Research Article

Design And Development Of Fast Dissolving Tablets Of Mefenic Acid Prepared By Spherical Crystallization Technique

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Abstract

Mefenamic acid is a Non Steroidal anti- inflammatory drug belonging to the BCS class II. It has a low oral bioavailability due to poor aqueous solubility and poor dissolution rate. The present study was undertaken to improve the dissolution, absorption, and bioavailability of Mefenamic acid 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 N,N-dimethyl formamide, water, and chloroform 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 Mefenic acid, thereby providing a faster onset of therapeutic action and improved patient compliance.

Keywords: LC-MS/MS, Mefenic acid, fast dissolving, In-vivo studies, pharmacokinetic parameters.

Introduction

Mefenamic acid is a non-steroidal anti-inflammatory drug (NSAID) that selectively inhibits release of certain chemical messengers that cause fever, pain and inflammation . 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 Mefenamic acid is essential to enhance its oral absorption and overall therapeutic efficacy [1].

In the present investigation, spherical agglomerates of Mefenamic acid were prepared using the quasi-emulsion solvent diffusion technique. To systematically optimize the formulation variables influencing spherical agglomeration, a 3^2 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 Mefenamic acid 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 Mefenic acid.

Materials and Methods

Mefenic acid 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 Mefenamic acid 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, Mefenamic acid (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 62.5 mL of distilled water containing different concentration of Pluronic F-68, which acted as the poor solvent phase. The dispersion was stirred continuously at 1000 rpm using a propeller-type mechanical stirrer (Remi Motors Ltd., Mumbai, India) at ambient temperature. Agitation was continued for 20 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 Mefenic acid Spherical Agglomerates as per 3^2 factorial design

Ingredients	MF1	MF2	MF3	MF4	MF5	MF6	MF7	MF8	MF9
Mefenic acid (g)	1	1	1	1	1	1	1	1	1
Pluronic F-68 (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
Chloroforme(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: Mefenic acid 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 (D**E)** 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 Mefenamic acid was used for dissolution study at 37 ± 0.5^0 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 225 nm UV/Visible spectrophotometer [6].

Table 2: In-vitro dissolution kinetics of Mefenamic acid spherical crystals as per 3^2 factorial design

S.No.	Formulation	T_{50} (min)	DE_{30} (%)
1	F_1	28.7	26.04
2	F_2	25.6	29.33
3	F_3	22.7	32.18
4	F_4	25.4	28.73
5	F_5	22.3	32.15
6	F_6	19.6	35.13
7	F7	22.0	30.68

Preparation of Mefenic acid tablets: To investigate the effect of co-processed superdisintegrants on the performance of Mefenamic acid 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 Mefenamic acid fast dissolving tablets

S.No	Ingredients	F_1	F_2	F_3
1	Mefenamic acid crystals prepared with Pluronic F-68 in 1:1 ratio	200	200	200
2	Croscarmalose sodium+ Crospovidone	15	15	15
3	Micro crystaline cellulose	81	81	81
4	Talc	2	2	2
5	Magnesium streate	2	2	2
	Total weight	300	300	300

Pharmacokinetic Study: The pharmacokinetic performance of pure Mefenamic acid and the optimized Mefenamic acid 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 Mefenamic acid 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 Mefenamic acid = 7.5mg.

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

$$= 100x3/70 = 4.287 \text{ mg} = 5\text{mg}$$

Estimation of Mefenamic acid in Plasma by LC–MS/MS

Mefenamic acid in plasma was estimated using a validated liquid chromatography–tandem mass spectrometry (LC-MS/MS) method. Chromatographic separation was performed using a Waters UPLC system coupled with an API 2000 mass spectrometer equipped with a heated nebulizer. The mass spectrometer was operated in negative ionization mode. Mefenamic acid was detected at *m/z* 240.2 as the parent ion and 196.0 as the product ion, while mefenamic acid-d4 was used as the internal standard (ISTD), with parent and product ions at *m/z* 244.2 and 200.2, respectively.

Separation was achieved using a Phenomenex Synergi 4 µ Polar-RP 80A column (4.6 × 75 mm). The column temperature was maintained at 35°C and the Peltier temperature at 10°C. The mobile phase consisted of ammonium formate and acetonitrile (30:70, v/v), delivered at a flow rate of 1.0 mL/min. The injection volume was 10 µL, with a total run time of 2 min. Mefenamic acid and the ISTD showed retention times within approximately 0.5–1.2 min.

For preparation of the mefenamic acid stock solution, a quantity of working standard equivalent to 5 mg was accurately weighed, transferred to a 5-mL volumetric flask, dissolved in methanol, and diluted to volume with the same solvent. The concentration was calculated considering the purity of the standard, and the solution was stored at 2–8°C. Similarly, 0.005 g of mefenamic acid-d4 was dissolved in methanol and diluted to 5 mL. The ISTD stock solution was further diluted with 60% acetonitrile in water to obtain a concentration of 75 µg/mL.

Calibration standards ranging from 50 to 7000 ng/mL were prepared in plasma and labeled CC1–CC8. Fresh calibration standards were prepared for each validation run.

Table 4: In-vitro dissolution kinetics of Mefenic acid fast dissolving tablets

S.No.	Formulation	T_{50} (min)	T_{90} (min)	DE_{15} (%)	K (min^{-1})	Correlation coefficient values	
						Zero Order	First order
1	F_1	5.9	20.1	48.78	0.115	0.8493	0.9751
2	F_2	4.7	15.6	56.37	0.148	0.8268	0.9762
3	F_3	3.1	10.3	66.31	0.222	0.8049	0.9833

For extraction, 0.25 mL plasma was transferred into a vial and 25 µL of ISTD solution was added. After vortex mixing, 2.5 mL of tert-butyl methyl ether was added. Samples were shaken for 15 min and centrifuged at 4000 rpm for 10 min at 20°C. The organic layer was transferred and evaporated under nitrogen at 45°C. The residue was reconstituted with 0.5 mL mobile phase, vortexed, and transferred to autosampler vials. Finally, 10 µL was injected into the LC-MS/MS system, and plasma concentrations were calculated from the calibration curve using the analyte-to-ISTD peak-area ratio.[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 Mefenamic acid 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 = 0.000160x - 0.000252, which was used for the determination of Mefenic acid concentrations in rabbit plasma.

Table 5: Analyte Concentrations of Stock Dilutions of Standard Mefenamic acid 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	254	513643	0	N/A	N/A
3	CC1	50.05	3879	528938	0.01	50.407	100.71
4	CC2	100.15	6997	506198	0.01	97.939	97.79
5	CC3	250.3	17284	484351	0.04	258.119	103.12
6	CC4	500.65	34646	504084	0.07	500.215	99.91
7	CC5	1001.25	77371	577631	0.13	978.007	97.68
8	CC6	2002.5	134349	520675	0.26	1887.085	94.24
9	CC7	5006.25	345626	529110	0.65	4782.401	95.53
10	CC8	7008.75	578109	544120	1.06	7780.67	111.01

Determination of Pharmacokinetic Parameters:

Pharmacokinetic parameters, including maximum plasma concentration (C_max), time to reach maximum plasma concentration (T_{max}), area under the plasma concentration–time curve (AUC), absorption rate constant (K_a), elimination rate constant (K_{el}), and elimination half-life ($t_{1/2}$), 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].

Result and Discussion

Spherical agglomerates of Mefenic acid 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 Mefenamic acid and the mutual miscibility of the solvents. N,N-Dimethylformamide (DMF) was selected as the good solvent owing to its excellent solubilizing ability for Mefenic acid , 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 Mefenamic acid 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 Mefenamic acid 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 Mefenic acid . 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 Mefenamic acid 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 Mefenamic acid 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 3^2 Factorial, nine different formulations of Mefenamic acid 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)= $Y1=22.33-2.90X1-3.25X2+0.120X1X2+0.13X1^2-0.03X2^2$. The polynomial equations for formulae for the time taken for Dissolution Efficiency is $Y2= Y2=32.15+3.20X1+2.45X2+0.130X1X2-0.22X1^2+0.37X2^2$.

Among all the formulations investigated, the spherical agglomerates prepared with Mefenic acid 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.

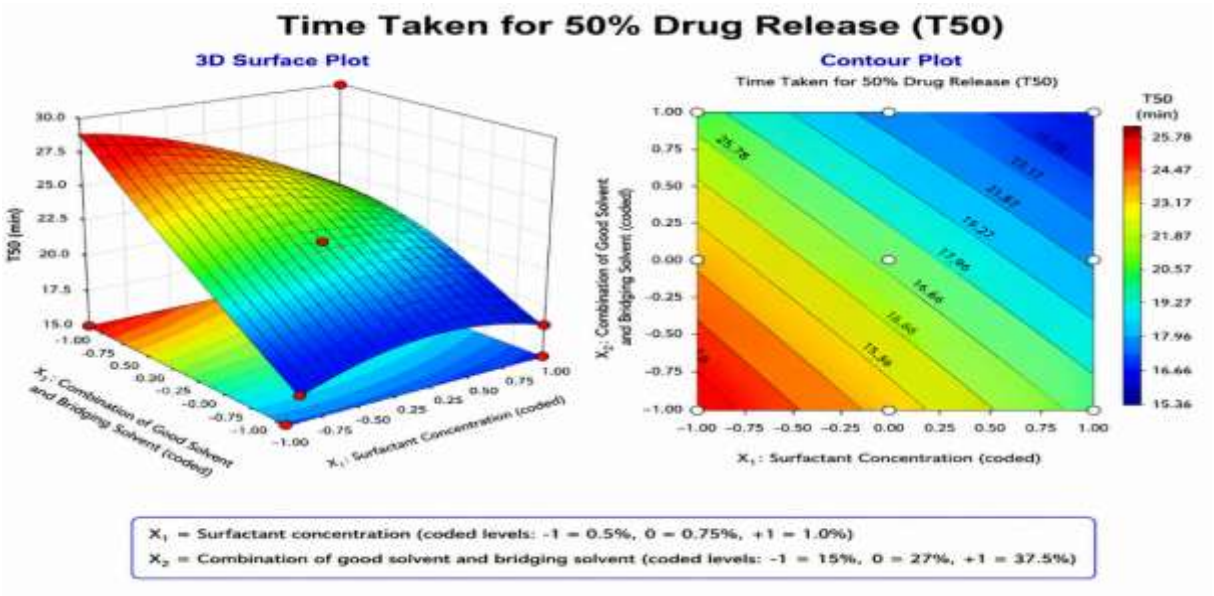

Figure1: 3D surface Plot and Contour Plot for Time Taken for 50% drug release (T_{50})

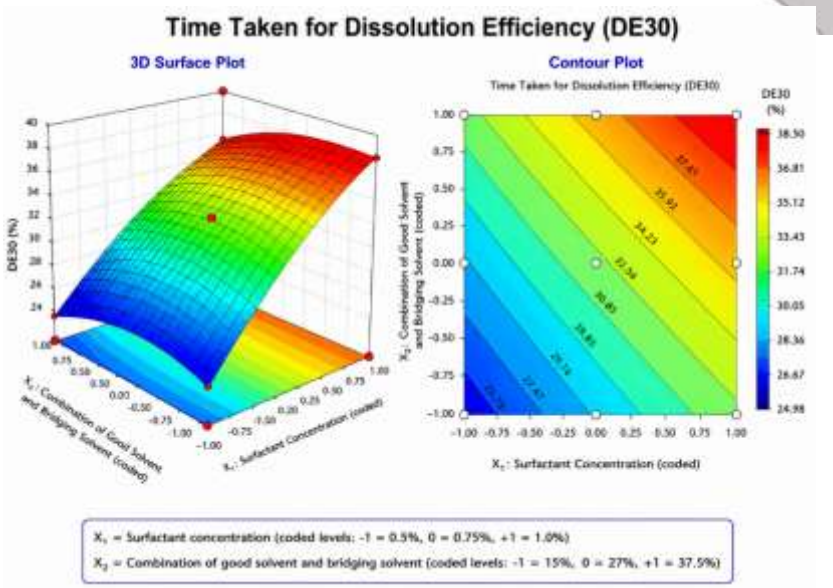

Figure2: 3D surface Plot and Contour Plot for Time Taken for dissolution efficiency **(DE_{30})**

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 Mefenamic acid fast dissolving tablets.

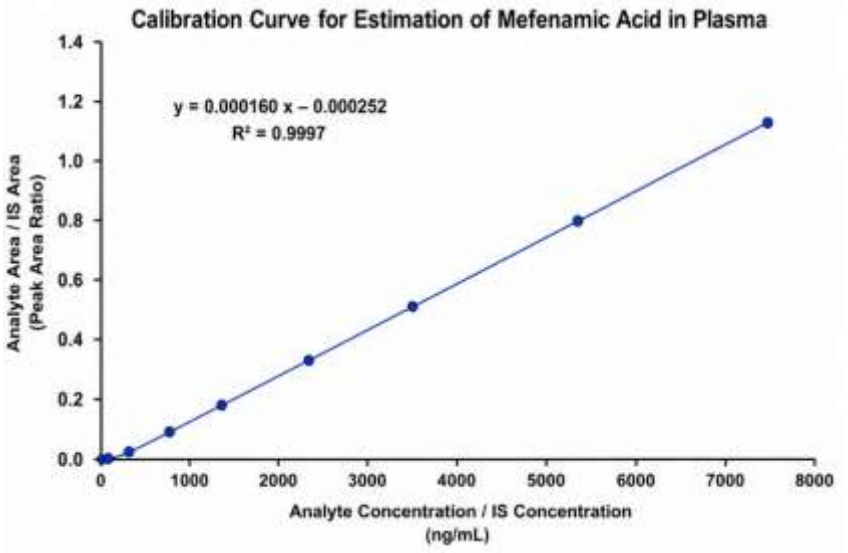

Figure 3: Calibration Curve for Estimation of Mefenic acid in Plasma

The vivo pharmacokinetic study was performed according to the experimental protocol described previously. Plasma concentrations of Mefenamic acid were quantified using a validated liquid chromatography–tandem mass spectrometry (LC–MS/MS) method, which demonstrated excellent sensitivity and selectivity for the determination of Mefenamic acid 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 Mefenamic acid 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.

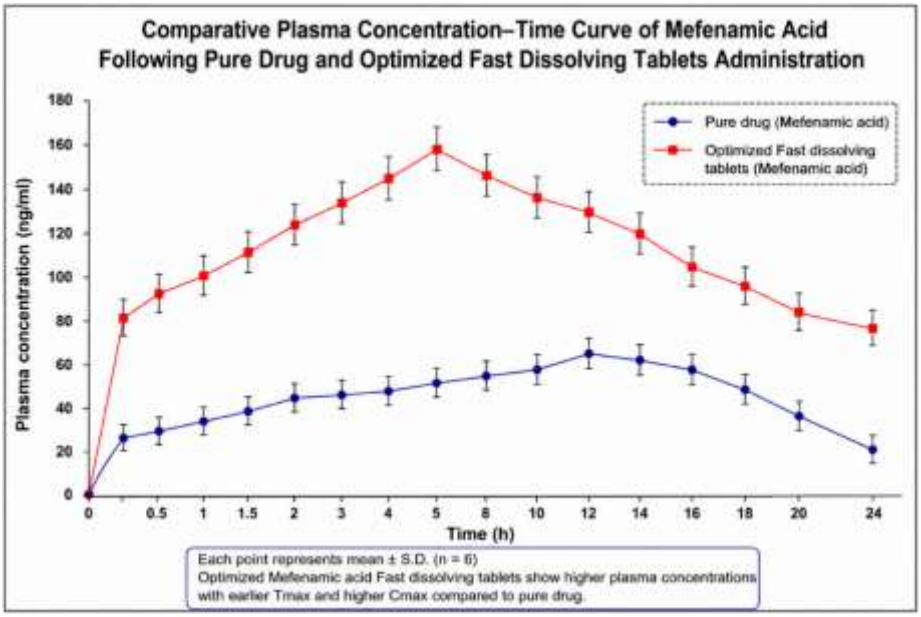

Figure 4: Concentration-Time Curve of Mefenic acid following oral administration of Pure Mefenic acid and optimized fast dissolving tablets

Table 6: Plasma Concentrations of Mefenamic acid following oral administration of Pure Mefenamic acid and optimized fast dissolving tablets

Time (h)	Plasma concentration (ng/ml) (Mean ± s.d)	
	Pure drug	Mefenamic acid fast dissolving tablets
0	0	0
0.5	27.52 ±1.32	82.34 ±0.25
1	31.24±1.45	94.83±0.15
1.5	34.67±1.53	102.36±0.51
2	39.54±1.12	113.45±0.13

3	46.75±1.43	124.83±0.72
4	48.28±1.23	135.47±0.49
5	50.46±1.24	145.43±0.55
6	54.49±1.37	158.46±0.47
8	57.45±1.68	147.17±1.52
10	60.39±1.54	137.42±1.59
12	67.56±1.24	129.52 ±1.68
14	64.35±1.26	119.64±1.26
16	59.46±1.47	105.52±1.38
18	48.72±1.39	97.45±1.15
20	35.67±1.214	83.62±1.67
24	22.43±1.28	77.34±1.38

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

Pharmacokinetic parameter	Pure Drug	Optimized fast disolving tablets	Calculated value of 't'
C_{max} (ng/ml)	67.56 ± 0.43	158.46 ± 0.15	12.52***
$t_{1/2}$ (h)	11.42 ± 0.32	6.15 ± 0.14	8.95***
K_{el} (h^{-1})	0.096 ± 0.004	0.045 ± 0.003	5.69***
K_a (h^{-1})	0.181 ± 0.01	0.375 ± 0.01	85.76***
$AUC_{0-\infty}$ (ng h/ml)	1405.51 ± 15.23	4443.22± 16.36	145.39***
Null hypothesis (H_o): There is no significant difference between the pharmacokinetic parameters of Mefenamic acid 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: H_o 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 158.46 ± 0.13 ng/mL, which was approximately 2.3-fold higher than that of pure Mefenamic acid (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 0.181 ± 0.01 h^{-1} for pure Mefenamic acid to 0.375 ± 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 0.095 ± 0.002 h^{-1} to **0.045** ± 0.001 h^{-1}, indicating prolonged systemic availability. The optimized FDT also produced a substantially higher AUC_0–∞ (4443.22 ± 1.27 ng·h/mL) compared with pure Mefenamic acid (1405.0 ± 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 Mefenic acid 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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