations are ideal carriers for oral administration of LV having a great potential to improve the oral bioavailability and sustain the drug release, thereby minimizing the dose dependent adverse effects and maximizing the patient compliance.

INTRODUCTION: Cardiovascular diseases, like atherosclerosis, are the most common reasons of mortality and morbidity worldwide [1, 2]. Atherosclerosis is a chronic, progressive disease that is characterized by continuous accumulation of plaque within the arterial wall, which is accelerated by risk factors such as hypercholesterolemia [3]. It is initiated by lipid retention, oxidation, and modification, which provoke chronic inflammation, ultimately causing thrombosis or stenosis [4].

QUICK RESPONSE CODE

DOI: 10.13040/IJPSR.0975-8232.6(11).4796-03

Article can be accessed online on: www.ijpsr.com

DOI link: http://dx.doi.org/10.13040/IJPSR.0975-8232.6(11).4796-03

Lovastatin belongs to the class of statins, and a class II drug according to Biopharmaceutical Classification Scheme (BCS), used for lowering cholesterol (hypolipidemic agent). It is a prodrug and after oral administration, the inactive parent lactone is hydrolyzed to the corresponding hydroxyacid form. Lovastatin is a fungal polyketide, which has a napthelin ring and a lactone ring, where the lactone ring binds to the 3-hydroxy-3-methylglutaryl-coenzym A (HMG-CoA) reductase enzyme and inhibits the formation of cholesterol. It's a poorly soluble drug, with a half-life of 1.1-1.7 h and less than 5% bioavailability. Lovastatin undergoes extensive first-pass metabolism. It is the drug of choice in primary hyperlipidemias with raised LDL and total cholesterol levels as well as for secondary i.e.

diabetes, nephritic syndrome, hypercholestoremia [5, 6, 7, 8].

An increased dose of molecularly targeted agents inside the diseased tissue will result in a satisfactory therapeutic response, creating a narrow efficiency/toxicity therapeutic window. An improvement of oral bioavailability of poor water-soluble drugs remains one of the most challenging aspects of drug development. Most data suggest that nanotechnologies could play a major role in the development of new therapies for pharmaceutical applications [9, 10]. Polymeric nanoparticles constitute a versatile drug delivery system, which can overcome physiological barriers and guide the drugs to specific cells/intracellular compartments. Methods used for preparing polymeric nanoparticles include ionic gelation, Co-acervation, solvent evaporation, spontaneous emulsification or solvent diffusion, salting out/emulsification-diffusion, supercritical fluid technology and polymerization using natural and synthetic polymers [11].

The objective of this work was to prepare the best formulation of Lovastatin nanoparticles with less particle size, uniform size distribution, higher entrapment efficiency, good percentage yield with good stability and to perform the comparative study of two formulation techniques. Two polymers (Chitosan and PVP K30) and two stabilizers (Sodium tripolyphosphate and Pleuronic F68) are used to formulate Lovastatin nanoparticles by two different techniques. Effects of stabilizers concentration on the formulation are studied. Formulated nanoparticles are evaluated for the parameters such as particle size, shape, zeta potential, drug loading capacity, *in vitro* release characteristics and stability studies.

MATERIALS AND METHODS:

Lovastatin was provided as a gift sample by Themis Pvt Ltd., Vapi, India. Chitosan and Sodium Tripolyphosphate were procured from Ozone International, Mumbai. PVP K30 and Pleuronic F68 were obtained from HiMedia Lab Pvt. Ltd, Mumbai. Acetone was obtained from RFCL Ltd., New Delhi, Methanol, Potassium dihydrogen phosphate and Sodium dihydrogen phosphate were obtained from Ranbaxy Fine Chem Ltd., New Delhi. All other chemicals used were of analytical grade.

Preparation of Lovastatin Nanoparticles by Ionic Gelation Technique: [12, 13]

Chitosan nanoparticles were prepared using ionic gelation of chitosan with TPP anions. Ionic gelation takes place when the positively charged amino groups in chitosan interact with the negatively charged TPP. Typically, different ratios of drug and polymer were dissolved in Methanol and 1.2% acetic acid solution respectively to get clear solution. pH was adjusted to 6.0 by adding 0.1N NaOH solution. Different concentrations of surfactants were designed to select the best concentration, which could provide high entrapment efficiency, percentage yield and desired particle size. STPP was dissolved in deionized water to obtain 0.1%, 0.2% and 0.3% solution. Drug solution and STPP solution was added drop wise to polymeric solution with continuous stirring using magnetic stirrer at 500rpm. Formulation was stirred for 30min and sonicated for 30min.The resultant nanoparticle suspensions were centrifuged at 10,000 rpm for 30min using centrifuge. Supernatants were discarded followed by freeze drying and nanoparticles were collected. Further evaluation studies were carried out for the freeze dried nanoparticles.

Preparation of Lovastatin Nanoparticles by Solvent Evaporation Technique: [10, 14]

Second method, Solvent evaporation method was adopted for the preparation of Lovastatin nanoparticles. Accurately weighed quantity of Lovastatin was dissolved in acetone. This was poured into solution containing different volume of water, PVPK-30 and PleuronicF68 maintained at room temperature and subsequently stirred at 1000rpm on magnetic stirrer for two hours to remove the volatile solvent. Organic solution was added to the aqueous solution containing surfactant by means of a syringe positioned with the needle directly into stabilizer/surfactant solution. The Nanoparticles were separated by centrifugation at 10,000rpm for 30min followed by separation of supernatant from precipitants. This precipitant containing nanoparticles was subjected for freeze drying and evaluation studies were carried out.

Effect of surfactants in nanoparticulate formulations:

Various concentrations of surface active agents were used as stabilizers and relationship between concentration of surfactant and particle size, PDI and entrapment efficiency are discussed. The optimal concentration of surfactant is important for optimal particles wetting. If the concentration is too low, particles float on the surface. If the concentration is too high bubbles appear. Effect of concentration was studied by keeping the Drug: Polymer proportion constant.

TABLE 1: FORMULATION OF LV-LOADED CHITOSAN NANOPARTICLES

Ingredients	IG1	IG2	IG3	IG4	IG_2A	IG_2B	IG_2C
Lovastatin (mg)	10	10	10	10	10	10	10
Chitosan (mg)	10	20	30	40	20	20	20
STPP (%)	0.2	0.2	0.2	0.2	0.1	0.2	0.3
Drug: Polymer	1:1	1:2	1:3	1:4	1:2	1:2	1:2

TABLE 2: FORMULATION OF LV-LOADED PVP K30 NANOPARTICLES

Ingredients	SE1	SE2	SE3	SE4	SE_4A	SE_4B	SE_4C
Lovastatin (mg)	10	10	10	10	10	10	10
PVP K30 (mg)	10	20	30	40	40	40	40
PleuronicF68(%)	0.03	0.03	0.03	0.03	0.01	0.02	0.03
Drug: Polymer	1:1	1:2	1:3	1:4	1:2	1:2	1:2

Characterization of prepared nanoparticles [15, 16]:

1. **Particle Size and PDI:**

   The size of drug nanoparticles was measured by dynamic laser scattering (NPA150, Microtrac, USA). The analysis was performed at a measuring angle of 180° and at a temperature of 25°C using samples appropriately diluted with Millipore filtered water (0.22 µm filter).

2. **Percentage yield:**

   The percentage yield of prepared nanoparticles was determined from equation (1).

$$\text{Percentage yield} = \frac{\text{Amount of nanoparticles}}{\text{Amount of drug and polymer}} \times 100 \quad \text{.....Eq (1)}$$

3. **Determination of drug content and entrapment efficiency:**

   Drug was extracted from the freeze-dried nanoparticles using buffer solution (pH 6.8) and the amount of drug was measured after suitable dilutions by UV spectroscopy at 238nm(Shimadzu UV 1800).

   Drug content and entrapment efficiency was calculated using following equation (2) and equation (3) respectively.

$$\text{Drug Content} = \frac{\text{Analyzed weight of drug in nanoparticle}}{\text{Theoretical weight of drug in nanoparticle}} \times 100 \quad \text{.....Eq (2)}$$

$$\text{The Entrapment Efficiency (\%)} = \frac{W_{initial} - W_{free\ drug}}{W_{initial}} \times 100 \quad \text{.....Eq (3)}$$

4. **Zeta potential:**

   It is a physical property of a suspension. It is defined as the potential difference between the bulk solution (dispersing medium) and the surface of the hydrodynamic shear (slipping plane). It can be used as an optimizing tool to determine stability of the nanoparticle formulation. It was measured by surface potential using dynamic light scattering technology (NPA152-31A Zetatrac, Microtrac, USA) joined with the interaction of random Brownian motion with driven electric field motion of particle suspensions.

5. **Shape and surface morphology:**

   Shape and surface morphology of LV loaded nanoparticles was done by Scanning Electron Microscopy (JSM-T330A, JEOL). SEM is the most commonly used method for characterizing the shape and surface structure of drug delivery systems because of its simplicity in sample handling and ease of operation.

6. **Differential scanning calorimetry:**
Differential scanning calorimetry (DSC) analyses of samples were carried out on DSC-60 (Shimadzu, Japan). Temperature and enthalpy were calibrated with the standard materials indium (melting point = 156.6^{o}C) and zinc (melting point = 419.5^{o}C) at a heating rate of 5^{o}C/min. DSC studies were performed to understand the behavior of the polymers on application of thermal energy.

7. ***In vitro* drug release study:**
The *in vitro* drug release studies were performed by using dialysis bag diffusion technique on optimized formulations of nanoparticles. Nanoparticles were dispersed in 5 ml of phosphate buffer (pH 6.8) and then put in the dialysis bags (Himedia Laboratories, Mumbai, India) with a cut-off molecular weight of 12,000–14,000 Da. The bags were hermetically sealed and immersed in a beaker containing 100 ml of phosphate buffer of pH 6.8. The contents were stirred continuously with a magnetic stirrer at 50 rpm. At predetermined time intervals, 1 ml of dispersion medium was withdrawn and analyzed for drug content by UV-spectrophotometry at 238nm after suitable dilution. The removed volume of dispersion medium was replaced with equivalent volume of fresh dispersion medium to maintain the sink conditions. The percentage cumulative drug release data was fitted into various release models (Zero order, First order, Higuchi model and Korsemeyer-Peppas model) to understand the mechanism of drug release. The release model having r^2 value (Regression Coefficient) close to one was considered as best fit model using the software PCP-Disso-V3.

8. **Stability Studies:**
Stability study was carried out for the optimized formulations obtained by both the methods respectively. Formulations were divided into three sets of samples and stored at -2˚C in refrigerator, room temperature (29˚C), 45 ± 2˚C/75% RH in humidity control chamber. Stability of the formulations were predicted from the results obtained for particle size distribution, PDI and entrapment efficiency after storing at room temperature, 45 ± 2˚C/75% RH and -2^{o}± 1^{o}C for 30days and 60days.

RESULTS AND DISCUSSION:

Physicochemical characterization of nanoparticles:

The average particle sizes of the prepared drug loaded nanoparticles by two methods were recorded. The minimum particle sizes of the nanoparticles prepared by the IG technique and SE technique were found to be approximately 108nm and 389nm. The PDI of optimized nanoparticles was found to be 0.447 and 0.557 for formulations IG_2B and SE_4B. PDI indicates the width of the particle size distribution, which ranges from 0 to 1. Theoretically, a monodisperse population indicates PDI equal to zero.

Nanoparticles prepared by IG technique using chitosan as polymer exhibited higher entrapment efficiency than nanoparticles prepared by SE technique using PVP K30 as polymer. This may be due to the larger size of nanoparticles prepared by IG technique than SE technique which could support a larger space for lovastatin encapsulation.

The results obtained for particle size, percentage yield and entrapment efficiency by Ionic gelation and Solvent evaporation method is displayed in **Table 3** and **Table 4** respectively.

The zeta potential of the optimized nanoparticle formulations was determined and it was found that formulation IG_2B showed better stability bearing value of 15.3mV in comparison with formulation SE_4B having the value of 13.5mV (**Figure 1**). These values indicated that the optimized formulations are moderately stable.

The SEM of LV nanoparticles prepared by both the techniques indicated that the nanoparticles have a nearly spherical structure with smooth surface. DSC is a useful tool to monitor the effect of additives on the thermal behavior of materials, and used to derive qualitative information about the

physicochemical status of drug in nanoparticles. The DSC thermograms of LV-loaded Chitosan nanoparticles and LV-loaded PVP K30 nanoparticles are shown in (**Fig. 2**). LV showed a sharp characteristic endothermic peak at 175.2^{o}C which corresponded to its intrinsic melting point indicating its crystalline nature. DCS thermogram of LV-Chitosan and LV-PVP K30 nanoparticles showed endothermic peaks at 170.4^{o}C and 165.4^{o}C respectively. However, no distinctive melting peak of LV was identified in the DSC curve obtained from LV-loaded nanoparticles suggesting that LV in nanoparticles was molecularly dispersed as an amorphous form.

TABLE 3: CHARACTERISTICS OF LV LOADED CHITOSAN NANOPARTICLES

Formulation Code	Drug : polymer ratio	LV entrapment (%)	Percentage Yield (%)	Particle size (nm)	PDI
IG1	1:1	51.5	61.5	108	0.825
IG2	1:2	68.2	70.8	202	0.447
IG3	1:3	69.2	72.3	315	0.779
IG4	1:4	71.1	73.6	486	0.350

TABLE 4: CHARACTERISTICS OF LV LOADED PVP K30 NANOPARTICLES

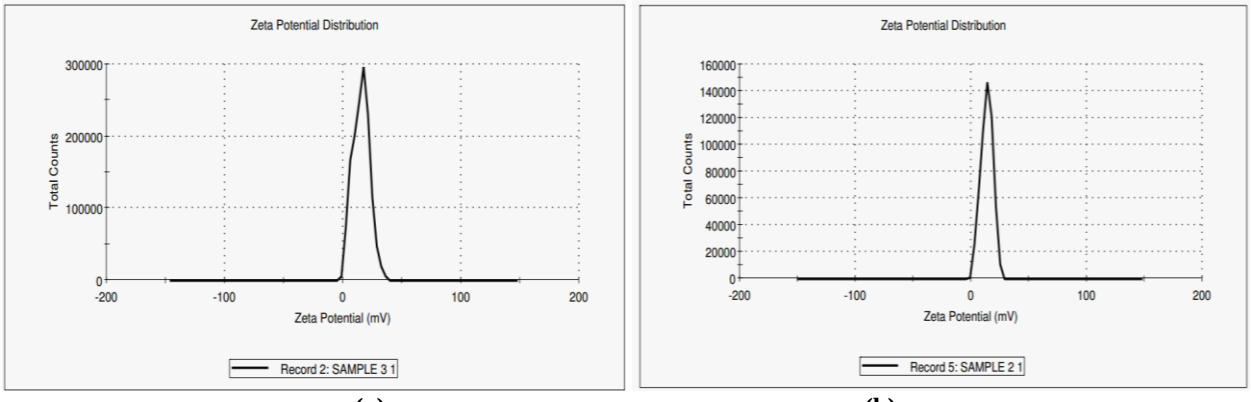
Formulation Code	Drug : polymer ratio	LV entrapment (%)	Percentage Yield (%)	Particle size (nm)	PDI
SE1	1:1	46.7	48.9	389	0.826
SE2	1:2	52.4	52.7	460	0.708
SE3	1:3	55.9	54.3	523	0.427
SE4	1:4	63.8	61.7	521	0.557

Study of the surfactant concentration:

Three different concentrations of surfactant for each optimized method were tried keeping drug polymer ratio constant and the results are listed in **Table 5**. When less concentration of surfactant was used, the size of nanoparticles was higher with greater entrapment efficiency and as the concentration of surfactant was increased the particle size was reduced with lesser entrapment efficiency. Based on this, 0.2% turned out to be the best concentration for LV-loaded chitosan nanoparticles and 0.02% turned out to be the best concentration for LV-loaded PVP K30 nanoparticles.

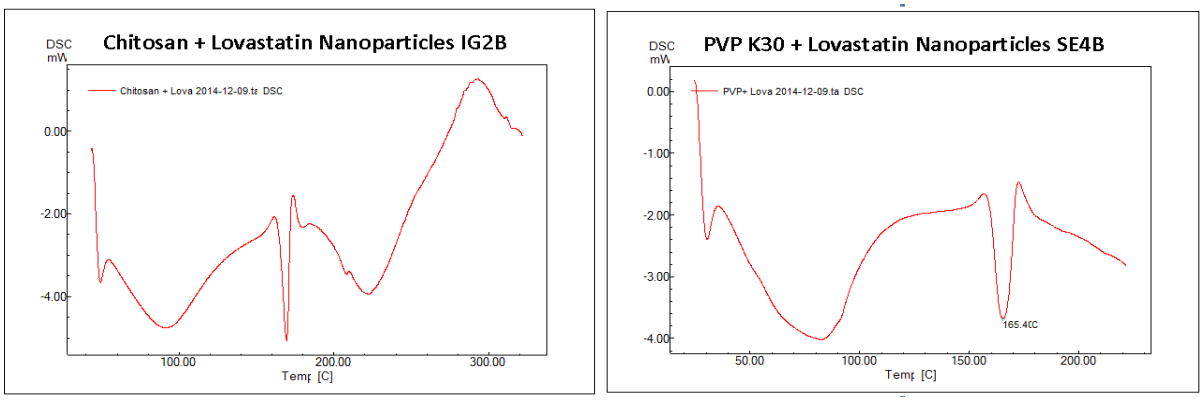
TABLE 5: EFFECT OF SURFACTANTS CONCENTRATION

Polymer	Formulation Code	Surfactant Conc (%)	Entrapment Efficiency (%)	Percentage Yield (%)	Particle Size (nm)	PDI
Chitosan	IG_2A	0.1	52.7	56.7	516	0.299
	IG_2B	0.2	68.2	70.8	202	0.447
	IG_2C	0.3	67.3	70.7	160.2	0.441
PVP K30	SE_4A	0.01	58.4	49.2	776	0.786
	SE_4B	0.02	63.8	61.7	521	0.557
	SE_4C	0.03	64.3	57.7	523	0.426



(a) **(b)**

FIG.1: ZETA POTENTIAL OF OPTIMIZED NANOPARTICLE FORMULATIONS:(a) IG_2B and (b) SE4B



(a) **(b)**

FIG.2: DSC THERMOGRAM OF OPTIMIZED NANOPARTICLE FORMULATIONS: (a) IG_2B and (b) SE_4B

***In-vitro* release study of the optimized nanoparticle formulations:**

Cumulative percentage drug released from the optimized formulations IG_2B and SE_4B after 10hrs were found to be 68.58% and 84.81% respectively (**Table 6, Fig. 3**). It was apparent that *in vitro* release of Lovastatin showed a very rapid initial burst, followed by a very slow drug release. An initial, fast release suggested that more amount of the drug was entrapped near the surface of the naonparticles due to larger surface area, rather than inside the particles. *In vitro* kinetics analysis showed that drug release was best explained by Korsmeyer-Peppas model than other model with highest value of Regression Coefficient (r^2=0.9974) and (r^2=0.9914) for IG and SE techniques respectively. The release was found to follow zero order release kinetics with Fickian diffusion mechanism for both the optimized formulation.

TABLE 6: *IN-VITRO* RELEASE PROFILE OF OPTIMIZED FORMULATIONS IG_2B AND SE_4B

Time (Hrs)	FORMULATION CODE	
	IG_2B (%CDR)	SE_4B (%CDR)
0	0	0
1	17.371	19.269
2	26.687	27.068
3	36.095	42.550
4	43.309	53.113
5	46.020	58.706
6	51.039	63.590
7	56.104	67.502
8	61.215	73.222
9	64.086	78.993
10	68.580	84.814

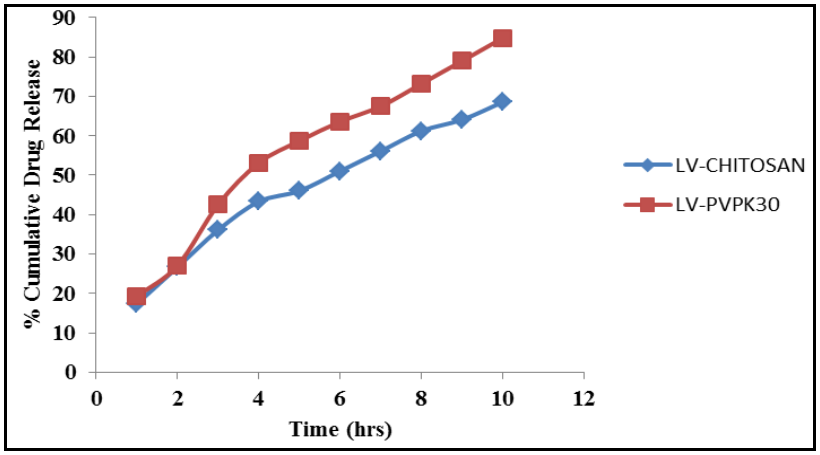


FIG.3: CUMULATIVE RELEASE OF NANOPARTICLES

Stability Studies:

The results of particle size and PDI of the optimized formulations IG_2B and SE_4B after 30 days and 60 days of stability testing at different storage conditions are shown in **Table 6 & 7.**

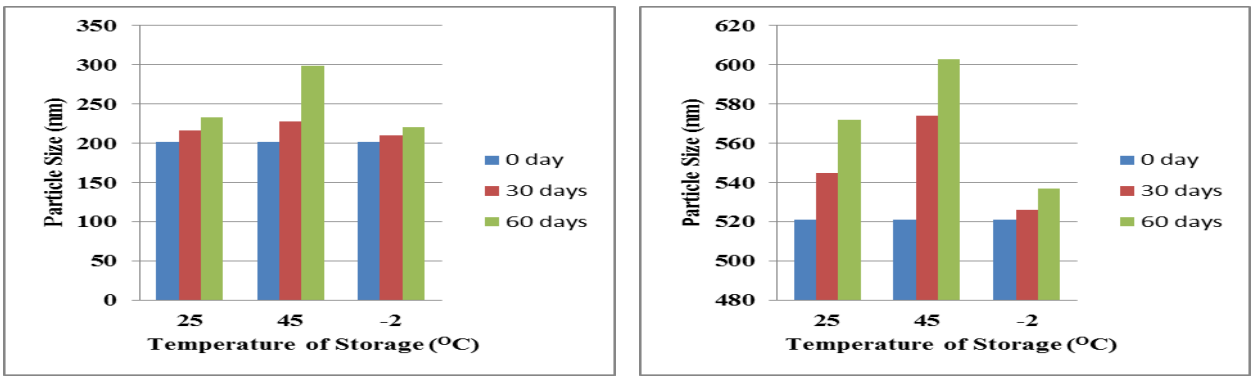
On comparing this data of formulations IG_2B and SE_4B **Fig.4 (a), (b)**, it was observed that there was slight increase in particle size when the formulation was stored at Room temperature, but there was a significant increase in particle size when stored at 45 ± 2˚C/75% RH, which indicated that high temperature can lead to aggregation and sedimentation of the particles after a period of time. Also it was observed that there was decrease in drug content when the formulations were stored at 45 ± 2˚C/75% RH, which suggested that drug gets degraded at that temperature hence decrease in the drug release was observed.

TABLE 6: PHYSICAL STABILITY RESULT OF IG_2B

Sr. no.	Time storage	Room temp.			45 ± 2˚C			-2^0c		
		Size	PDI	%EE	Size	PDI	%EE	Size	PDI	%EE
1.	0 day	202.0	0.44	68.2	202.0	0.44	68.2	202.0	0.44	68.2
2.	30 days	216.6	0.48	65.9	228	0.53	59.3	210.4	0.49	67.1
3.	60 days	233	0.56	63.3	299	0.62	51.7	220	0.54	65.0

TABLE 7: PHYSICAL STABILITY RESULT OF SE_4B

Sr. no.	Time storage	Room temp.			45 ± 2˚C			-2^0c		
		Size	PDI	%EE	Size	PDI	%EE	Size	PDI	%EE
1.	0 day	521	0.55	63.8	521	0.55	63.8	521	0.55	63.8
2.	30 days	545	0.57	58.6	574	0.61	55.6	526	0.59	60.3
3.	60 days	572	0.65	56.4	603	0.72	49.0	537	0.61	59.6



(a) **(b)**

FIG.4: COMPARITIVE STABILITY STUDY OF PARTICLE SIZE OF FORMULATION (a) IG_2B AND (b) SE_4B AT -2˚C, ROOM TEMPERATURE (25± 2˚C/60% ± 5% RH) AND 45 ± 2˚C/75% RH

CONCLUSION: Based on particle size, drug content, drug entrapment efficiency and polydispersity index formulations IG_2B and SE_4B were selected as an optimum formulation prepared by Ionic gelation method and solvent evaporation method respectively. Stability studies showed that LV nanoparticles prepared using IG technique are more stable as compared to nanoparticles prepared by SE technique. Also chitosan nanoparticles showed more sustained effect in comparison to PVP K30 nanoparticles. On comparing the *in vitro* drug release profile of formulations prepared by IG and SE, SE_4B was showing maximum drug release (84.81%) in a time period of 10hrs. The maximum drug release was may be because of poor entrapment of the drug.

ACKNOWLEDGEMENTS: The authors thank to Shivaji University Kolhapur and Manipal College of Pharmacy for providing SEM and Zeta Potential facilities to carry out this work.

REFERENCES:

1. Dhanalakshmi R, Balamurugan K and Manavalan R: Hypolipidemic and Antiatherosclerotic Activity of Some Medicinal Plants: A Review. World Journal of Pharmacy and Pharmaceutical Sciences 2014; 3:328-340.
2. Srinivas M, Annapurna A and Reddy YN: Anti-atherosclerotic effect of atorvastatin and clopidogrel alone

and in combination in rats. Indian Journal of Experimental Biology 2008; 46:698-703.
3. Davidson MH, Gandhi SK and Ohsfeldt RL, Fox KM: Hypercholesterolemia Treatment Patterns and Low-Density Lipoprotein Cholesterol Monitoring in Patients with a Diagnosis of Atherosclerosis in Clinical Practice. The American Journal of Medicine 2009; 122:51-9.
4. Insull WJ: The Pathology of Atherosclerosis: Plaque Development and Plaque Responses to Medical Treatment. The American Journal of Medicine 2009; 122:3-14.
5. Raja RK, Abbulu K, Sudhakar M, Vishwanadham M and Tejaswini MS: Studies on Dissolution Enhancement of Lovastatin Using Soluplus by Solid Dispersion Technique. International Journal of Pharmacy and Pharmaceutical Sciences 2012; 4:124-128.
6. Neduri K, Bontha VK and Vemula SK: Different Techniques to Enhance the Dissolution Rate of Lovastatin: Formulation and Evaluation. Asian Journal of Pharmaceutical and Clinical Research 2013; 6:56-60.
7. Rao BB, Saikat D, Kumar TA and Swathi V: Formulation and In Vitro Evaluation Of Lovastatin Buccal Tablets. International Research Journal of Pharmacy 2013; 4(12):16-19.
8. Radha KV, Lakshmanan D: A Review: Lovastatin Production and Applications. Asian Journal of Pharmaceutical and Clinical Research 2013; 6:21-26.
9. Agoston-Coldea L: Advances in Atherosclerotic Plaque Targeting, Imaging and Treatment Using Nanotechnology and Stem Cells Research. Biotechnology, Molecular Biology and Nanomedicine 2013; 1:21-27.
10. Patel DJ, Patel JK, Pandya VM and Patel RD: Effect of Formulation variables on Nanosuspension Containing Famotidine Prepared by Solvent Evaporation Technique. International Journal of Pharmaceutical Sciences and Nanotechnology 2010; 2:707-713.
11. Sreelola V and Sailaja AK: Preparation and Characterisation of Ibuprofen Loaded Polymeric Nanoparticles by Solvent Evaporation Technique. International Journal of Pharmacy and Pharmaceutical Science 2014; 6:416-421.
12. Kaur SP, Rao R, Hussain A and Khatkar S: Preparation and Characterization of Rivastigmine Loaded Chitosan Nanoparticles. Journal of Pharmaceutical sciences and Research 2011; 3:1227-1232.
13. Kumar P, Kumar P, Rajoria G and Narang RK: Techniques for Preparation of Pharmaceutical Coated Nanoparticles: A Comprehensive Review. American Journal of Pharmtech Research 2012; 2:121-135.
14. Nagavarma BVN, Yadav HKS, Ayaz A, Vasudha LS and Shivakumar HG: Different Techniques for Preparation of Polymeric Nanoparticles-A Review. Asian Journal of Pharmaceutical and Clinical Research 2012; 5:16-24.
15. Nesalin JAJ and Smith AA: Preparation and evaluation of chitosan nanoparticles containing zidovudine. Asian Journal of Pharmaceutical Sciences 2012; 7:80-84.
16. Bhosale UV and Devi VK: Preparation and *In Vitro* Evaluation of Acyclovir Loaded Eudragit RLPO Nanoparticles as Sustained Release Carriers. RGUHS Journal of Pharmaceutical Sciences 2011; 1:85-92.

How to cite this article:
Mannur VS, Majik KK, Mastiholimath VS and Furtado DA: Formulation and Comparative Studies of Lovastatin Loaded Polymeric Nanoparticles Prepared by Ionic Gelation and Solvent Evaporation Technique. Int J Pharm Sci Res 2015; 6(11): 4796-03.doi: 10.13040/IJPSR.0975-8232.6(11).4796-03.