INTRODUCTION

Lornoxicam (LX), chemically 6-chloro-4-hydroxy-2-methyl-N-2-
pyridinyl-2H-thienol [1, 2], 1,2-thiazin-3-carboxamide-1,1-dioxide, is a
member of the oxicam class of non-steroidal anti-inflammatory
drugs (NSAIDs) with having analgesic, anti-inflammatory and
antipyretic properties [1, 2]. LX also shows a significant therapeutic
effect in pain like osteoarthritis and rheumatoid arthritis [3, 4]. LX
acts by non-selective inhibition of cyclooxygenase-1 and-2.
Quantification of the active component in a dosage form is essential
for the quantification of lornoxicam in rat plasma. A simple, reliable,
sensitive and validated reversed phase-high performance liquid chromatography (RP-HPLC) method was developed for
quantification of lornoxicam (LX) in rat plasma.

Methods: Solid lipid nanoparticle (SLN) and nanostructured lipid carriers (NLC) gel formulations containing lornoxicam were prepared using high
speed homogenization followed by ultra-sonication. Pharmacokinetic study of formulated LX loaded SLN and NLC were performed on Wister albino
rats.

Results: The chromatographic separation was performed on hypersil octadecylsilane (ODS)-18 column using a mobile phase of 10 mmol. Phosphate
buffer (pH, 4.5) and acetonitrile (65:35 v/v). Elute was monitored at 377 nm with a flow rate of 1 ml/min. Calibration curve was linear over the
concentration range of 25.38–2046.45 ng/ml. Retention times of LX and internal standard (piroxicam) were 9.3 and 10.2 min, respectively. Maximum plasma drug
concentration, the area under drug concentration versus time curve and elimination half-life for LX loaded SLN gel were found 6.91±0.27, 6.53±0.28 and
6.22±0.19 h. respectively.

Conclusion: A novel simple, simple, sensitive, precise, rapid, accurate, and economical and reliable RP-HPLC method was developed and validated
for the estimation of LX in rat plasma.

Keywords: Lornoxicam, SLN, NLC, RP-HPLC, Pharmacokinetic

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antipyretic properties [1, 2]. LX also shows a significant therapeutic
effect in pain like osteoarthritis and rheumatoid arthritis [3, 4]. LX
acts by non-selective inhibition of cyclooxygenase-1 and-2.
Quantification of the active component in a dosage form is essential
to the quality control of these systems. Quality control checks the
suitability of a drug delivery system for the intended application. It
serves as a marker for the consistency and predictability of the
performance of dosage forms. RP-HPLC methods are widely
reported for the quantitative estimation of LX but to this day, no
reports are available on the quantification of LX in nanostructured
delivery systems such as solid lipid nanoparticles (SLN) and
nanostructured lipid carriers (NLC) gel. Reversed phase high
performance liquid chromatography (RP-HPLC) assembled with
photodiode array (PDA) detector is most widely used in industries
requiring simple sample preparation and short running time for the
determination of LX in biological samples. However, most of the published methods
described the quantification of LX along with other drugs by RP-
HPLC technique. To best our knowledge, a validate RP-HPLC method
for the determination of LX loaded SLN and NLC in a biological
sample have not been reported.

Hence in this paper, we reported a simple, sensitive, precise, rapid,
accurate, and economical, reliable, and validated RP-HPLC method
requiring simple sample preparation and short running time for the
determination of pharmacokinetic profile of LX after transdermal
administration of SLN and NLC in rats.

MATERIALS AND METHODS

LX was obtained as gift sample from Akumbs Drugs, (Hridwar,
India). Stearic acid, pluronic F68, carbopol 940 P, and oleic acid were
purchased from Himedia, Mumbai, India. phospholipon90G
(phosphatidylcholine 90%) was collected as gift sample from GmbH,
Germany. HPLC grade acetonitrile, methanol, and dichloromethane
were purchased from E-Merck, Mumbai. Potassium dihydrogen
phosphate (KH2PO4) and orthophosphoric acid (H3PO4) were
purchased from SD Fine Chem. Ltd., Mumbai, India. All other
chemicals and solvents used were of analytical grade. Water used in
the HPLC analysis was prepared by the water purifier (AriumR,
611UF, Sartorius, Germany). The mobile phase and all the solutions
were filtered through a 0.45 µm ultraport®N66 membrane filter (Pall
Life Sciences, USA) prior to use.

Instruments

HPLC system (Waters, USA) consisting of the quaternary pump
(WaterTM600), 7725i rhodyme manual injector, PDA detector, and
empower-II software and these assembled were used for analysis. They
were processed by using of micropipettes (Ependruff, USA). spinix
Experimental animals

Wistar rats of either sex weighing 130-140 gm, housed at a temperature of 22±1 °C and relative humidity of 55±10% in controlled room were used in the experiments. The pharmacokinetic studies were conducted under protocol number MC/ICMS/AEC/DU/12 of the Institutional Animal Ethical Committee of Department of Pharmaceutical Sciences, Dibrugarh University, Dibrugarh, Assam. The experiments were conducted in accordance with the guidelines provided by the Committee for Purpose of Control and Supervision of Experiments on Animals (CPCSEA, Govt. of India).

Preparation of LX-loaded SLN and NLC

SLN and NLC were prepared by high-speed homogenization and ultrasonication method [11]. Briefly, LX and phospholipon 90G were dissolved in methanol. Stearic acid was dissolved in acetone and mixed with methanol containing LX and phospholipon 90G. The mixture was added dropwise to an aqueous solution of pluronic F68 and maintained at 75°C (5 °C above the melting point of the lipid). A pre emulsion thus obtained was stirred using an ultra-turrax T25 (IKA-Werke GmBH, Germany) at 15000 rpm for 3 min. This preemulsion was immediately placed in a probe-type sonicator (6 mm diameter, 20 W; Malvern Instruments, UK) by an ultrasonic processor to prevent crystallization. After 15 min of ultrasonication, the nanodispersion was kept for cooling under continuous stirring. During this process, SLN was formed by recrystallization. The prepared SLN dispersions were lyophilized for further studies. NLC was prepared in a similar manner wherein only the "solid lipid" (Stearic acid) was replaced by oleic acid in different proportions [12]. The formulated nanoparticles were evaluated for drug entrapment efficiency, particle size measurement, X-Ray diffraction study, scanning electron microscopy and in vitro drug release study. The in vitro drug release study was performed in Franz diffusion cell with the magnetic stirring rate at 800 rpm. The release medium was contained 25 ml of phosphate buffer (pH 7.4). At predetermined intervals 2 ml of samples were withdrawn from receptor compartment and replaced with equal volume of release medium [11].

Chromatographic conditions

HPLC analysis was performed using a hyper sim ODS C18 column (250 mm × 4.6 mm, particle size 5 μm). The mobile phase consisted of methanol, acetonitrile, water and di-chloromethane in a spinix vortexer extracted by vortexing with 1.5 ml of selected extracting solvents (acetonitrile, methanol and di-chloromethane) in a spinix vortexer for 10 min. followed by centrifugation at 10,000 rpm for 5 min at 4 °C. The supernatant was withdrawn and dried under nitrogen at 25 psi for 10 min at 40 °C. The residue was reconstituted with 100 μl of mobile phase and 20 μl was injected onto the RP-HPLC column [13].

Validation of method

The validation of an analytical method confirms the characteristics of the method to satisfy the requirements of the application domain [13]. The method was validated according to ICH guidelines [14, 15] for specificity, recovery, linearity, precision and stability. Under the validation programme the following parameters were studied:

Specificity

The specificity criterion demonstrates that the result of the method is not affected by the presence of interferences, i.e. whether the compound of interest elutes without interfering with other compounds and components of plasma. The specificity of the method was determined by comparing the chromatograms obtained from the aqueous solutions of LX and IS with those obtained from blank plasma. Blank plasma samples from each of five rats were processed in the presence of IS and another set of five samples processed with LX and IS to evaluate the presence of interference around the peak of LX. The median quality control solution (406.12 ng/ml) of LX was injected into the column under the optimized chromatographic conditions to obtain the chromatographic peaks of LX and IS so as to differentiate them from the interfering peaks of plasma components.

Selection of solvent for recovery of drug

The recovery of an analyte is the extraction efficiency of an analytical process, reported as a percentage of the known amount of an analyte carried through the sample extraction and processing steps of the method. Different organic extraction solvents (acetoniitrile, methanol, ethylæne, dichloro methane and chloroform) were tried in the experiment to recover LX from plasma samples. Quality control samples were prepared in triplicate at three levels of 101.53, 406.12 and 1244.24 ng/ml of LX and assayed by HPLC method as described above. The extraction efficiency of LX was determined by comparing the peak areas obtained from extracted quality control samples with the peak area of an aqueous working solution containing the same concentration of LX at three levels.

Linearity

Quantitative analytical results are highly influenced by the quality of the calibration curve [16, 17]. Nine different concentrations of LX with a fixed concentration of IS in blank plasma were processed, and a calibration curve was constructed in the specified concentration range (25.38, 50.77, 101.53, 203.06, 406.12, 846.09, 1244.24, 1637.16, 2046.45 ng/ml). All the solutions were prepared once and analyzed daily over a period of 3 d for the inter-day precision of the method. These solutions were stored at −20°C until further study [13].

Quality control standards

Lowest quality control standards, medium quality control standards, and highest quality control standards were prepared by spiking drug-free plasma with LX to give solutions containing 101.53, 406.12 and 1244.24 ng/ml, respectively. They were stored at −20°C til analysis.

Sample preparation

An aliquot quantity of 100 μl of rat plasma spiked with 10 μl of calibration standard solution of LX was taken in a 2 ml stopper centrifuge tube and mixed for 10 s. To this, 10 μl of internal standard (IS) solution (50 μg/ml) was added and mixed for 20 s. The drug was extracted by vortexing with 1.5 ml of selected extracting solvents (acetonitrile, methanol and di-chloromethane) in a spinix vortexer for 10 min. followed by centrifugation at 10,000 rpm for 5 min at 4 °C. The supernatant was withdrawn and dried under nitrogen at 25 psi for 10 min at 40 °C. The residue was reconstituted with 100 μl of mobile phase and 20 μl was injected onto the RP-HPLC column [13].
for LX concentrations by validated RP-HPLC method. The first order experiment was conducted at 20 °C until analyzed. The plasma samples were analyzed after transdermal application of formulated nanoparticle containing 2.5 mg of LX. 2 ml of blood samples were collected from the tail vein at 0.25, 0.5, 1, 2, 3, 4, 6, 9, 12 and 24 h time points into heparinized collection tubes. The blood was immediately centrifuged (1000 × g) for 10 min at an ambient temperature. The supernatant plasma layer was separated and stored at −20 °C until analyzed. The plasma samples were analyzed for LX concentrations by validated RP-HPLC method. The first order experimentation. After transdermal application of formulated

Animals) guidelines. The rats weighing 130–150 gm were housed with free access to food and water, except for the final 12 h before experiment. After transdermal application of formulated nanoparticle containing 2.5 mg of LX. 2 ml of blood samples were collected from the tail vein at 0.25, 0.5, 1, 2, 3, 4, 6, 9, 12 and 24 h time points into heparinized collection tubes. The blood was immediately centrifuged (1000 × g) for 10 min at an ambient temperature. The supernatant plasma layer was separated and stored at −20 °C until analyzed. The plasma samples were analyzed for LX concentrations by validated RP-HPLC method. The first order elimination rate constant (k_e) was estimated by the least square regression of plasma concentration–time data points of the curves describing the terminal log-linear decay phase. The plasma half-life (t_1/2) was calculated from k_e (t_1/2 = 0.693/k_e). The area under the plasma concentration–time curve from zero to the last measurable plasma concentration at time t (AUC(t)) was calculated by applying the trapezoidal rule. The area was extrapolated to infinity (AUC(∞)) by the addition of C(t)/k_e to AUC(∞), where C(t) is the last detectable drug concentration. The absorption rate constant (k_a) was determined by the residual method. The maximum observed LX concentration (C_max) and the time at which C_max was observed (T_max) were obtained directly from the profile. The AUMC/AUC(0–∞) is the area under the plot of time vs. the product of time and concentration extrapolated to infinity and was calculated by trapezoidal rule. The mean residence time (MRT) was determined by AUMC divided by AUC. All the pharmacokinetic parameters were calculated using Microsoft office excel 2003 (Microsoft Corporation, USA) software application. [12]

The Wagner–Nelson method [18] was applied to deconvolute the percentage of the LX absorbed using Eq. (1).

\[ F_t = C_t + K_{AUC(t)} AUC(0–t) \]  

Where, F_t is the amount of drug absorbed. The fraction absorbed (FRA) was calculated using eq. (2) and was plotted against the fraction of drug dissolved (FRD) at the same time and the linear regression analysis was used to examine the in vitro–in vivo relationship.

\[ \text{Fraction absorbed(FRA)} = C_t + K_{AUC(t)} AUC(0–t)/K_a AUC(0–t) \]  

Establishment of in vivo in vitro correlation (IVIVC)

An IVIVC refers to the predictive mathematical model describing the relationship between in vitro property of a controlled-release dosage form (usually the rate or extent of drug dissolution or release) and a relevant in vivo response, such as plasma drug concentration or amount of drug absorbed. A level A correlation is usually estimated by a two-stage procedure: deconvolution followed by comparison of the fraction of drug absorbed (FRA) to the fraction of drug dissolved (FRD). A correlation of this type represents a point-to-point relationship between in vitro dissolution and the in vivo input rate [19]. Accordingly, the deconvolution procedure was done on nanoparticles using mean LX plasma concentration vs. time profile using the method of wagner–nelson. The data of FRA (obtained by deconvolution) and FRD for each formulation were then plotted to develop an IVIVC model. The linear, quadratic, and cubic models (Eq. (2) bearing the following forms were tested to obtain the best fit:

\[ Y = a + bX, Y = a + bX + cX^2, Y = a + bX + cX^2 + dX^3 \]  

where a, b, c, d represent regression parameters associated with each function, Y is the FRA in vivo and X is the FRD in vitro. The coefficients of determination (r^2) for all developed models were determined. The highest r^2 value equation was considered as the best fitting model.

Statistical analysis

The linearity of the proposed method was evaluated by measuring the single factor analysis of variance (ANOVA) of the linear regression data. Statistical significance was established by a P-value<0.05, which indicates that the model is explained by the proposed regression at a 95% confidence interval.

RESULTS AND DISCUSSION

Preparation of SLN and NLC

Both SLN and NLC formulations were successfully prepared using high-speed homogenization method. The particle size, zeta potential, and poly dispersity index were found to be within the range of 140–193 nm±0.220, −22 to −32 mV, and 0.354–0.301 for SLN formulations and 146–201 nm±0.232, −23 to −30 mV, and 0.355–0.345±0.145 for NLC formulations, respectively. The entrapment efficiency of the SLN formulations was found within the range of 42%–72% and that for the NLC formulations was 61%–79%. Thermal analyses such as DSC, XRD showed good results. In vitro permeation rate and controlled release property of carbopol-loaded SLN, NLC gel was studied.

Selection and development of chromatographic method

Normal phase chromatography can be used for the separation of non-ionic and non-polar substances, while reversed-phase chromatography (C8 and C18) can be used for the separation of non-ionic as well as ionic non-polar to semi-polar substances. Thus, LX (an ionizable semi-polar weak acid) can satisfactorily be separated by reversed phase chromatography. However, octylsilsesquioxane columns are less retentive as compared to octadecylsilane. The majority of the ionizable pharmaceutical compounds can be very well separated in octadecylsilane reversed phase columns [16]. Therefore, octadecylsilane column was considered for isolation of LX from the plasma sample. A mixture of methanol and phosphate buffer (pH 4.5) was used as a mobile phase for the analysis of LX [14]. The optimum ratio of acetonitrile to phosphate buffer (pH 4.5) used in the current investigation was 65.35%v/v, which was selected on the basis of best resolution and absence of tailing and fronting. The best resolution and sensitivity of the peaks of LX and IS were obtained at 377 nm and flow rate of 1 ml/min of the mobile phase.

Validation of methods

Specificity

Typical chromatogram (fig. 1) of a mixture of LX and IS revealed that they are well separated under the RP-HPLC conditions applied. A chromatogram of blank plasma sample is shown in fig. II. Retention time was found 9.3 min for LX and 10.4 min for IS. In the comparison of a chromatogram of LX and IS (fig. 1) with the chromatogram of blank plasma (fig. 2), the absence of interference of plasma components is observed around the zone of the retention time of LX and IS. The chromatogram of the medium level quality control sample [i.e. 406.12 ng/ml] of LX spiked with rat plasma (fig. 3) showed a good resolution peaks for LX and IS which are well differentiated from the peaks of plasma components.

Selection of extracting solvent for recovery of drug

On the basis of capability of solvent to extract the maximum amount of drug from plasma was selected for extracting of LX from rat plasma. The recovery efficiency of LX from rat plasma was found to be 83.52±0.78, 82.11±0.56, 79.04±0.78, 76.46±0.89, 68.28±1.05, and 71.08±1.25% in acetonitrile, ethanol, methanol, hexane, dichloromethane and chloroform, respectively. Among the different solvents, acetonitrile showed maximum recovery efficiency, and therefore, acetonitrile was selected as the extracting solvent for extraction of LX from rat plasma.
Linearity
The ratio of peaks area of LX to IS at various concentrations of LX in plasma was determined. The chromatographic responses (ratio of peaks area of LX to IS vs. LX concentration) were found to be linear over an analytical range of 25.38–2046.45 ng/ml with regression coefficient (r²) value 0.999 which showed good linearity. The linear regression equation obtained was Y = 0.001X + 0.013.

Precision and accuracy
The accuracy of the proposed RP-HPLC method was determined by using three quality control samples, and the results are reported in table 1. The relative standard deviation (RSD) of the intra-day assay of the drug was ranged from 3.51 to 5.35 % and for the inter-day assay was from 2.77 to 3.16 % (table 2).

Stability
The result of the stability of LX in rat plasma at different conditions is presented in table 3. The result revealed that the final drug concentration of each quality control sample at three freeze-thaw cycles and the sample stored at room temperature for 24 h and 1 mo were almost similar with the initial concentration. The RSD value (n = 6) of final concentration of LX after three freeze-thaw cycles, 24 h and 1 mo was <10.87, <9.69 and <7.01, respectively.
Table 1: Peak area of the chromatogram of lornoxicam and I. S. at different concentration of lornoxicam

<table>
<thead>
<tr>
<th>Concentration of LX (ng/ml)</th>
<th>Peak area of the chromatogram</th>
<th>Ratio of peak area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lornoxicam</td>
<td>I. S. (Piroxicam)</td>
</tr>
<tr>
<td>25.38</td>
<td>10590</td>
<td>315383</td>
</tr>
<tr>
<td>50.77</td>
<td>19414</td>
<td>326485</td>
</tr>
<tr>
<td>101.53</td>
<td>48744</td>
<td>330127</td>
</tr>
<tr>
<td>203.06</td>
<td>90937</td>
<td>296772</td>
</tr>
<tr>
<td>406.12</td>
<td>189793</td>
<td>298161</td>
</tr>
<tr>
<td>846.09</td>
<td>417630</td>
<td>340716</td>
</tr>
<tr>
<td>1244.24</td>
<td>580504</td>
<td>333671</td>
</tr>
<tr>
<td>1637.16</td>
<td>799309</td>
<td>333077</td>
</tr>
<tr>
<td>2046.45</td>
<td>960772</td>
<td>335589</td>
</tr>
</tbody>
</table>

LX: Lornoxicam IS: internal standard, ng/ml: nanogram per milliliter

Table 2: Intra-and inter-day precision and accuracy for lornoxicam

| QC sample (ng/ml) | Intra-day variation | Inter-day variation | | | | |
|-------------------|---------------------|---------------------|---|---|---|
|                   | Observed value*     | R. SD%              | Accuracy % | Observed value* | R. SD% | Accuracy % |
| 101.53            | 96.42±5.16         | 5.35                | 94.97     | 103.14±3.26     | 3.16   | 101.59     |
| 406.12            | 428.31±12.63       | 2.95                | 105.46    | 395.49±10.72    | 2.71   | 97.38      |
| 1244.24           | 1115.18±39.17      | 3.51                | 89.63     | 1106.47±30.69   | 2.77   | 88.93      |

(mean±SD; n = 6), QC: Quality control, RSD: relative standard deviation ng/ml: nanogram per milliliter

Table 3: Stability of LX in rabbit plasma

<table>
<thead>
<tr>
<th>Stability</th>
<th>QC sample (ng/ml)</th>
<th>Observed value*</th>
<th>R. SD%</th>
<th>Accuracy %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Freeze-thaw stability</td>
<td>101.53</td>
<td>105.23±9.38</td>
<td>8.91</td>
<td>103.64</td>
</tr>
<tr>
<td></td>
<td>406.12</td>
<td>384.75±41.81</td>
<td>10.87</td>
<td>94.74</td>
</tr>
<tr>
<td>Short term (24 h)</td>
<td>1244.24</td>
<td>1121.47±68.58</td>
<td>6.12</td>
<td>90.13</td>
</tr>
<tr>
<td></td>
<td>101.53</td>
<td>96.98±6.9</td>
<td>6.90</td>
<td>95.52</td>
</tr>
<tr>
<td></td>
<td>406.12</td>
<td>374.99±36.24</td>
<td>9.69</td>
<td>92.11</td>
</tr>
<tr>
<td></td>
<td>1244.24</td>
<td>1167.57±81.14</td>
<td>6.95</td>
<td>93.84</td>
</tr>
<tr>
<td>Long term (30 d)</td>
<td>101.53</td>
<td>109.08±7.14</td>
<td>6.55</td>
<td>107.44</td>
</tr>
<tr>
<td></td>
<td>406.12</td>
<td>384.57±26.94</td>
<td>7.01</td>
<td>94.69</td>
</tr>
<tr>
<td></td>
<td>1244.24</td>
<td>1178.41±101.65</td>
<td>8.63</td>
<td>94.71</td>
</tr>
</tbody>
</table>

(mean±SD; n = 6). ng/ml: nanogram per milliliter RSD: relative standard deviation LX: Lornoxicam

Pharmacokinetic study in rats

The validated RP-HPLC method was applied to carry out a pharmacokinetic study of LX in rats. The mean plasma concentration of LX versus time profile following a single transdermal application of prepared LX loaded SLN and NLC on six rats is presented in fig. 4. The various pharmacokinetic parameters are summarized in table 4.

In vitro–in vivo correlation (IVIVC)

To assess the viability and validity of the sustaining nature of nanoparticles, IVIVC study is essential, since prolonged release products may be especially suited for this kind of study. When the FRD from nanoparticles in pH 7.4 was plotted against the FRA, a linear correlation was obtained (fig. 5).

![Fig 4: Mean plasma concentration versus time profile of loraxicam following transdermal delivery of lipid nanocarrier to rats (n = 6).](image)
Hence, it can be inferred that LX was stable in rat plasma up to one month at room temperature. In the IVIVC study, a higher value of correlation coefficient suggested that a good correlation existed between in vitro-in vivo data. Finally a novel simple, simple, sensitive, precise, rapid, accurate, and economical and reliable RP-HPLC method was developed and validated for the estimation of LX in rat plasma using PDA detector. A maximum recovery of drug from plasma resulted by using acetonitrile as extracting solvent in comparison to other solvents. The results obtained proved that the method was accurate and reproducible, and drug was stable in rat plasma.

**CONCLUSION**

Therefore, it can be concluded that the validated chromatographic condition is suitable for determination of pharmacokinetic profile of LX in rat plasma after transdermal application of SLN and NLC on rat and is also applicable to the routine therapeutic monitoring of the LX. A linear relationship was observed between FRD and FRA in IVIVC study.

**ACKNOWLEDGEMENT**

We acknowledge the financial support provided by University Grants Commission (UGC). We also acknowledge Akumbs Drugs, Hridwar, India for supplying Lornoxicam. We also acknowledge Lipoid, GmbH Germany for supplying phospholipon 90G.

**CONFLICTS OF INTERESTS**

Declared none

**REFERENCES**


**Table 4: Pharmacokinetic parameters of Lornoxicam as lipid nanocarrier to healthy rabbit volunteers**

<table>
<thead>
<tr>
<th>Pharmacokinetic parameter</th>
<th>Observed value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum plasma concentration, C_max (ng/ml)</td>
<td>6381.5±971.27 (SLN)</td>
</tr>
<tr>
<td>Time required to reach maximum plasma concentration, T_max (h)</td>
<td>4.0±0.00 (SLN)</td>
</tr>
<tr>
<td>Area under the curve, AUC_0→∞ (ng h/ml)</td>
<td>19917.21±711.24 (SLN)</td>
</tr>
<tr>
<td>Area under momentum curve, AUMC_0→∞ (ng h²/ml)</td>
<td>122052.26±25847.08 (SLN)</td>
</tr>
<tr>
<td>Elimination half-life, t_1/2 (h)</td>
<td>7.27±1.21 (SLN)</td>
</tr>
<tr>
<td>Elimination rate constant, K_e (h⁻¹)</td>
<td>0.095±0.101 (SLN)</td>
</tr>
<tr>
<td>Mean residence time, MRT (h)</td>
<td>6.128±1.057 (SLN)</td>
</tr>
</tbody>
</table>

(mean±SD; n = 6). SLN: solid lipid nanoparticle formulation, NLC: nanostructured lipid carrier formulation.

**Fig. 5: Standard curve for In vitro & In vivo co-relation between LX & Internal standard VS. Conc. of LX**


