Development of Lacidipine loaded nanostructured lipid carriers (NLCs) for bioavailability enhancement

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ABSTRACT
Nanostructured Lipid Carriers (NLCs) are new generation Nanoparticle system, which have shown a lot of advantages over conventional Solid lipid nanoparticles, such as improved drug incorporation and release properties. The purpose of this study is to prepare an optimized nanostructured lipid carrier formulation for “Lacidipine”, and to estimate the potential of NLCs as an oral drug-delivery system. In this work, solvent injection technique was used to prepare Lacidipine–loaded NLCs. The Lacidipine loaded NLCs showed smooth surface with spherical morphology under scanning electron microscope (SEM) and transmission electron microscope (TEM) analysis. The maximum encapsulation efficiency observed was 92.65±0.5%. In In-Vitro release study, Lacidipine loaded NLCs exhibited a sustained release profile of Lacidipine and no burst release was shown. The oral bioavailability study was performed by using Wistar Albino rats. The relative bioavailability of Lacidipine loaded NLCs was found to be 3.9. In conclusion, the NLC formulation significantly improved the oral bioavailability of Lacidipine and revealed a positive aspect for oral delivery of poorly water-soluble drugs.

1. Introduction

New drug molecules are been introduced into the pharmaceutical industry everyday but only the development of new drugs alone is not sufficient to assure the progress in drug therapy. The most common problem faced is low-solubility of drug molecule which ultimately leads to low bioavailability. Therefore, there is an increasing requirement to develop a drug carrier system that overcomes these drawbacks. The carrier system should have some important characteristics such as no toxicity (acute and chronic), have a sufficient drug loading capacity and the feasibility of drug targeting and controlled release. The carrier system should also provide chemical and physical stability for the incorporated drug. The possibility of production scaling up with reasonable overall costs should be available[1-3]. Lipid-based nanoparticle formulations may also increase the drug absorption by improving dissolution and solubility in the intestinal milieu, by reducing gastric emptying rate and increase in mucosal permeability. Lipids are used to increase lymph formation and also promote lymph flow rate[4]. NLCs are composed of biocompatible solid lipid matrices and liquid lipid which have different chemical structure from the solid lipid[5]. Besides, NLCs have the usual particle diameter ranging 10–1000 nm. NLCs drug delivery system have many advantages like high biocompatibility, controlled drug release, high bioavailability, and the possibility of large industrial scale production.Drug delivery system based on NLCs also have no problems with different routes of administration, such as oral, intravenous, pulmonary and transdermal administration[6-11]. However, the various kinds of lipid NLC components results in the imperfections type structures, amorphous state type or multiple type to adjust more drug and decrease the drug leakage during storage[12]. Poorly water soluble drugs loaded by lipid formulations have been studied for oral route and have reported to enhance the oral bioavailability by numerous research teams[13,14] but there are very less reports for oral administration on NLC system.

Lacidipine, a calcium channel blocker used in hypertension and atherosclerosis treatment. It also contains antioxidant effect and is the most vascular selective dihydroy pyridine[15-16]. Lacidipine shows high first-pass hepatic metabolism and have about 10% of mean absolute bioavailability. The complete metabolism of Lacidipine takes place in the liver by cytochrome P450 3A4 to pharmacologically inactive metabolites[16]. Lacidipine is white to pale yellow crystalline, water insoluble (84µg/lit), freely soluble in acetone and sparingly soluble in absolute alcohol[17].

2. Materials and methods

2.1 Materials

Lacidipine was a kind gift from Aarti Industries Ltd, Mumbai, India. Glycerol monostearate (M.P. 52–54°C; molecular weight 358.63) was purchased from Yarrow Chem products, Mumbai, India. Poloxamer 407 (molecular weight 12.5) was purchased from Leo Chem, Bangalore, India. Linoleic acid was purchased

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from Otto Chem products, India. Other chemicals were of analytical grade.

### 2.2 Preparation of Lacidipine loaded NLCs

Solvent injection technique was used to prepare the NLCs with slight modification\[18,19\]. Lacidipine, specified amount of Glycerol monostearate (GMS) and Linoleic acid as given in Table 1 were dissolved in 4 ml of isopropyl alcohol (boiling point 81–83°C) and heated at the melting temperature of GMS. The resulting solution injected rapidly in 20 ml of aqueous phase containing specified amount of poloxamer 407 as given in Table 1. Then, it was continuously stirred at 400 rpm for 30 min on a magnetic stirrer and then 0.1 N HCl (8 ml) was added to the dispersion. Thereafter, centrifugation was done at 10,000 rpm for 30 min at 10°C in REMI cooling centrifuge (Model C- 24BL, VACO-779, Vasai, India), and 4% poloxamer 407 (by weight) in 10 ml double distilled water was used to re-suspend the aggregates with stirring at 1000 rpm for 10min\[18\]. Dialysis technique was used for the purification of Lacidipine loaded NLCs. In the dialysis bag re-suspended suspension was taken and sealed at both ends. The dialysis bag was then dipped into 100 ml of double distilled water containing 0.2% (w/v) sodium lauryl sulphate and stirred at 100 rpm for 20 min. The un-entrapped drug was removed in 20 min. The HPLC was performed by using Youglin HPLC model equipped with Binary pump. A mixture of acetonitrile: ammonium acetate buffer pH 5.0 (90:10 v/v) was used as mobile phase\[20\]. The flow rate of mobile phase, injection volume and detection wavelength were 1.0 ml/min, 20µl and 283nm respectively. Lacidipine showed linear calibration curve with R²=0.997 in the range 50-250µg/ml.

### Table 1: Formulation Design of NLCs.

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Amount of drug(mg)</th>
<th>Amount of Linoleic acid(mg)</th>
<th>Amount of Glycerol monostearate(mg)</th>
<th>Surfactant concentration(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>30</td>
<td>10</td>
<td>100</td>
<td>0.8</td>
</tr>
<tr>
<td>F2</td>
<td>30</td>
<td>15</td>
<td>100</td>
<td>0.8</td>
</tr>
<tr>
<td>F3</td>
<td>30</td>
<td>20</td>
<td>100</td>
<td>0.8</td>
</tr>
<tr>
<td>F4</td>
<td>30</td>
<td>20</td>
<td>100</td>
<td>0.8</td>
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<tr>
<td>F5</td>
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<td>30</td>
<td>100</td>
<td>0.8</td>
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<td>30</td>
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<td>150</td>
<td>0.8</td>
</tr>
<tr>
<td>F7</td>
<td>30</td>
<td>20</td>
<td>200</td>
<td>0.8</td>
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<tr>
<td>F8</td>
<td>30</td>
<td>20</td>
<td>150</td>
<td>0.8</td>
</tr>
<tr>
<td>F9</td>
<td>30</td>
<td>20</td>
<td>150</td>
<td>1.0</td>
</tr>
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<td>F10</td>
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<td>1.2</td>
</tr>
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<td>F11</td>
<td>30</td>
<td>20</td>
<td>150</td>
<td>1.0</td>
</tr>
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<td>F12</td>
<td>10</td>
<td>20</td>
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<td>20</td>
<td>20</td>
<td>150</td>
<td>1.0</td>
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<td>F14</td>
<td>30</td>
<td>20</td>
<td>150</td>
<td>1.0</td>
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<td>F15</td>
<td>40</td>
<td>20</td>
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<td>1.0</td>
</tr>
<tr>
<td>F16</td>
<td>50</td>
<td>20</td>
<td>150</td>
<td>1.0</td>
</tr>
</tbody>
</table>

### 2.3 Characterization of NLC

#### 2.3.1 Particle size

The nanostructured lipid carrier formulations were characterized for their size by using digital microscope (BA-310, Motic, USA). Nanostructured lipid carriers were dispersed in 10ml of water. From the dispersion of NLCs, a drop of sample was placed on glass slide and covered with cover slip. The prepared slide then analysed under digital microscope under 40X magnification. The size of nanostructured lipid carriers were also analysed by Zetasizer at 25°C at an angle of 90°, taking the average of three measurements.

#### 2.3.2 Drug Entrapment Efficiency (DEE %)

The drug entrapment was determined by RP-HPLC method using acetonitrile: ammonium acetate buffer (pH 5.0) (90:10 v/v) as a mobile phase. 1ml of Lacidipine loaded NLCs colloidal solution centrifuged for 10 min at 4000rpm. Then the solution was filtered through a 0.45µm membrane filter. After that, it analysed by HPLC\[21\]. Drug entrapment efficiency (DEE) of nanostructured lipid carriers calculated using the following equation:

\[
\text{DEE (\%) = } \frac{\text{Totalamountofdrugrecovered}}{\text{Totalamountofdrugadded}} \times 100
\]

#### 2.3.3 In vitro release studies

The release studies were conducted by using USP Type II (paddle) apparatus with 900ml of simulated intestinal fluid (SIF) as medium at 37°C with stirring at 100 RPM. The medium was replaced every 2 h until complete release of drug. The concentration of drug was determined by using UV-Visible Spectrophotometer at 283nm. The cumulative release was plotted against time to obtain release kinetic models. The drug release was determined by using zero order, first order, Higuchi and Korsmoe models. The Kinetic models were evaluated by using C-E fit of drug release data.
The dialysis technique was used for *In vitro* drug release from the NLCs\[22\]. Dialysis bag of cellulose dialysis membrane (MW cut-off 10,000 Da) was soaked in the distilled water overnight and then 1ml of drug loaded NLCs preparation was taken in dialysis bag with both the ends sealed with threads. Initial studies were carried out in 100 ml of 0.1N HCl (pH 1.2) for 2 hours and then in phosphate-buffered saline (PBS) pH 6.8 at 37°C on magnetic stirrer moving at a speed of 50 rpm for 24hrs[23]. The pH was adjusted with 2N HCl or 2N NaOH. Samples were withdrawn at predetermined time intervals and replaced with fresh media. Samples were filtered and analysed by using HPLC at $\lambda_{\text{max}}$ of 283 nm[24]. All the values obtained were expressed as mean ± standard error mean (S.E.M.). Each data represents mean ± SD (n=3).

2.3.4 **Scanning electron microscopy**

Lacidipine loaded NLC was visualized by scanning electron microscopy for the surface morphology[25]. Before observation, the nanoparticles were fixed on a double-sided sticky tape which had previously been secured on aluminum stubs and then coated with gold with thickness about 450 Å using Sputter gold coater and were visualized under scanning electron microscope.

2.3.5 **Transmission electron microscopy**

The morphology of Lacidipine loaded NLCs colloidal solution was observed by transmission electron microscopy. The sample was prepared by placing a drop of formulation which was diluted with double-distilled water on to copper grid coated with carbon film and followed by negative staining with 2% phosphotungstic acid. Then the sample was dried in the air before TEM observation (Figure 2).

2.5 **In vivo pharmacokinetics**

The male albino rats were used for *In vivo* pharmacokinetic study. Before drug administration, these rats were fasted overnight with free access to water. Lacidipine suspension and Lacidipine-NLCs suspension were administered orally to the rats. The
administration dose of Lacidipine was 2.5 mg/kg. At defined time points (1, 2, 4, 6, 8, 12 and 24 h), the collected blood The withdrawn blood sample volume was replaced immediately with an equal volume of physiological saline. The tubes were placed in a centrifuge for 20 min at 3000 rpm to separate the serum and then serum was stored at -20°C until drug analysis was carried out using HPLC.

The standard pharmacokinetic parameters were collected from each of the individual rat plasma and plasma concentration Vs. time profiles of Lacidipine were determined by non compartmental method using the Win Nonlin computer program. The Cmax and tmax were calculated directly from the plasma concentration vs. time graph of Lacidipine. The trapezoidal method was used to obtain AUC. The t1/2 was calculated by linear regression of log linear portion of the plasma concentration time profile. The apparent plasma clearance (CL) was obtained by dividing the dose with AUC. Win Nonlin software was used to determine the mean residence time (MRT). The relative bioavailability of NLCs formulations was obtained by using the following formula:

\[
\text{Relative bioavailability} = \frac{\text{AUC}_{\text{Sample}}}{\text{AUC}_{\text{Standard}}}
\]

3.0 Results and discussion

NLCs were successfully prepared by solvent injection technique that depends on rapid diffusion of the solvent over the solvent–lipid interface with the aqueous phase and this physical phenomenon is critical for the precipitation of nanosized lipid particle. The formed small size NLCs may couple with low density of lipids. To overcome this limitation, the pH was decrease to 1.5–2 to maintain the zeta potential to a level that raise the aggregation of nanoparticles. Purity of the product obtained is another significant aspect in preparation of NLCs. A feasibility of existence of free Lacidipine particles in the sediment of Lacidipine-loaded NLCs can’t be refused. Both, the in vitro and in vivo release behavior of Lacidipine can affect the free drug particles. Therefore, dialysis technique was used to remove the free drug particles from the sediment of NLCs.

sample were centrifuged for 10 min at 4000 rpm[21].

Lacidipine have low molecular weight of 455.543 g/mol so that this technique was considered suitable to remove the free drug particles. Free drug could be efficiently removed by dialysis from sediment of NLCs in 20 min and was used throughout the experiment. Glycerol monostearate demonstrated higher bioavailability because of higher lipophilic nature of the former that is responsible for more sustained release of the drug[26].

3.1 Analysis of dependent variables

3.1.1 Effect of formulation variables

In formulation of nanostructured lipid carriers (NLCs), the variables such as the amount of liquid lipid, amount of solid lipid, concentration of surfactant and amount of drug may affect the particle size and drug entrapment efficiency. The effect of formulation variables was seen on nanostructured lipid carriers to get desired particle size and maximum drug entrapment efficiency (%) and the following variables were optimized;

- Amount of liquid lipids (linoleic acid)
- Amount of solid lipid (GMS)
- Surfactant concentration (Poloxamer407)
- Amount of Drug (Lacidipine)

Effect of amount of linoleic acid

The amount of linoleic acid (10mg, 15mg, 20mg, 25mg, and 30mg) was varied. Formulation batches from F1 to F5 were prepared to investigate the effect of amount of linoleic acid on entrapment and particle size. All other parameters like drug amount (30mg), amount of solid lipid (100mg), concentration of surfactant (0.8%) and stirring speed (400rpm) were kept constant.

Optimization parameters such as particle size, size distribution and drug entrapment efficiency (%) were evaluated. The obtained results are tabulated in Table 2.

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Amount of linoleic acid (mg)</th>
<th>Particle Size(\bar{b}) (nm)±S.D</th>
<th>Polydispersity index</th>
<th>Drug Entrapment Efficiency (%) ±S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>10</td>
<td>259.5±6.2</td>
<td>0.462±0.36</td>
<td>75.92±0.20</td>
</tr>
<tr>
<td>F2</td>
<td>15</td>
<td>257.4±9.6</td>
<td>0.357±0.63</td>
<td>86.38±0.08</td>
</tr>
<tr>
<td>F3</td>
<td>20</td>
<td>252.8±6.5</td>
<td>0.342±0.73</td>
<td>88.23±0.09</td>
</tr>
<tr>
<td>F4</td>
<td>25</td>
<td>269.8±6.5</td>
<td>0.371±0.62</td>
<td>84.14±0.10</td>
</tr>
<tr>
<td>F5</td>
<td>30</td>
<td>264.8±9.6</td>
<td>0.359±0.24</td>
<td>78.72±0.05</td>
</tr>
</tbody>
</table>

(Mean ± S.D.)\((n = 3)\)

Effect of amount of solid lipid

The amounts of liquid lipid (20mg linoleic acid), concentration of surfactant (poloxamer 0.8%) and amount of drug (30mg Lacidipine) were kept constant. The amount of Glycerol...
monostearate (100mg, 150mg, and 200mg) was varied. Total three batches (F6 to F8) were prepared for evaluating the effect of solid lipid amount on particle size and entrapment efficiency. The obtained results are tabulated in Table 3.

### Table 3: Effect of amount of solid lipid with linoleic acid

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Amount of Glycerol monostearate(mg)</th>
<th>Particle Size* (nm)±S.D</th>
<th>Polydispersity index</th>
<th>Drug Entrapment Efficiency (%) ±S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>F6</td>
<td>100</td>
<td>259.5±6.2</td>
<td>0.342±0.34</td>
<td>77.24±0.07</td>
</tr>
<tr>
<td>F7</td>
<td>150</td>
<td>257.1±7.3</td>
<td>0.329±0.52</td>
<td>81.12±0.02</td>
</tr>
<tr>
<td>F8</td>
<td>200</td>
<td>261.3±3.6</td>
<td>0.432±0.73</td>
<td>75.66±0.11</td>
</tr>
</tbody>
</table>

*(Mean ± S.D.)(n = 3)*

**Effect of surfactant concentration**

The amounts of liquid lipid (20mg linoleic acid) and solid lipid (150mg glycerol monostearate) were kept constant. Different formulation batches (F9-F11) were prepared with varying amount of poloxamer 407 (0.8%, 1.0%, and 1.2%). Three batches were prepared for evaluating the effect of surfactant concentration on particle size and drug entrapment efficiency (%). The obtained results tabulated in Table 4.

### Table 4: Effect of surfactant concentration

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Surfactant concentration(%)</th>
<th>Particle Size* (nm)±S.D</th>
<th>Polydispersity index</th>
<th>Drug Entrapment Efficiency (%) ±S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>F9</td>
<td>0.8</td>
<td>252.7±5.6</td>
<td>0.342±0.36</td>
<td>88.23±0.02</td>
</tr>
<tr>
<td>F10</td>
<td>1.0</td>
<td>243.4±5.4</td>
<td>0.324±0.24</td>
<td>90.25±0.03</td>
</tr>
<tr>
<td>F11</td>
<td>1.2</td>
<td>246.8±4.2</td>
<td>0.391±0.44</td>
<td>80.90±0.18</td>
</tr>
</tbody>
</table>

*(Mean ± S.D.)(n = 3)*

**Effect of drug (Lacidipine) amount**

The amounts of liquid lipid (20mg linoleic acid), solid lipid (150mg glycerol monostearate) and poloxamer 407 (1%) were kept constant. The amount of drug (Lacidipine) was varied from 10 mg – 50 mg and the formulation was loaded and stirring speed (400rpm) was kept constant. Five batches (F12 to F16) were prepared for evaluating the effect of drug amount on particle size and entrapment efficiency. The obtained results are tabulated in Table 5.

### Table 5: Effect of drug (Lacidipine) amount

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Amount of Drug (mg)</th>
<th>Particle Size* (nm)±S.D</th>
<th>Polydispersity index</th>
<th>Drug Entrapment Efficiency (%) ±S.D</th>
</tr>
</thead>
<tbody>
<tr>
<td>F12</td>
<td>10</td>
<td>255.1±7.3</td>
<td>0.363±0.42</td>
<td>86.4±0.1</td>
</tr>
<tr>
<td>F13</td>
<td>20</td>
<td>248.2±6.9</td>
<td>0.385±0.73</td>
<td>88.34±0.2</td>
</tr>
<tr>
<td>F14</td>
<td>30</td>
<td>241.4±8.4</td>
<td>0.246±0.47</td>
<td>92.65±0.5</td>
</tr>
<tr>
<td>F15</td>
<td>40</td>
<td>245.7±6.3</td>
<td>0.372±0.74</td>
<td>90.27±0.3</td>
</tr>
<tr>
<td>F16</td>
<td>50</td>
<td>254.1±3.7</td>
<td>0.361±0.53</td>
<td>80.14±0.7</td>
</tr>
</tbody>
</table>

Values of the particle size of the developed NLCs are documented in Table 2,3,4 and 5. The results showed that the amounts of GMS and linoleic acid were critical parameters in governing the particle size. After production, the particles size ranged between 241.4±8.4nm and 269.8±6.5nm and polydispersity was between 0.246±0.47 and 0.462±0.36. The mean particle size was least when Glycerol monostearate was 150mg and Linoleic acid and poloxamer407 concentration were 20mg and 1.0% (F14) and the particle size was largest when Glycerol monostearate was 150mg and linoleic acid was 25 mg (F4). Thus, the linoleic acid amount in the lipid matrix affects the mean particle size. The size of NLCs was analyzed by zeta sizer as shown in Figure 3. The entrapment efficiency of Lacidipine within the different prepared nanostructured lipid carrier formulations is shown in Tables 1, 2, 3 & 4. The highest entrapment efficiency of Lacidipine in all the prepared NLCs was observed in batch F14 using 150mg GMS, 20mg linoleic acid, 30mg Lacidipine and 0.1% Poloxamer407 concentration.
Concerning liquid lipid type, Linoleic acid increased the entrapment efficiency, being mixture of triglycerides of different chain length (C8, C10) form less perfect crystals with many imperfections offering space to accommodate the drug.

3.1.2 In vitro drug release

The optimized batch was subjected to in vitro drug release studies for 2 hrs in 0.1N HCl and further upto 24 hrs in phosphate buffer (pH 6.8) by dialysis bag technique using dialysis membrane. In vitro release rate of Lacidipine loaded NLCs is graphically presented in Figure 4. As both particle size and entrapment efficiency are determinants of drug release from a given carrier system, the in vitro release profile were expected to vary accordingly. In 2hrs, 12hrs and 24hrs of the release study, the %CDR observed in NLCs formulated with linoleic acid was 1.12±0.004%, 59.63±0.13% and 92.96±0.19 %. The formulation F14 with smallest particle size of 241.4nm and highest entrapment efficiency displayed maximum %CDR in a sustained manner.

3.2 In vivo studies

Lacidipine NLCs and Lacidipine suspension were orally administrated to Male Albino rats. The Plasma concentration-time plots in rats after oral administration are shown in Figure 5. The $T_{\text{max}}$ was 2h and the $C_{\text{max}}$ value was 571.770ng/ml after oral administration of Lacidipine suspension. However, the $T_{\text{max}}$ value (4.03 h) of Lacidipine NLCs was two hours later than that of Lacidipine suspension. The visible difference between $T_{\text{max}}$ value of Lacidipine NLCs and Lacidipine suspension manifested that the rates of absorption of two formulations were not the same. Lacidipine in suspension dissolved in the intestinal tract and absorbed directly into systemic circulation. However, Lacidipine in NLC could hardly be released into the gastrointestinal tract, as was supported in the in vitro release studies. Therefore, the intact Lacidipine NLCs were directly absorbed into the blood circulation and released the drug gradually. The $C_{\text{max}}$ value of Lacidipine NLCs was 813ng/ml which was significantly higher than that obtained with the Lacidipine suspension (571.770ng/ml). The corresponding pharmacokinetic parameters are listed in Table 6. The AUC after oral administration of Lacidipine NLCs was 3143.9±574.9 ng/ml/h, which was approximately 3.9fold higher than that of Lacidipine suspension (975.8±109.4 ng/ml/h). The results

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**Figure 3:** Particle size of nanostructured lipid carriers (Zeta sizer)

**Figure 4:** In vitro release profile of Lacidipine loaded NLCs

---

**Table 6**

<table>
<thead>
<tr>
<th>Material</th>
<th>Particle Size (nm)</th>
<th>$C_{\text{max}}$ (ng/ml)</th>
<th>$T_{\text{max}}$ (h)</th>
<th>AUC (ng/ml/h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lacidipine NLC</td>
<td>241.4</td>
<td>813</td>
<td>4.03</td>
<td>3143.9</td>
</tr>
<tr>
<td>Lacidipine suspension</td>
<td>200.0</td>
<td>571.770</td>
<td>2.00</td>
<td>975.8±109.4</td>
</tr>
</tbody>
</table>
indicated that systemic absorption of Lacidipine as significantly enhanced by incorporating into NLC compared with Lacidipine suspension. The NLCs showed a promising potential for enhancing oral bioavailability of poorly water-soluble drugs.

### Table 6: Mean pharmacokinetic parameters of nanostructured lipid carriers formulations

<table>
<thead>
<tr>
<th>Formulation</th>
<th>AUC (h*ng/ml)</th>
<th>C_{max} (ng/ml)</th>
<th>Plasma clearance (ml/hr)</th>
<th>MRT (h)</th>
<th>t_{1/2} (h)</th>
<th>Relative bioavailability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug suspension</td>
<td>2064.7586</td>
<td>571.770</td>
<td>5392.32</td>
<td>2.35</td>
<td>1.32</td>
<td>1</td>
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<tr>
<td>Lacidipine loaded nanostructured lipid carriers (NLCs)</td>
<td>8225</td>
<td>813</td>
<td>1236.82</td>
<td>10.0606</td>
<td>4.03</td>
<td>3.9</td>
</tr>
</tbody>
</table>

**Figure 5:** Plasma–drug profile curve

**4. Conclusion**

Using solvent injection technique, Lacidipine was successfully incorporated in NLCs formulations which can be potentially useful for delivery of this drug. From *in vitro* drug release study, it was concluded that the NLCs formulation delayed the drug release for two hours and controlled drug release up to 24 hrs. It can be concluded from the result obtained that the NLCs developed for oral delivery of Lacidipine possessed site specific targeting ability, better stability and higher entrapment efficiency, easy to scale up. Pharmacokinetic study revealed prolonged T_{max}, and improved relative bioavailability(4-fold) of Lacidipine loaded NLCs to Lacidipine suspension in rats after oral administration. The results of the present investigation showed that the problems associated with the oral bioavailability of Lacidipine could be overcome by incorporating it into a new gastrointestinal drug delivery system, nanostructured lipid carriers.

**References**


carriers (NLC) for improved oral bioavailability. Int. J.


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