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Formulation And In Vitro Characterization Felodipine Loaded Liposphere to Enhace Its Oral Bioavailbility

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ABSTRACT: The present study focuses on the formulation and in vitro characterization of felodipine-loaded lipospheres for oral drug delivery. Felodipine is a lipophilic calcium channel blocker used in the treatment of hypertension and stable angina. The study was undertaken to investigate the feasibility of incorporating felodipine into a lipid-based carrier system and to characterize the resulting formulations. Preformulation studies were performed to evaluate the organoleptic properties, melting point, solubility, partition coefficient, and Fourier-transform infrared (FTIR) characteristics of the drug. Felodipine-loaded lipospheres were prepared using the melt-dispersion method, with stearic acid as the lipid carrier and poloxamer 188 as the stabilizing surfactant. Ten formulations (FL1–FL10) were developed by varying the quantities of stearic acid and poloxamer 188 and the homogenization speed. The prepared formulations were evaluated for physical appearance, percentage yield, drug entrapment efficiency, drug loading, particle size, and in vitro drug release. The results demonstrated variation in formulation characteristics depending on the composition and preparation conditions. The study describes the development and preliminary in vitro evaluation of felodipine-loaded lipospheres and provides a basis for further investigation of their drug-release behaviour and suitability for oral delivery.

KEYWORDS: Felodipine, Lipospheres, Lipid-based drug delivery, Stearic acid, Drug entrapment

I. Introduction

Lipospheres are lipid based water dispersible solid particles bearing particle size between 0.01 and 100 µm in diameter, composed of a solid hydrophobic lipid core containing active drug moiety dissolved or dispersed in a solid fat matrix, which is stabilized by a layer of phospholipid molecules as external coat.[1-5] Lipospheres are composed of solid lipid core surrounded by a single unit phospholipid layer that may entrap the drug or enrich its coat with the drug. The emulsifier or stabilizer is used to form uniform coat around the core material and to facilitate partitioning of the drug between the lipid and aqueous phases.[3,4] Low molecular polyethylene glycols (PEGs), as plasticizers could impart tensile strength to the external lipid coat. Improved stability of the drug in the formulation, freeze dry and reconstitution properties, controlled particle size, high-drug load, well controlled drug release and no carrier toxicity made liposphere systems superior over other particulate delivery systems such as emulsions, liposomes and microspheres.[6,7] In addition, lipospheres protect the drug candidates from hydrolysis, corroborate the shelf life facilitating high bioavailability and prolonged plasma levels.[8] The lipospheres offer well controlled delivery to a variety of drug candidates like antiinflammatory compounds, local anesthetics, antibiotics and anticancer agents. The lipid entrapped vaccines were administered with an adjuvant effect through liposphere systems.

Felodipine is a medication of the calcium channel blocker type that is used to treat high blood pressure. Felodipine has additionally been found to act as an antagonist of the mineralocorticoid receptor, or as an antimineralocorticoid. Felodipine is used to treat stable angina.It should not be used for people who are pregnant, have acute heart failure, are having a heart attack, have an obstructed heart valve, or have obstructions that block bloodflow out of the heart.For people with liver failure the dose needs to be lowered, because felodipine is cleared by the liver.

Stearic acid is a hard, white or faintly yellow-colored, somewhat glossy, crystalline solid or a white or yellowish white powder. It has a slight odor and taste suggesting tallow. Stearic acid is widely used in oral and topical pharmaceutical formulations. It is mainly used in oral formulations as a tablet and capsule lubricant; [9.10], although it may also be used as a binder or in combination with shellac as a tablet coating. It has also been suggested that stearic acid may be used as a sustained-release drug carrier. In topical formulations, stearic acid is used as an emulsifying and solubilizing agent. [11]

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II. MATERIAL AND METHOD

1.1. MATERIAL

Felodipine was obtained from TCI and excipients Ethanol was obtained from Chamgshu Yangyuan Chemical, China, Methanol from Merck Ltd., n-Octanol, Potassium dihydrogen phosphate, Di-sodium hydrogen phosphate, Stearic acid, Sodium Hydroxide, and Chloroform from S.D. Fine chemicals Ltd., Dichloromethane was obtained from Loba Chemie, Mumbai, Span 80 from Avarice lab. Pvt. Ltd. and Poloxamer 188 from BASF.

2. Experimental work

2.1. Preformulation studies

2.1.1. Melting point

This determination was made using the capillary fusion method and a digital capillary melting point device. The experiment was performed in triplicate.[12]

2.1.2. Solubility

2 mL of each solvent and almost 100 mg of drug were put to a glass culture tube. After that, the combinations were shaken in a water bath for 24 hours. Sample temperatures were 25.0±0.1 °C. After suitable dilution and interpolation from previously created calibration curves, UV absorbance at 250 nm was measured to estimate the solution concentrations. The experiment was performed in triplicate. [12]

2.1.3. Partition coefficient studies

4ml of the mixture of n-octanol and water in the glass culture tube received close to 100 mg of the drug. After that, the combinations were shaken in a water bath for 24 hours. Sample temperatures were 25.0 0.1 °C. Drug concentration in octanol to drug concentration in water was used to calculate the partition coefficient, and the results were given as log P.[12]

$$\text{Log p} = \frac{\textit{concentration of drug in non aqueous phase}}{\textit{concentration of drug in aqueous phase}}$$

2.1.4. Preparation of standard plot of felodipine in methanol

10 mg of the medication were dissolved in 100 ml of methanol in a volumetric flask, and a stock solution containing 100 g/ml was created. Appropriate dilutions were made from this working standard solution to yield 4–40µg/ml. All sample solutions were made in triplicate using stock, and a UV-visible spectrophotometer was used to measure absorbance at 362 nm wavelength against the solvent methanol as a blank. The calibration curve was drawn by plotting the absorbances versus concentration [12].

2.1.5. FT-IR Analysis

Infrared Fourier transform to identify that specific compound; spectroscopies of other substances were run. FT-IR Spectroscopy of the final, improved formulation of the pure medication felodipine was carried out using KBr pellets. Different peaks in the FT-IR spectrum were interpreted to identify various groups in the pure drug's optimized formulation. The investigation and forecasting of any physicochemical interactions between various components can also be done using FT-IR spectroscopy. [12]

2.2. Preparation of liposphere using melt dispersion method

By utilizing the melt dispersion (homogenization) approach, felodipine-loaded lipospheres were created. Felodipine was used to create the lipid phase that contained stearic lipid. Felodipine was then added to the lipid phase after it had melted at 70°C. By mixing surfactant Poloxamer 188 in hot distilled water above the melting point of the lipid phase at 80°C and dissolving it, the aqueous phase was generated separately. The addition of hot, external, 80°C-maintained aqueous phases containing an appropriate surfactant was used to emulsify the lipid phase. Using an HIGH speed homogenizer, the emulsion was homogenised while being kept at a temperature of 80 °C. In order to achieve uniform liposphere dispersion, the emulsion formulation was then quickly chilled to around 10 °C by submerging it in an ice bath while still being stirred. Following a water wash, the isolated lipospheres were filtered through whattman filter paper. [13]

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Table 1: Composition of felodipine loaded oral liposphere

S.No.	Formulation code	Felodipine (mg)	Stearic acid (mg)	Poloxamer 188 (mg)	Homogenization (rpm)
1	FL1	10	250	100	7000
2	FL2	10	350	100	7000
3	FL3	10	450	100	7000
4	FL4	10	550	100	7000
5	FL5	10	650	100	7000
6	FL6	10	450	50	7000
7	FL7	10	450	150	7000
8	FL8	10	450	150	6000
9	FL9	10	450	150	8000
10	FL10	10	450	150	9000

2.3. Characterization and evaluation of liposphere of felodipine:

2.3.1. Percentage (%) yield

Weighing was done after the prepared liposphere was gathered. The total weight of the drug and excipients was divided by the measured weight. The % yield was calculated using following formula:

$$\text{Percentage Yield} = \frac{\text{Total formulation weight}}{\text{Total weight of excipient + drug}} \times 100$$

2.3.2. Particle size analysis

The optical microscopy method was used to measure the liposphere's particle size. For the purpose of measuring particle size, 100 lipospheres were counted using a calibrated optical microscope. [13]

$$\text{Particle Size} = \frac{\sum nd}{\sum n} * \text{Least count}$$

Here, $\sum n$ = no. of particles

$\sum nd$ = average diameter

2.3.3. Percentage drug entrapment

By dissolving the top lipid layer of the lipospheres in chloroform, it was possible to determine the drug content. Dried lipospheres weighing precisely 100 mg per batch were dissolved in a 9 ml methanol. To get a clear solution, the obtained solution was sonicated for five minutes at a speed of 15000 rpm. Whatman filter paper 42 was used to filter the sediment, which was then utilized to determine the amount of felodipine present in the methanol. Following dilutions in methanol solution, a wavelength of 250 nm was used for spectrophotometric scanning. Straight line equation was used to compute the drug content.[14,15]

Percentage drug entrapment =Initial amount- Final amount/ Initial amount *100

2.3.4. In vitro dissolution studies

The USP Basket technique of dissolving was used to examine the drug release of felodipine from the lipospheres. A capsule was loaded with enough lipospheres to make up 10mg of felodipine in total. Using a USP type I basket dissolution apparatus maintained at 37°C 0.5°C, under stirring at 100 rpm, in vitro drug release was carried out in acidic buffer 0.1 N HCl (pH-1.2) for 2 hours and 6.8 Phosphate buffer for 12 hours. Periodically, samples were taken out (0 min, 30 min, 1 hr, 2 hr, 4 hr, 6 hr, 8 hr, 10 hr, 12 hr), and the same volume was immediately replaced with new medium. Sample solutions were filtered, properly diluted, and examined using a UV-visible spectrophotometer to measure absorbance at 250 nm.[16]

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3. Result and discussion

3.1. Preformulation study

3.1.1. Organoleptic properties

Drug felodipine was discovered to have organoleptic qualities that matched the literature. The observation confirmed it appeared as White to pale yellow crystalline powder.

3.1.2. Melting point

Melting point of drug was determined by capillary fusion method.

Table 2: Melting point of Felodipine

Drug	Specification	Observation
Felodipine	141-145°C	141±1°C-145±1°C

The melting point of drug was found to be range 141±1°C-145±1°C, hence drug sample was free from any type of impurities.

3.1.3. Preparation of Standard Calibration curve of felodipine in methanol

Table 3: Calibration curve of felodipine in methanol

S.No.	Concentration (µg/ml)	Absorbance
1	5	0.173±0.002
2	10	0.267±0.003
3	15	0.365±0.002
4	20	0.456±0.002
5	25	0.538±0.005
6	30	0.640±0.003
7	35	0.748±0.003
8	40	0.845±0.003

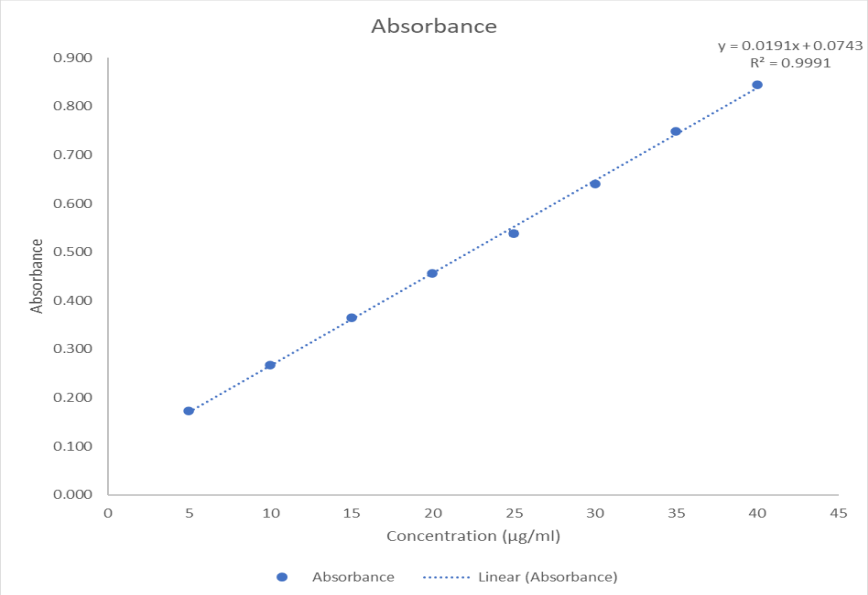

Figure 1: Calibration curve of felodipine in methanol

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The 5 to 40 µg/ml solution of felodipine in methanol was used to create the calibration curve for felodipine. At 362 nm, the absorbance was measured. Figure 1 representation of the felodipine calibration curve revealed the regression equation y = 0.0191x + 0.0743and an R^2 value of 0.999, indicating good linearity.

3.1.4. Solubility studies of drug

The solubility of drug in different solvent as given below:

Table 4: Solubility of the felodipine

S.No.	Solvent	Solubility (mg/ml)
1	Water	0.088±0.004
2	Methanol	81.016±0.419
3	Ethanol	50.859±0.583
4	Phosphate Buffer 6.8pH	0.257±0.005

3.1.5. Partition coefficient of drug

The shake flask method was used to carry out the investigation on partition coefficient determination. Felodipine was discovered to have a partition coefficient of 4.178±0.162 in n- Octanol: Water. This suggests that the medication has a lipophilic character.

3.1.6. FTIR analysis

Figure 2: FTIR spectrum of felodipine

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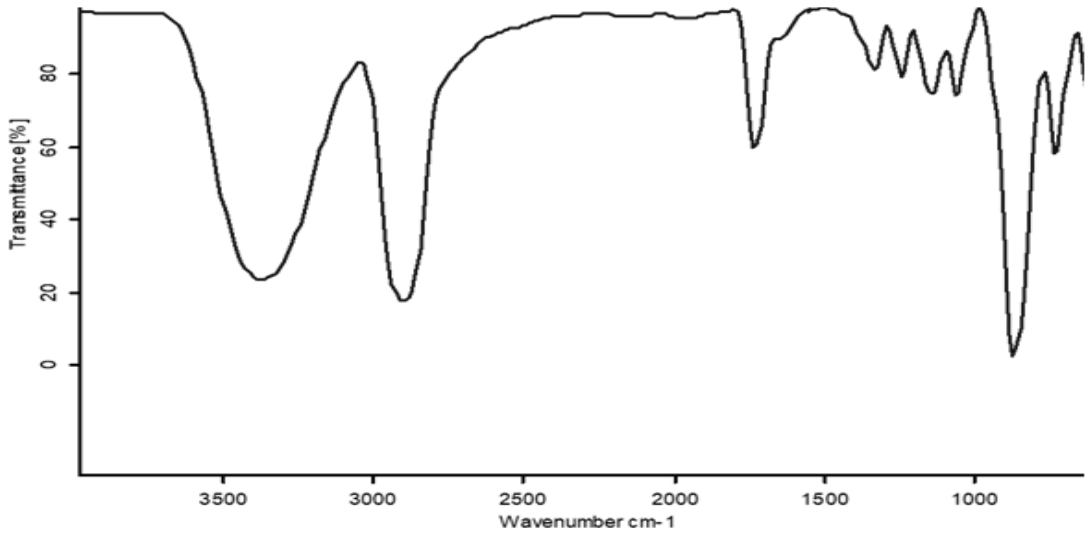

Figure 3: FTIR spectrum of optimized formulation

The FTIR spectral analysis of FD alone showed that the principal peaks were observed at wave numbers of 3437.47 cm−1 (N-H stretching), 1431.12 cm−1 (C-H stretching), and 1679.09 cm−1 (C=O stretching). Less intense peaks were seen in the felodipine liposphere properties, indicating that the drug had been incorporated into the lipid matrix.

3.2. Evaluation of felodipine containing liposphere

3.2.1. Appearance and percentage yield

Appearance and percentage yield of drug containing different liposphere was given below.

Table 5: Appearance and percentage yield of drug containing different liposphere

S.no.	Formulation code	Appearance
1	FL1	Spherical shape, uniform particle was formed
2	FL2	Spherical shape, uniform particle was formed
3	FL3	Spherical shape, uniform particle was formed
4	FL4	Spherical shape, uniform particle was formed
5	FL5	Spherical shape, uniform particle was formed
6	FL6	Spherical shape, uniform particle was formed
7	FL7	Spherical shape, uniform particle was formed
8	FL8	Spherical shape, uniform particle was formed
9	FL9	Spherical shape, uniform particle was formed
10	FL10	Spherical shape, uniform particle was formed

Table 5 demonstrated that all lipospheres formulations were spherical in shape and uniform.

3.2.2. Percentage yield

Percentage yield of all different liposphere formulations were given below.

Table 6: Percentage yield of different liposphere formulation

S.No.	Formulation code	Percentage yield
1	FL1	96.514±0.534
2	FL2	97.545±0.048
3	FL3	98.420±0.024
4	FL4	98.798±0.009

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5	FL5	99.000±0.019
6	FL6	98.193±0.113
7	FL7	99.236±0.031
8	FL8	99.723±0.023
9	FL9	99.936±0.025
10	FL10	99.785±0.014

It showed the percentages yield for the entire drug-loaded liposphere formulation, which were respectively determined to range from 96.514±0.534% 99.936±0.025%. The percentage yield increased along with the lipid content, and at the same time.

3.2.3. Percentage drug entrapment and Percentage Drug loading

Percentage drug entrapment and percentage drug loading of all different liposphere formulations were given below.

Table 7: Percentage Drug entrapment of different liposphere formulation

S.No.	Formulation code	Percentage drug entrapment
1	FL1	21.774±0.948
2	FL2	55.276±0.975
3	FL3	90.284±0.612
4	FL4	89.587±1.218
5	FL5	91.327±1.057
6	FL6	86.635±0.080
7	FL7	95.921±0.850
8	FL8	75.792±0.669
9	FL9	96.670±0.981
10	FL10	92.495±1.033

Table 8: Percentage Drug loading of different liposphere formulation

S.No.	Formulation code	Percentage drug loading
1	FL1	2.464±0.047
2	FL2	2.455±0.063
3	FL3	2.576±0.054
4	FL4	2.374±0.003
5	FL5	2.428±0.010
6	FL6	2.420±0.023
7	FL7	2.497±0.091
8	FL8	2.557±0.086
9	FL9	2.453±0.067
10	FL10	2.436±0.096

These showed the drug entrapment and drug loading for the entire drug-loaded liposphere formulation, which were respectively determined to range from 21.774±0.948% to 96.670±0.981% and 2.374±0.003% to 2.557±0.086%. The percentage drug loading increased along with the lipid content, and at the same time, the percentage of drug entrapment increased.

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3.2.4. Particle size

Particle size of different liposphere formulation was given below.

Table 9: Particle size of different formulation

S. no.	Formulation code	Particle size (µm)
1	FL1	2.593±0.035
2	FL2	4.910±0.040
3	FL3	6.200±0.026
4	FL4	8.987±0.041
5	FL5	10.517±0.386
6	FL6	8.937±0.032
7	FL7	7.077±0.020
8	FL8	10.560±0.330
9	FL9	5.457±0.197
10	FL10	3.130±0.046

Table 9 showed that the range of particle sizes for all microparticle formulations was 2.593±0.035µm to 10.560±0.330 µm. The mean particle size increased as lipid concentration increased.
The FL9 formulation was chosen for additional examination based on the aforementioned in vitro assessment of all liposphere formulations.

3.2.5. *In-Vitro* Drug Release Studies

Percentage in-vitro drug release study FL9 formulation and pure drug was given below.

Table 10: Percentage Drug Release of FL9 Formulation

Time(min.)	Percentage Drug release of pure drug suspension	Percentage Drug release of formulationFL9
0	0.000±0.00	0.000±0.00
0.5	40.618±0.090	5.749±1.670
1	59.937±0.340	15.408±0.560
2	99.990±0.667	24.832±0.335
4		45.330±0.565
6		52.634±0.100
8		69.361±0.236
10		85.382±0.356
12		100.461±0.489
24		100.225±0.659

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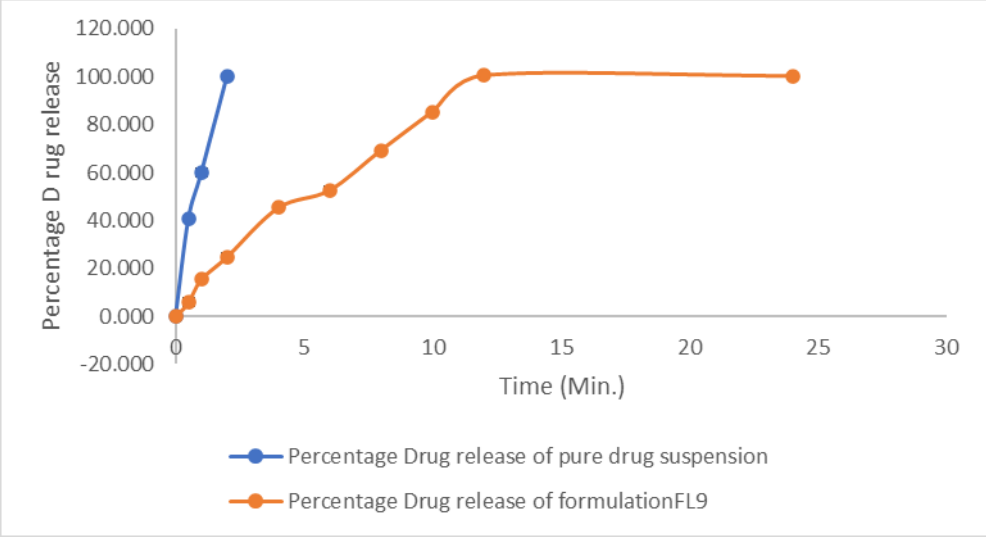

Figure 4: Percentage Drug Release of FL9 Formulation and pure drug suspension

When compared to the pure drug suspension, which had an in-vitro drug release of 99.990±0.667 after 2 hours, the manufactured liposphere of felodipine showed sustained release at a higher rate of 100.225±0.659%.

V. Conclusion

In current study Felodipine loaded liposphere was prepared. Drug felodipine was discovered to have organoleptic qualities that matched the literature. the observation confirmed it appeared as White to pale yellow crystalline powder.

The melting point of drug was found to be range 141±1°C-145±1°C. The 5 to 40 µg/ml solution of felodipine in methanol was used to create the calibration curve for felodipine. At 362 nm, the absorbance was measured. Figure 3 representation of the felodipine calibration curve revealed the regression equation y = 0.0191x + 0.0743and an R2 value of 0.999, indicating good linearity. Felodipine was found to be maximum in alcohol. Felodipine was discovered to have a partition coefficient of 4.178±0.162 in n- Octanol: Water. This suggests that the medication has a lipophilic character. The Melt Method was used to prepare the liposphere. All lipospheres formulations were spherical in shape and uniform except formulation code FL1, FL5, FL6 and FL8. The percentages yield for the entire drug-loaded liposphere formulation, which were respectively determined to range from 96.514±0.534% 99.936±0.025%. The percentage yield increased along with the lipid content, and at the same time. The drug entrapment and drug loading for the entire drug-loaded liposphere formulation, which were respectively determined to range from 21.774±0.948% to 96.670±0.981% and 2.374±0.003% to 2.557±0.086%. The range of particle sizes for all microparticle formulations was 2.593±0.035µm to 10.560±0.330 µm. On the basis of above in vitro characterization of all liposphere formulations FL9 formulation was selected for further analysis. When compared to the pure drug suspension, which had an in-vitro drug release of 99.990±0.667 after 2hours, the manufactured liposphere of felodipine showed sustained release at a higher rate of 100.225±0.659%. FL9 formulation follow the Zero model for drug release.

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Conflict of interest: No conflict of interest

References

[1]. Ravi Kumar MN. Nano and microparticles as controlled drug delivery devices. J Pharm Pharm Sci 2000;3:234-58.
[2]. Jenning V, Thünemann AF, Gohla SH. Characterisation of a novel solid lipid nanoparticle carrier system based on binary mixtures of liquid and solid lipids. Int J Pharm 2000;199:167-77.
[3]. Domb AJ, Bergelson L, Amselem S. Lipospheres for controlled delivery of substances. In: Benita S, editor.

Microencapsulation, Methods and Industrial Applications. New York: Marcel Dekker; 1996. p. 377-410.
[4]. Maniar MH, Hannibal D, Amselem S, Xie X, Burch R, Domb A. Characterization of lipospheres: Effect of carrier and phospholipid on the loading of drug into the lipospheres. Pharm Res 1991;8:175-185.
[5]. Bekerman T, Golenser J, Domb A. Cyclosporin nanoparticulate lipospheres for oral administration. J Pharm Sci 2004;93:1264-70.
[6]. Reithmeier H, Herrmann J, Göpferich A. Lipid microparticles as a parenteral controlled release device for peptides. J Control Release 2001;73:339-50.
[7]. Almeida AJ, Souto E. Solid lipid nanoparticles as a drug delivery system for peptides and proteins. Adv Drug Deliv Rev 2007;59:478-90.
[8]. Souto EB, Muller RH. Lipid nanoparticles (SLN and NLC) for drug delivery. In: Domb AJ, Tabata Y, Ravi Kumar MN, Farber S, editors. Nanoparticles for Pharmaceutical Applications.
[9]. California: American Scientifi c Publishers; 2007. p. 103-22.
[10]. Domb AJ. Lipospheres for controlled delivery of substances. In: Benita S, editor. Microencapsulation, Methods and Industrial Applications. Boca Raton: Taylor and Francis; 2006. p. 297-314.
[11]. Amselem S, Domb AJ. Liposphere delivery systems for vaccines. In: Bernstein H, Cohen S, editors. Microparticulate Systems for Drug Delivery. New York: Marcel Dekker; 1996. p. 149-68.
[12]. Amselem S, Alving CR, Domb AJ. Polymeric biodegradable lipospheres as vaccine delivery systems. Polym Adv Technol 1992;3:351-57.
[13]. Amselem S, Domb AJ, Alving CR. Lipospheres as a vaccine carrier systems: Effects of size, charge, and phospholipid composition. Vaccine Res 1992;1:383-95.
[14]. Zhang L, Long C, Qian Y, Liu L. Stabilizer distribution on the surface of solid lipid microparticles and SLM stability: Mesoscale simulation and experiments. J Chem Ind Eng 2007;58:181-89.
[15]. Lewis L, Boni R, Adeyeye CM. Effect of emulsifi er blend on the characteristics of sustained release diclofenac microspheres. J Microencapsul 1998;15:283-98.
[16]. Cortesi R, Esposjto E, Luca G, Nastruzzi C. Production of lipospheres as carriers for bioactive compounds. Biomaterials 2002;23:2283-94.
[17]. El-Gibaly I, Abdel-Ghaffar SK. Effect of hexacosanol on the characteristics of novel sustained-release allopurinol solid lipospheres (SLS): Factorial design application and product evaluation. Int J Pharm 2005;294:33-51.
[18]. Toongsuwan S, Li LC, Erickson BK, Chang HC. Formulation and characterization of bupivacaine lipospheres. Int J Pharm 2004;280:57-65.
[19]. Zimmermann E, Müller RH. Electrolyte- and pH-stabilities of aqueous solid lipid nanoparticle (SLN) dispersions in artificial gastrointestinal media. Eur J Pharm Biopharm
[20]. 2001;52:203-10.
[21]. Mehnert W, Mäder K. Solid lipid nanoparticles: Production, characterization and applications. Adv Drug Deliv Rev 2001;47:165-96.
[22]. Gasco MR, Inventor. Method for producing solid lipid microspheres having a narrow size distribution. United States Patent US 5250236A; 1993.
[23]. van Krevelen DW, Hoftyzer PJ. Properties of Polymers. 3rd ed. New York: Elsevier; 1990.
[24]. Zhang LJ, Qian Y, Long CX, Chen Y. Systematic procedures for formulation design of drug-loaded solid lipid microparticles: Selection of carrier material and stabilizer. Ind Eng Chem Res 2008;47:6091-100.
[25]. Müller RH, Radtke M, Wissing SA. Solid lipid nanoparticles (SLN) and nanostructured lipid carriers (NLC) in cosmetic and dermatological preparations. Adv Drug Deliv Rev 2002;54 Suppl 1:S131-55.
[26]. Long CX, Zhang LJ, Qian Y. Mesoscale simulation of drug molecules distribution in the matrix of solid lipid microparticles (SLM). Chem Eng J 2006;119:99-106.
[27]. Domb AJ, Maniar M, Inventor. Nova Pharmaceutical Corp. Lipospheres for controlled delivery of pharmaceuticals, pesticides, and fertilizers. United States Patent 90-US6519 (9107171); 1990.
[28]. Tursilli R, Casolari A, Iannuccelli V, Scalia S. Enhancement of melatonin photostability by encapsulation in lipospheres. J Pharm Biomed Anal 2006;40:910-4.

[29]. Favaro-Trindade CS, Santana AS, Monterrey-Quintero ES, Trindade MA, Netto FM. The use of spray drying technology to reduce bitter taste of casein hydrolysate. Food Hydrocoll 2010;24:336-40.
[30]. Rasiel A, Sheskin T, Bergelson L, Domb AJ. Phospholipid coated poly (lactic acid) microspheres for the delivery of LHRH analogue. Polym Adv Technol 2002;13:127-136.
[31]. Eldridge JH, Staas JK, Meulbroek JA, McGhee JR, Tice TR, Gilley RM. Biodegradable microspheres as a vaccine delivery system. Mol Immunol 1991;28:287-94.
[32]. Morel S, Gasco MR, Cavalli R. Incorporation in lipospheres of [D-Trp-6] LHRH. Int J Pharm 1995;119:126.
[33]. Morel S, Ugazio E, Cavalli R, Gasco MR. Thymopentin in solid lipid nanoparticles. Int J Pharm 1996;132:259-61.
[34]. Shukla D, Chakraborty S, Singh S, Mishra B. Lipid-based oral multiparticulate formulations - advantages, technological advances and industrial applications. Expert Opin Drug Deliv 2011;8:207-24.
[35]. Bahrami M, Ranjibarian S. Production of micro and nano composites by super critical carbon dioxide. J Supercrit Fluids 2007;40:263-83.
[36]. Amidi M, Pellikaan HC, de Boer AH, Crommelin DJ, Hennink WE, Jiskoot W. Preparation and physicochemical characterization of supercritically dried insulin-loaded microparticles for pulmonary delivery. Eur J Pharm Biopharm 2008;68:191-200.
[37]. Johnson KA. Preparation of peptide and protein powders for inhalation. Adv Drug Deliv Rev 1997;26:3-15.
[38]. Barbosa CM, Morais HA, Delvivo FM, Mansur HS, Oliveira MC, Silvestre MP. Papain hydrolysates of casein: Molecular weight profile and encapsulation in lipospheres. J Sci Food Agric 2004;84:1891-900.
[39]. Yajima T, Umeki N, Itai S. Optimum spray congealing conditions for masking the bitter taste of clarithromycin in wax matrix. Chem Pharm Bull (Tokyo) 1999;47:220-5.
[40]. Albertini B, Passerini N, González-Rodríguez ML, Perissutti B, Rodriguez L. Effect of aerosil on the properties of lipid controlled release microparticles. J Control Release 2004;100:233-46.
[41]. Passerini N, Perissutti B, Albertini B, Voinovich D, Moneghini M, Rodriguez L. Controlled release of verapamil hydrochloride from waxy microparticles prepared by spray congealing. J Control Release 2003;88:263-75.
[42]. Fini A, Rodriguez L, Cavallari C, Albertini B, Passerini N. Ultrasound-compacted and spray-congealed indomethacin/ polyethyleneglycol systems. Int J Pharm 2002;247:11-22.
[43]. Maschke A, Becker C, Eyrich D, Kiermaier J, Blunk T, Göpferich A. Development of a spray congealing process for the preparation of insulin-loaded lipid microparticles and characterization thereof. Eur J Pharm Biopharm 2007;65:175-87.
[44]. Jin X, Zhang ZH, Li SL, Sun E, Tan XB, Song J, et al. A nanostructured liquid crystalline formulation of 20(S)-protopanaxadiol with improved oral absorption. Fitoterapia 2013;84:64-71.
[45]. Domb AJ. Long acting injectable oxytetracycline-liposphere formulations. Int J Pharm 1995;124:271-8.
[46]. zur Mühlen A, Schwarz C, Mehnert W. Solid lipid nanoparticles (SLN) for controlled drug delivery — Drug release and release mechanism. Eur J Pharm Biopharm 1998;45:149-55.
[47]. Pietkiewicz J, Sznitowska M, Placzek M. The expulsion of lipophilic drugs from the cores of solid lipid microspheres in diluted suspensions and in concentrates. Int J Pharm 2006;310:64-71.
[48]. Cavalli R, Morel S, Gasco MR, Chetoni P, Saettone MF. Preparation and evaluation in vitro of colloidal lipospheres containing pilocarpine as ion pair. Int J Pharm 1995;117:243-46.
[49]. Sawant KK, Dodiya SS. Recent advances and patents on solid lipid nanoparticles. Recent Pat Drug Deliv Formul 2008;2:120-35.
[50]. Das S, Chaudhury A. Recent advances in lipid nanoparticle formulations with solid matrix for oral drug delivery. AAPS PharmSciTech 2011;12:62-76.
[51]. Drake B, Prater CB, Weisenhorn AL, Gould SA, Albrecht TR, Quate CF, et al. Imaging crystals, polymers, and processes in water with the atomic force microscope. Science 1989;243:1586-9.

[52]. Fenske DB. Structural and motional properties of vesicles as revealed by nuclear magnetic resonance. Chem Phys Lipids 1993;64:143-62.
[53]. Mukherjee S, Ray S, Thakur RS. Solid lipid nanoparticles: A modern formulation approach in drug delivery system. Indian J Pharm Sci 2009;71:349-58.
[54]. Gander B, johansen P, Nam-Tran H, Merkle HP. Thermodynamic approach to protein microencapsulation into poly (D,L-lactide) by spray drying. Int J Pharm 1996;129:51-61.
[55]. Brown SA, Chime SA, Attama AA, Agu CI, Onunkwo GC. In-vito and In-vivo characterization of piroxicam loaded Dika wax lipospheres. Trop J Pharm Res 2013;12:33-8.
[56]. Naeem M, Bhise KS. Formulation and development of Fenofi brate loaded liposphere system. J Drug Deliv Ther 2013;3:1-10.
[57]. Liu X, Zhang Y, Tang X, Zhang H. Determination of entrapment effi cogency and drug phase distribution of submicron emulsions loaded silybin. J Microencapsul 2009;26:180-6.
[58]. Muchow M, Maincent P, Muller RH. Lipid nanoparticles with a solid matrix (SLN, NLC, LDC) for oral drug delivery. Drug Dev Ind Pharm 2008;34:1394-405.