RESEARCH PAPER

Development and QbD-Based Optimization of Fast Dissolving Tablets of Meloxicam Prepared by Spherical Crystallization Technique.

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ABSTRACT

Meloxicam, a poorly water-soluble selective cyclooxygenase-2 (COX-2) inhibitor, exhibits low oral bioavailability owing to its limited aqueous solubility and slow dissolution rate. The present study was undertaken to improve the dissolution, absorption, and bioavailability of Meloxicam by employing spherical agglomeration followed by the development of fast dissolving tablets (FDTs). Spherical agglomerates were prepared using the quasi-emulsion solvent diffusion technique with methanol, water, and dichloromethane as the good solvent, poor solvent, and bridging liquid, respectively. Pluronic F-68 was used as carrier in drug-to-carrier ratios of 1:0.5, 1:0.75, and 1:1. The prepared agglomerates were evaluated for practical yield, drug content, solubility, flow properties, particle size, scanning electron microscopy, and in vitro dissolution. Microscopic studies confirmed the formation of spherical agglomerates with improved flowability and significantly enhanced dissolution. Optimized agglomerates were compressed into FDTs using co-processed superdisintegrants containing croscarmellose sodium and crospovidone in ratios of 1:1, 1:2, and 1:3. The formulation containing a 1:3 ratio (F9) exhibited the fastest drug release and was selected for pharmacokinetic evaluation in New Zealand white rabbits using a validated LC-MS/MS method following a crossover design. Compared with the pure drug, the optimized FDT demonstrated significantly higher Cmax (158.46 ± 0.15 vs. 67.56 ± 0.43 ng/mL), shorter Tmax (6.15 ± 0.14 vs. 11.42 ± 0.32 h), higher Ka (7.76 ± 0.01 vs. 2.92 ± 0.01 h^{-1}), and greater $AUC_{0-\infty}$ (564.9 ± 1.36 vs. 126 ± 1.23 ng·h/mL). These findings indicate that spherical agglomeration combined with optimized FDT formulation markedly enhances the dissolution, oral absorption, and bioavailability of Meloxicam, thereby providing a faster onset of therapeutic action and improved patient compliance.

Keywords: LC-MS/MS, Meloxicam, fast dissolving, In-vivo studies, pharmacokinetic parameters

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INTRODUCTION

Meloxicam is a non-steroidal anti-inflammatory drug (NSAID) that selectively inhibits cyclooxygenase-2 (COX-2) and is widely prescribed for the management of chronic inflammatory conditions such as osteoarthritis, rheumatoid arthritis, ankylosing spondylitis, and other musculoskeletal disorders. Its poor water solubility results in a slow dissolution rate, delayed onset of action, variable oral bioavailability, and inconsistent therapeutic response. Furthermore, prolonged residence of undissolved drug particles in the gastrointestinal tract may contribute to local gastric irritation. Therefore, improving the dissolution characteristics of Meloxicam is essential to enhance its oral absorption and overall therapeutic efficacy 1.

In the present investigation, spherical agglomerates of Meloxicam were prepared using the quasi-emulsion solvent diffusion technique. To systematically optimize the formulation variables influencing spherical agglomeration, a 32 factorial design was employed as a statistical screening tool. The statistical analysis enabled the identification of the most influential factors governing the quality of spherical agglomerates, thereby facilitating formulation optimization 2. The resulting spherical crystals exhibited improved micromeritic properties, making them suitable for direct compression into tablet dosage forms while simultaneously enhancing the drug dissolution rate.

The optimized spherical agglomerates were subsequently incorporated into fast dissolving tablets (FDTs) to achieve rapid drug release and improved patient compliance. To evaluate whether the enhanced in vitro dissolution translated into improved in vivo performance, pharmacokinetic studies were conducted in New Zealand white rabbits using a crossover study design. The pharmacokinetic comparison demonstrated that the optimized fast dissolving tablets significantly enhanced the rate and extent of Meloxicam absorption compared with the pure drug 3. Overall, the present investigation demonstrates that the combination of spherical agglomeration, statistical experimental design, and fast dissolving tablet technology represents a promising strategy for improving the physicochemical properties, pharmacokinetic performance, and therapeutic effectiveness of poorly water-soluble drugs such as Meloxicam.

MATERIALS AND METHODS

Meloxicam was obtained from Dr. Reddy's Laboratories, Hyderabad, India. Pluronic F-68was purchased from S.D. Fine Chemicals Ltd., Mumbai, India. All other chemicals used were of analytical grade.The in vivo study was conducted according to CPCSEA guidelines after obtaining approval from the Institutional Animal Ethics Committee (IAEC), Nirmala College of Pharmacy (Approval No. 12/PHD/IAEC/NCPA, dated 29-04-2024).

Preparation of Spherically Agglomerates: Spherical agglomerates of Meloxicam were prepared by the quasi-emulsion solvent diffusion technique in the presence and absence of stabilizers. The compositions of the stabilizers employed in the formulations are presented in Table 1. Initially, Meloxicam (1.0 g) was dissolved in 25.0 mL of N,N-dimethylformamide, which served as the good solvent. Chloroform (12.5 mL) was then incorporated as the bridging liquid, and the resulting solution was added dropwise into 100 mL of distilled water containing different concentration of Poloxamer F118, which acted as the poor solvent phase. The dispersion was stirred continuously at 500 rpm using a propeller-type mechanical stirrer (Remi Motors Ltd., Mumbai, India) at ambient temperature. Agitation was continued for 30 minutes to facilitate the formation and growth of spherical agglomerates through solvent diffusion and particle coalescence 4. The resulting agglomerates were separated by filtration using Whatman filter paper No.[42], washed appropriately to remove residual solvents, and dried before further physicochemical characterization.

Table 1. Composition of Meloxicam Spherical Agglomerates as per 32 factorial design

Ingredients	MF1	MF2	MF3	MF4	MF5	MF6	MF7	MF8	MF9
Meloxicam(g)	1	1	1	1	1	1	1	1	1
Poloxomer -F338 (g)	0.5	0.75	1	0.5	0.75	1	0.5	0 .75	1
N,N-dimethylformamide	10	10	10	18	18	18	25	25	25
Dichloromethane(ml)	5	5	5	9	9	9	12.5	12.5	12.5
Water (ml)	85	85	85	73	73	73	62.5	62.5	62.5

Experimental design: Meloxicam spherical agglomerates were prepared by varying two independent formulation variables, namely surfactant concentration (X_1) and the combination of good solvent and bridging solvent (X_2), according to a 3^2 full factorial design, a three-level, two-factor experimental design. The effects of these variables on the formulation were evaluated using time taken for 50% drug release (T_{50}) and dissolution efficiency (DE) as the dependent responses 5. Polynomial equations were generated by multiple regression analysis, and statistically significant model terms were identified at a 95% confidence level ($p < 0.05$) using analysis of variance (ANOVA). Factor X_1 (surfactant concentration) was investigated at three levels (0.5, 0.75, and 1.0% w/v), whereas factor X_2 (combination of good solvent and bridging solvent) was evaluated at three levels (15, 27, and 37.5%, respectively).

In Vitro Drug release study: In-vitro dissolution studies of pure drug and spherical agglomerates were carried out for 60 minutes using USP Dissolution test apparatus type II (Lab India DISSO 2000, eight stages) at 50 rpm.Spherical agglomerates equivalent to 100 mg of Meloxicam was used for dissolution study at 37±0.50 C in 900ml of 6.8 pH phosphate buffer as dissolution medium. Aliquot equal to 5 ml was withdrawn at regular time intervals (10, 20, 30, 40, 50, 60 min), an equal volume of fresh dissolution medium was replaced to maintain the sink condition and aliquots were measured at 372 nm UV/Visible spectrophotometer 6.

Preparation of Meloxicam tablets: To investigate the effect of co-processed superdisintegrants on the performance of Meloxicam fast dissolving tablets, three formulations (F1, F2, and F3) were prepared using croscarmellose sodium and crospovidone in different ratios of 1:1, 1:2, and 1:3, respectively. The required quantities of all formulation ingredients (Table 3) were accurately weighed, passed through a suitable sieve, and blended uniformly. The prepared powder blend was lubricated with magnesium stearate and mixed gently to ensure uniform distribution. Finally, the lubricated blend was compressed into tablets by the direct compression method using a Cadmach single-punch tablet compression machine fitted with a 7 mm round flat-faced punch 7.

Table 3. Composition of ingredients for Meloxicam fast dissolving tablets

S.No	Ingredients	F1	F2	F3
1	Meloxicam crystals prepared with Poloxomer -F118 in 1:1 ratio	15	15	15
2	Croscarmalose sodium+ Crospovidone	5	5	5
3	Micro crystaline cellulose	76	76	76
4	Talc	2	2	2
5	Magnesium streate	2	2	2
	Total weight	100	100	100

Pharmacokinetic Study: The pharmacokinetic performance of pure Meloxicam and the optimized Meloxicam fast dissolving tablet (FDT) formulation was evaluated in healthy New Zealand white rabbits using a randomized two-period, two-treatment crossover study design. Twelve healthy rabbits (10 ± 2 weeks old) weighing 3.0 ± 0.2 kg were included in the study. The animals were randomly allocated into two groups (n = 6) and acclimatized under standard laboratory conditions. Prior to dosing, the rabbits were fasted overnight with unrestricted access to water to minimize variability in drug absorption. All animals were handled carefully throughout the study to reduce stress 8.

The study consisted of two treatment periods separated by a washout interval of two weeks to eliminate any residual drug from the previous treatment. In the first treatment period, one group received pure Meloxicam while the other received the optimized FDT formulation. Following the washout period, the treatments were crossed over between the two groups. Both formulations were administered orally by gastric intubation.The animal dose was calculated from the recommended human therapeutic dose using body weight conversion according to the following equation 9:

Human dose of Meloxicam = 7.5mg.

$$\text{Animal dose} = \frac{\text{Human dose} \times \text{Animal weight}}{\text{Human weight}}$$

$$= 7.5 \times 3/70 = 0.3214\text{mg} = 0.4\text{mg}$$

Estimation of Meloxicam in Plasma by LC–MS/MS

Plasma concentrations of Meloxicam were determined using a validated UPLC–MS/MS method with Piroxicam as the internal standard (IS). Chromatographic analysis was performed using a Waters UPLC system coupled with an API 2000 triple quadrupole mass spectrometer equipped with a heated nebulizer operating in positive electrospray ionization mode. Separation

was achieved on an Agilent Zorbax Eclipse XDB C18 column (4.6 × 150 mm, 5 µm) maintained at 35°C. The mobile phase consisted of 5 mM ammonium formate and acetonitrile (30:70, v/v), delivered at a flow rate of 1.0 mL/min with an injection volume of 15 µL. The total run time was 2 min, and both Meloxicam and Piroxicam were detected within 0.8–1.5 min using multiple reaction monitoring (MRM) transitions of m/z 352.1→115.1 for Meloxicam and m/z 332.2→121.0 for Piroxicam.

Stock solutions of Meloxicam and Piroxicam (1 mg/mL) were prepared in methanol and stored at 2–8°C. Working standard solutions were prepared by serial dilution with 60% acetonitrile in water. Calibration standards ranging from 10 to 2000 ng/mL were prepared by spiking blank rabbit plasma with appropriate volumes of the working standard solutions. Plasma samples (200 µL) were mixed with 20 µL of the internal standard solution and extracted using Phenomenex Strata-X solid-phase extraction cartridges. The cartridges were conditioned with methanol and water, washed with water, and the analytes were eluted with methanol. The eluates were evaporated under a gentle stream of nitrogen at 50°C, and the dried residues were reconstituted with 300 µL of the mobile phase. After vortex mixing, 15 µL of each sample was injected into the UPLC–MS/MS system 10-11.

Chromatographic data were acquired and processed using Analyst® software version 1.4.2 (Applied Biosystems, Canada). Quantification was based on the peak area ratio of Meloxicam to the internal standard using a weighted ($1/x^2$) linear regression model. The calibration curve showed good linearity over the concentration range of 10–2000 ng/mL with the regression equation $y = 0.00232x - 0.00133$, which was used for the determination of Meloxicam concentrations in rabbit plasma.

Determination of Pharmacokinetic Parameters:

Pharmacokinetic parameters, including maximum plasma concentration (C_max), time to reach maximum plasma concentration (Tmax), area under the plasma concentration–time curve (AUC), absorption rate constant (Ka), elimination rate constant (Kel), and elimination half-life (t1/2), were determined using standard non-compartmental analysis. The pharmacokinetic profiles of the optimized FDT formulation were compared with those of the pure drug to assess the improvement in oral absorption and systemic bioavailability 12.

RESULTS AND DISCUSSION:

Spherical agglomerates of meloxicam were successfully prepared by the quasi-emulsion solvent diffusion (QESD) technique employing a three-solvent system consisting of a good solvent, a bridging solvent, and a poor solvent. The selection of the solvent system was based on the solubility characteristics of meloxicam and the mutual miscibility of the solvents. N,N-Dimethylformamide (DMF) was selected as the good solvent owing to its excellent solubilizing ability for meloxicam, chloroform served as the bridging solvent because of its immiscibility with water and ability to wet the drug crystals, while distilled water was employed as the poor solvent. This solvent combination facilitated efficient spherical crystallization of meloxicam through the quasi-emulsion solvent diffusion process.

During the QESD process, the drug solution containing the good solvent and bridging solvent was introduced into the external poor solvent phase containing different concentrations of Pluronic F-68under continuous stirring. Initially, quasi-emulsion droplets were formed, followed by gradual diffusion of the good solvent from the droplets into the surrounding aqueous phase. Simultaneously, water diffused into the droplets, reducing the solubility of meloxicam and inducing crystal nucleation and growth. The bridging solvent preferentially wetted the crystal surfaces, promoting the formation of liquid bridges between adjacent crystals, which subsequently coalesced to form dense, spherical agglomerates with improved micromeritic properties.

The incorporation of Pluronic F-68during the agglomeration process markedly enhanced the dissolution characteristics of meloxicam. The hydrophilic polymer improved wettability, reduced the interfacial tension between the drug particles and the dissolution medium, and increased the effective surface area available for dissolution. Consequently, the spherical agglomerates exhibited immediate wetting and rapid sinking in the dissolution medium, whereas pure meloxicam powder remained floating on the surface for a longer period because of its hydrophobic nature. The improved wettability and reduced diffusion layer thickness significantly accelerated the dissolution rate of the agglomerated crystals.

Response surface analysis demonstrated that both formulation variables significantly influenced the dissolution characteristics of meloxicam spherical agglomerates. Increasing the concentration of Pluronic F-68(X_1) resulted in a significant reduction in the time required for 50% drug release (T_{50}), indicating a faster dissolution rate. Similarly, increasing the good solvent–bridging solvent ratio (X_2) also reduced the T_{50} values. In contrast, dissolution efficiency (DE) increased with increasing levels of both formulation variables. These findings indicate that higher surfactant concentration and an optimized solvent ratio synergistically improved drug wettability, crystal morphology, and dissolution performance. Using chosen X1, X2, combos of the two elements according to the 32 Factorial, nine different formulations of Meloxicam Spherical Agglomerates were prepared. These formulations were then assessed to determine the importance of the mixed results of X1, X2, in order to determine the optimal blend as well as the focus needed to achieve the desired drug release in 1 hour. Three concentration levels of Surfactant concentration were chosen and assigned the codes -1 = 0.5%, 0 = 0.75%, and +1 = 1%. Using DESIGN EXPERT 7 software, polynomial equations were produced for the 50 % of drug release (T 50) and Dissolution Efficiency. Figure 1-2 displays the response surface and contour plots for the 50 % of drug release (T 50) and Dissolution Efficiency applying X1 and X2, respectively, on both axes. The formula $Y= b0 + b1\ X1 + b2\ X2 + b12\ X1\ X2 + b11\ X1^2 + b22\ X2^2$ is the polynomial equation for 3^2 full factorial designs. If Y represents the dependent variable, b0 is the nine batches' mathematical mean answer, and b1 is the factor X1 estimated co-efficient. The average effect of adjusting each factor one from a low to a high value over time is represented by the primary effects (X1 and X2). When two factors are altered at the same time, the response changes as indicated by the interaction term (X1X2). The polynomial expressions ($X1^2$ and $X2^2$) are included in order to explore non-linearity. The correctness of the obtained equations was proved by generating one check point formulations of intermediate concentration (VF). Polynomial equation for Time taken for 50% drug release (T_{50}) (Y_1)= $Y1=19.878-2.833X1-2.700X2 +0.350X1X2+0.733X12-0.067X22$. The polynomial equations for formulae for the time taken for Dissolution Efficiency is Y2= $Y2=36.237+2.890X1+2.828X2+0.018X1X2-0.660X12 +0.185X22$.

Among all the formulations investigated, the spherical agglomerates prepared with Meloxicam and Pluronic F-68in a 1:1 ratio exhibited the highest dissolution performance, releasing the maximum amount of drug within 60 min. The enhanced dissolution behaviour can be attributed to improved particle morphology, increased surface wettability, reduced particle aggregation, and enhanced penetration of dissolution medium into the agglomerates.

To evaluate the influence of co-processed superdisintegrants on the performance of fast dissolving tablets, spherical agglomerates exhibiting superior dissolution characteristics were compressed into tablets using different ratios of croscarmellose sodium and crospovidone (1:1, 1:2, and 1:3). Among the formulations evaluated (F1–F3), tablets containing the co-processed superdisintegrants in a 1:3 ratio (F3) demonstrated the fastest disintegration and the highest drug release. The improved dissolution profile is attributed to the synergistic action of

crospovidone, which promotes rapid water uptake through capillary action, and croscarmellose sodium, which facilitates tablet swelling, resulting in rapid tablet disintegration and enhanced drug dissolution. Dissolution kinetic analysis revealed that all formulations followed first-order release kinetics, as evidenced by the linear relationship between log percentage of drug remaining and time. These findings suggest that the optimized spherical agglomerates, in combination with an appropriate ratio of co-processed superdisintegrants, significantly improve the dissolution behaviour of meloxicam fast dissolving tablets.

The in vivo pharmacokinetic study was performed according to the experimental protocol described previously. Plasma concentrations of Meloxicam were quantified using a validated liquid chromatography–tandem mass spectrometry (LC–MS/MS) method, which demonstrated excellent sensitivity and selectivity for the determination of Meloxicam in rabbit plasma. Calibration curves were constructed using blank plasma, blank plasma spiked with the internal standard (IS), and eight calibration standards covering the required concentration range. The developed analytical method showed satisfactory linearity, precision, and accuracy for pharmacokinetic analysis.

The mean plasma concentration–time profiles of pure Meloxicam and the optimized fast dissolving tablet (FDT) formulation are presented in Figure 4, while the corresponding plasma drug concentrations are summarized in Table 6. Pharmacokinetic parameters, including maximum plasma concentration (C_max), time to reach maximum plasma concentration (T_max), absorption rate constant (K_a), elimination rate constant (K_el), area under the plasma concentration–time curve (AUC), elimination half-life (t1/2), and mean residence time (MRT), were calculated by non-compartmental analysis and are presented in Table 7.

Table 6. Plasma Concentrations of Meloxicam following oral administration of Pure Meloxicam and optimized fast dissolving tablets

Time (h)	**Plasma concentration (ng/ml) (Mean s.d)**	**Plasma concentration (ng/ml) (Mean s.d)**
Time (h)	Pure drug	Meloxicam fast dissolving tablets
0	0	0
0.5	08.52 1.87	28.22 1.37
1	11.361.75	36.451.77
1.5	12.521.53	42.211.55
2	14.621.15	45.231.22
3	16.741.66	49.631.14
4	18.821.36	54.131.66
5	19.631.44	61.191.68
6	21.921.25	68.321.86
8	22.771.42	62.161.73
10	24.911.23	57.431.24
12	27.731.25	49.22 1.35
14	24.631.35	42.211.42
16	21.971.54	35.251.62
18	18.851.33	28.551.19
20	15.931.22	23.131.66
24	12.281.37	17.191.46

Table 7. Statistical Treatment of Pharmacokinetic Parameters (Mean S.D.) of following oral administration of Pure Meloxicam and optimized fast dissolving tablets

Pharmacokinetic parameter	**Pure Drug**	**Optimized fast disolving tablets**	**Calculated value of 't'**
Cmax (ng/ml)	67.57 0.42	158.45 0.13	12.52***
t1/2 (h)	11.43 0.31	6.14 0.13	8.95***
Kel (h-1)	0.95 0.002	0.81 0.001	5.69***
Ka (h-1)	2.91 0.01	7.75 0.01	85.76***
AUC0-□ (ng h/ml)	125 1.11	465.4. 1.27	145.39***
Null hypothesis (Ho): There is no significant difference between the pharmacokinetic parameters of Meloxicam obtained with pure drug and optimized fast disolving tablets.Table value of 't' with 10 DF at the 0.001 level is 4.587.	Null hypothesis (Ho): There is no significant difference between the pharmacokinetic parameters of Meloxicam obtained with pure drug and optimized fast disolving tablets.Table value of 't' with 10 DF at the 0.001 level is 4.587.	Null hypothesis (Ho): There is no significant difference between the pharmacokinetic parameters of Meloxicam obtained with pure drug and optimized fast disolving tablets.Table value of 't' with 10 DF at the 0.001 level is 4.587.	Null hypothesis (Ho): There is no significant difference between the pharmacokinetic parameters of Meloxicam obtained with pure drug and optimized fast disolving tablets.Table value of 't' with 10 DF at the 0.001 level is 4.587.
Result: Ho is not accepted as the calculated 't' value more than the table Value of't' with 10 DF at 0.001 levels of significance. It was therefore concluded that there was significant difference between the pharmacokinetic parameters of obtained with pure drug and optimized fast disolving tablets.	Result: Ho is not accepted as the calculated 't' value more than the table Value of't' with 10 DF at 0.001 levels of significance. It was therefore concluded that there was significant difference between the pharmacokinetic parameters of obtained with pure drug and optimized fast disolving tablets.	Result: Ho is not accepted as the calculated 't' value more than the table Value of't' with 10 DF at 0.001 levels of significance. It was therefore concluded that there was significant difference between the pharmacokinetic parameters of obtained with pure drug and optimized fast disolving tablets.	Result: Ho is not accepted as the calculated 't' value more than the table Value of't' with 10 DF at 0.001 levels of significance. It was therefore concluded that there was significant difference between the pharmacokinetic parameters of obtained with pure drug and optimized fast disolving tablets.

The optimized FDT formulation exhibited a significantly improved pharmacokinetic profile compared with the pure drug. The mean C_max of the optimized FDT was 158.45 ± 0.13 ng/mL, which was approximately 2.3-fold higher than that of pure Meloxicam (67.57 ± 0.42 ng/mL), indicating enhanced systemic absorption. Furthermore, the optimized formulation achieved a significantly shorter T_max (6.14 ± 0.13 h) compared with the pure drug (11.43 ± 0.31 h), demonstrating a faster onset of absorption.

The absorption rate constant (K_a) increased markedly from 2.91 ± 0.01 h^{-1} for pure Meloxicam to 7.75 ± 0.01 h^{-1} for the optimized FDT, confirming rapid drug absorption following administration of the optimized formulation. In contrast, the elimination rate constant (K_el) was slightly reduced from 0.95 ± 0.002 h^{-1} to 0.81 ± 0.001 h^{-1}, indicating prolonged systemic availability. The optimized FDT also produced a substantially higher $AUC_{0-\infty}$ (465.4 ± 1.27 ng·h/mL) compared with pure Meloxicam (125.0 ± 1.11 ng·h/mL), representing nearly a four-fold increase in the extent of drug absorption.

The improved pharmacokinetic performance can be attributed to the enhanced dissolution rate of the spherical agglomerates and the rapid disintegration of the fast dissolving tablet, which increased the effective surface area available for dissolution and facilitated faster gastrointestinal absorption. Overall, the optimized Meloxicam FDT significantly enhanced both the rate and extent of oral drug absorption, resulting in improved bioavailability compared with the conventional pure drug formulation.

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Table 2. In-vitro dissolution kinetics of Meloxicam spherical crystals as per 32 factorial design

S.No.	Formulation	T 50 (min)	DE 30 (%)
S.No.	Formulation	T 50 (min)	DE 30 (%)
1	F1	26.5	30.12
2	F2	22.2	33.23
3	F3	20.3	36.11
4	F4	23.5	32.88
5	F5	20.1	36.34
6	F6	17.5	38.17
7	F7	20.2	35.43
8	F8	17.2	39.51
9	F9	15.4	41.49

Table 4. In-vitro dissolution kinetics of Meloxicam fast dissolving tablets

S.No.	Formulation	T 50 (min)	T 90 (min)	DE 15 (%)	K (min-1)	Correlation coefficient values	Correlation coefficient values
S.No.	Formulation	T 50 (min)	T 90 (min)	DE 15 (%)	K (min-1)	Zero Order	First order
1	F1	6.0	20.1	48.78	0.115	0.8493	0.9751
2	F2	4.7	15.6	56.37	0.148	0.8268	0.9762
3	F3	3.1	10.3	66.31	0.222	0.8049	0.9833

Table 5. Analyte Concentrations of Stock Dilutions of Standard Meloxicam Solution with Plasma

S.NO	Sample Name	Analyte Concentration (ng/ml)	Analyte peak area	IS Peak Area	Area Ratio	Calculated Concentration (ng/ml)	Accuracy (%)
1	Plasma blank	0	0	0	0	N/A	N/A
2	Blank+ISTD	0	0	82222	0	N/A	N/A
3	CC1	10	2158	100544	0.02	9.845	98.47
4	CC2	20	4281	92611	0.05	20.523	102.63
5	CC3	50.050	11617	100612	0.12	50.412	100.72
6	CC4	150.100	35541	100598	0.35	153.055	101.98
7	CC5	500.350	111503	98126	1.14	490.983	98.12
8	CC6	1000.750	224912	95368	2.36	1018.373	101.77
9	CC7	1501.100	318306	95017	3.35	1446.322	96.36
10	CC8	2001.500	415352	89596	4.64	2001.258	99.98

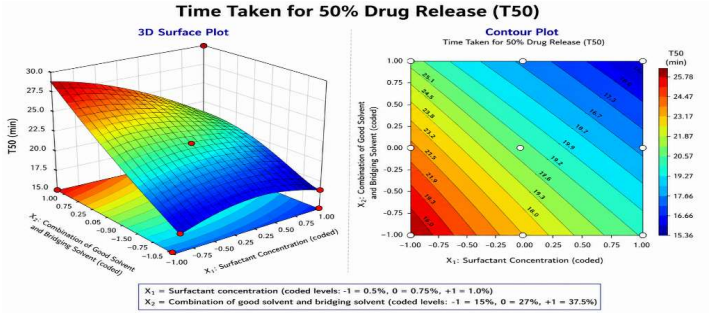

Figure 3D surface Plot and Contour Plot for Time Taken for 50% drug release (T_{50})

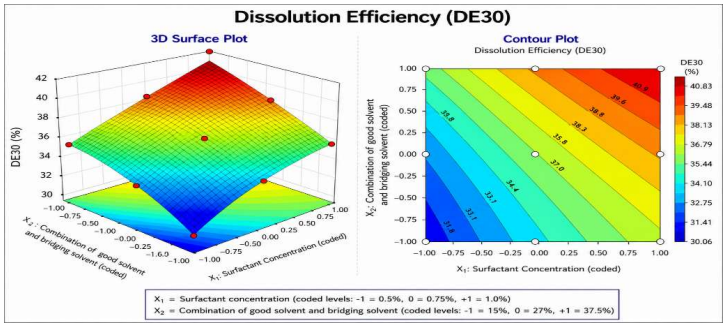

Figure 3D surface Plot and Contour Plot for Time Taken for dissolution efficiency (DE30)

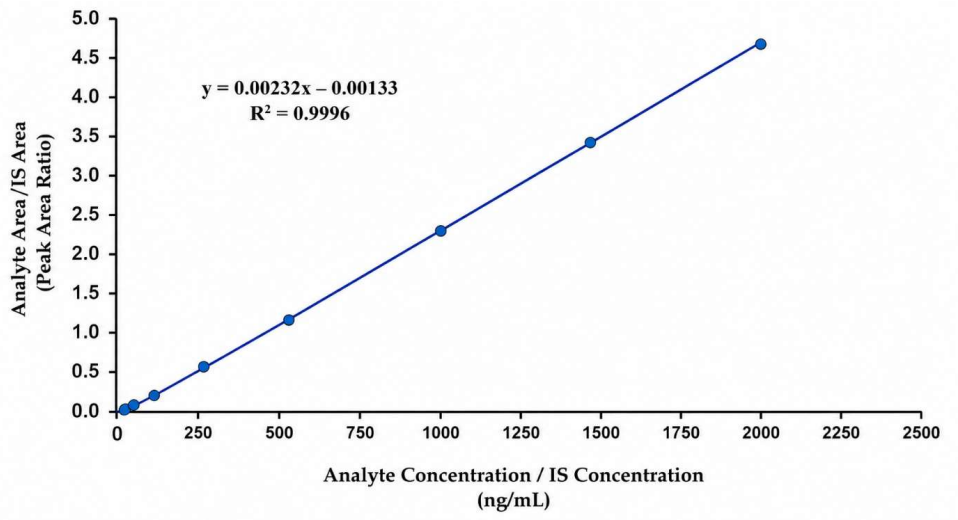

Figure Calibration Curve for Estimation of Meloxicam in Plasma

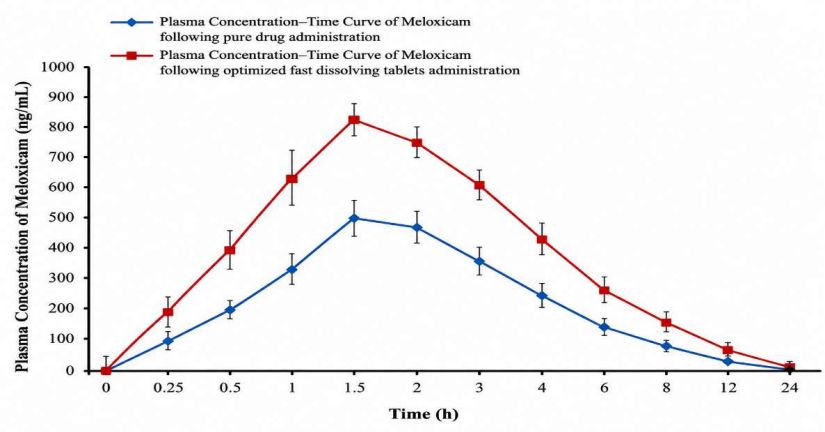

Figure Concentration-Time Curve of Meloxicam following oral administration of Pure Meloxicam and optimized fast dissolving tablets