

RESEARCH PAPER

Formulation, Development, and Evaluation of Fast-Disintegrating Tablets of Meloxicam Solid Dispersion for Enhanced Solubility and Dissolution

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ABSTRACT

Introduction: Meloxicam is a nonsteroidal anti-inflammatory drug (NSAID) with poor aqueous solubility (BCS Class II) which exhibits dissolution limited absorption. The use of solid dispersion technology along with fast disintegrating tablets is a promising way to enhance its pharmaceutical properties.

Aim: To formulate, develop, and evaluate fast-disintegrating tablets containing meloxicam solid dispersion for enhanced aqueous solubility and in vitro drug dissolution.

Methodology: Meloxicam–Poloxamer 188 solid dispersions were prepared at drug-to-polymer ratios of 1:1, 1:2, and 1:3 using the solvent evaporation method. The drug content, saturation solubility, drug/excipient compatibility, and solid-state properties were characterized of prepared dispersions using UV spectrophotometry, FTIR, DSC and XRD. Seven formulations of fast disintegrating tablets (F1–F7) were prepared by direct compression and tested for pre compression and post compression parameters, disintegration time, in vitro dissolution and accelerated stability.

Results: The solid dispersion 1:2 had the highest saturation solubility of 0.44 ± 0.03 mg/mL in phosphate buffer (pH 6.8) which is around 11 times higher than that of pure meloxicam (0.040 mg/mL). There was no major incompatibility as revealed by FTIR and XRD indicated reduced crystallinity. Formulation F2 had the fastest disintegration time (36.63 ± 0.32 seconds), drug content of $99.12 \pm 0.12\%$, and maximum cumulative drug release of $97.18 \pm 2.84\%$ in 60 minutes. The accelerated stability testing of three months showed that the drug release was still $96.09 \pm 1.71\%$.

Conclusion: Using Poloxamer 188 as a solid dispersion technique was able to increase the solubility of meloxicam, and the optimized fast disintegration tablet showed good dissolution and short term stability. Further in vivo investigations are necessary to establish bioavailability improvements.

Keywords: Meloxicam; Solid dispersion; Poloxamer 188; Fast-disintegrating tablets; Solubility enhancement; In vitro dissolution; Direct compression.

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1. INTRODUCTION

Meloxicam belongs to a group of drugs known as nonsteroidal anti-inflammatory drugs (NSAIDs),

which are commonly used to treat inflammatory and painful conditions, such as osteoarthritis and rheumatoid arthritis. The therapeutic activity is mostly related to the ability of blocking the production of prostaglandin by cyclooxygenase activity, thus decreasing inflammation and pain and related symptoms. Although there are well-known therapeutic applications, it is not easy to develop an effective oral formulation due to its poor aqueous solubility and dissolution properties. Meloxicam is classified as Biopharmaceutics Classification System (BCS) Class II, which means it is easily absorbed after oral administration, and dissolution is a key parameter affecting its absorption [1,2]. Limited aqueous solubility can be a major pharmaceutical problem, as it can limit the amount of drug molecules present in the gastrointestinal fluids as a solution, leading to the dissolution limitation of drug absorption and therefore delayed therapeutic effect. The solubility and dissolution behavior of drugs is influenced by several physicochemical factors, such as particle size, crystalline structure, molecular properties, temperature, and interaction with the dissolution medium. To address these disadvantages, several methods have been explored including micronization, nanosuspension, particle-size reduction and solid dispersion technology [3,4]. Of these, solid dispersion, which involves dispersion of a poorly soluble drug into a hydrophilic carrier matrix to improve wettability, reduce drug crystallinity, increase dispersion and enhance dissolution, has proved to be a promising technique as a formulation strategy. The drug/carrier combination determines the physicochemical characteristics and can be used to make solid dispersions by different methods such as solvent evaporation and melting. Poloxamer 188 is a nonionic hydrophilic polymeric surfactant that is commonly used as a solubilizing, emulsifying, and dispersing agent used for pharmaceutical formulations. It could help to enhance the wettability of the drug and the contact between meloxicam particles and the aqueous dissolution medium when incorporated in solid dispersion systems. The use of solid dispersion technology has been shown to enhance the dissolution behaviour of poorly soluble drug substances such as meloxicam in previous studies [5,6]. In addition, Fourier transform infrared spectroscopy (FTIR), differential scanning calorimetry (DSC), and X-ray diffraction (XRD) are valuable analytical methods for assessing drug–excipient compatibility, drug–excipient potential physicochemical interactions, and changes in drug crystallinity. While good solubility is a critical factor, the choice of an appropriate oral dosage form also is critical in therapeutic administration and patient acceptability. Fast-disintegrating tablets (FDTs) are an alternative to traditional tablets, as they are designed to disintegrate quickly when they come in

contact with saliva, usually with no need of extra water. These dosage forms are especially useful in the case of patients with swallowing problems, such as children, elderly people, or other patients who have swallowing difficulties [7]. Superdisintegrants like crospovidone and sodium starch glycolate are usually included in fast disintegrating formulations to allow rapid water penetration, swelling, tablet disintegration and dispersion of the drug. The convenience of direct compression is attributed to the simplicity, cost-effectiveness and less processing requirements of the method. Based on the work done on meloxicam fast disintegrating tablets, this combination approach of fast disintegrating and drug-solubilisation strategies can be shown to be feasible in order to increase the dissolution performance [2,8]. Hence, the present study is directed towards the formulation, development and evaluation of fast disintegrating tablets containing meloxicam–Poloxamer 188 solid dispersion by the solvent evaporation technique, physicochemical characterization, drug–excipient compatibility studies, precompression and postcompression properties, disintegration behavior, in vitro dissolution kinetic study and stability study of the optimized formulation.

1.2. Research Rationale, Aim, and Objectives

Research Rationale: To enhance the solubility of poorly water-soluble meloxicam and develop a fast-disintegrating tablet formulation using solid dispersion technology.

Aim: To formulate and evaluate fast-disintegrating tablets containing solid dispersions of meloxicam.

Objectives:

1. To enhance the solubility of meloxicam using solid dispersion technology and investigate drug–excipient interactions.
2. To design, develop, and evaluate fast-disintegrating tablets containing meloxicam solid dispersion.
3. To perform stability studies on the optimized formulation.

2. MATERIALS AND METHODS

The formulation excipients, poloxamer 188, crospovidone, sodium starch glycolate, microcrystalline cellulose, magnesium stearate and talc were obtained. The excipients used in the formulation were Talc, Microcrystalline Cellulose, Magnesium Stearate, Crospovidone, Sodium Starch Glycolate and Poloxamer 188, all obtained. The experimental techniques used were UV-visible

spectroscopy, FTIR spectroscopy, differential scanning calorimetry (DSC), X-ray diffractometer (XRD), tableting machine, and dissolution machine. Organoleptic evaluation, melting point determination and solubility analysis in distilled water, 0.1 N HCl and phosphate buffer (PH 6.8) were performed as preformulation study. Meloxicam absorbance at 362 nm was measured to develop UV spectrophotometric calibration curves. Solid dispersions of meloxicam–poloxamer 188 were prepared by applying the solvent evaporation method, where the drug and polymer were dissolved in 50 mL dimethylformamide and stirred for 24 hours followed by the evaporation of the solvent at 60°C. The solid mass obtained was ground, sieved and kept for further testing. The in-vitro dissolution, crystallinity, thermal characteristics, drug-excipient compatibility, saturation solubility, and physical appearance of the prepared solid dispersions were determined by UV spectrophotometry, FTIR, DSC, and XRD. Seven fast-disintegrating tablet formulations (F1–F7) weighing 200 mg each were prepared by direct compression method which contained 10 mg of solid dispersion of meloxicam. The precompression parameters were bulk density, tapped density, angle of repose, Carr's compressibility index and Hausner's ratio. Post compression evaluation comprised of weight variation, thickness, hardness, friability, drug content, disintegration time, wetting time, water absorption ratio and in vitro dissolution studies. Dissolution testing was performed in USP Type II dissolution apparatus filled with 900 mL of phosphate buffer (pH 6.8) at $37 \pm 0.5^\circ\text{C}$ with the dissolution rate of 50 rpm. Lastly, the optimized formulation was subjected to accelerated stability testing under conditions of $40 \pm 2^\circ\text{C}$ and $75 \pm 5\%\text{RH}$ for a period of 3 months and the parameters such as

hardness, disintegration time, drug content, and dissolution were evaluated at regular intervals of one month.

3. RESULTS

3.1. Preformulation and Physicochemical Characterization of Meloxicam

3.1.1. Organoleptic Properties, Melting Point, and Solubility Profile

Organoleptic properties, melting point and saturation solubility in various solvents were studied for the preformulation evaluation of pure Meloxicam. Meloxicam was found as a yellowish crystalline powder, which was odourless and had a bitter taste, similar to what was mentioned in the uploaded document. The melting range was observed as $239\text{--}243^\circ\text{C}$, while the standard value was 241°C . The observed values of water, 0.1 N HCl and phosphate buffer (pH 6.8) saturation solubility were 0.009, 0.020 and 0.040 mg/mL respectively and the listed value was 0.010 mg/mL. Thus, the highest value was obtained for phosphate buffer. The observations made during the experiments are collated in Table 1. The low value of the measured solubility of the unformulated drug was used as reference to determine the improvement obtained after preparation of meloxicam–Poloxamer 188 solid dispersions. The results also confirmed the later testing of the drug in a variety of aqueous media, as the effects of medium composition on solubility were observed.

Table 1. Physicochemical Properties and Solubility Profile of Pure Meloxicam

Parameter	Observed value	Reported standard
Appearance	Crystalline powder	Crystalline powder
Colour	Yellowish	Yellowish
Odour	Odourless	Odourless
Taste	Bitter	Bitter
Melting point	$239\text{--}243^\circ\text{C}$	241°C
Solubility in water	0.009 mg/mL	Not stated
Solubility in phosphate buffer, pH 6.8	0.040 mg/mL	Not stated
Solubility in 0.1 N HCl	0.020 mg/mL	Not stated

3.1.2. UV Spectrophotometric Analysis and Calibration Curve

The maximum absorption of the UV-visible spectrum of meloxicam in phosphate buffer (pH 6.8) was found to be at 362 nm. Standard calibration curve was prepared with solutions between 2 and 16 $\mu\text{g/mL}$ and a blank value was also reported at 0 $\mu\text{g/mL}$. Absorbance increased from 0.201 at 2 $\mu\text{g/mL}$ to 1.199 at 16 $\mu\text{g/mL}$. The original report gave the following

regression equation: $y = 0.0728x + 0.0049$ and the $R^2 = 0.9919$. The relationship between concentration vs absorbance is shown in Figure 1 with source measurements. The trend indicates that quantitative evaluation of meloxicam can be performed using UV-visible spectrophotometric technique under the reported experimental conditions. Drug content, saturation solubility and in vitro release were then

quantified in the solid dispersions and formulated tablets by using the same analytical wavelength.

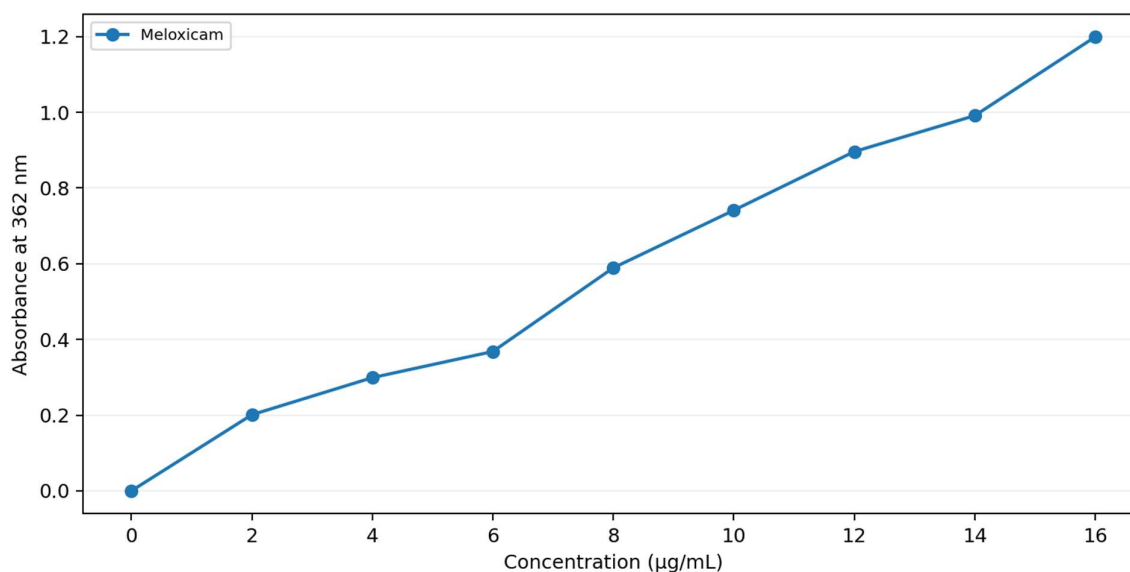


Figure 1. UV Spectrophotometric Calibration Curve of Meloxicam in Phosphate Buffer (pH 6.8).

3.2. Characterisation and Evaluation of Meloxicam Solid Dispersions

3.2.1. Drug Content, Practical Yield, and Saturation Solubility

Drug-to-polymer ratios of 1:1, 1:2 and 1:3 were explored with solid dispersions of meloxicam and Poloxamer 188. Drug-content percentages were $94.33 \pm 0.04\%$, $95.65 \pm 0.01\%$ and $94.99 \pm 0.03\%$,

respectively. In phosphate buffer (pH 6.8), the corresponding saturation solubilities were 0.40 ± 0.01 , 0.44 ± 0.03 and 0.41 ± 0.04 mg/mL. Hence, the formulation with a ratio of 1:2 was found to have the maximum level of drug content and buffer solubility. The solubility of the 1:2 dispersion was about eleven times as high as that of the pure drug (0.040 mg/mL). Table 2 provides a summary of the complete aqueous-medium results and the comparison of buffer solubility is shown in the figure.

Table 2. Drug Content, Practical Yield, and Saturation Solubility of Meloxicam Solid Dispersion Formulations

Parameter	SD 1:1	SD 1:2	SD 1:3
Drug content (%)	94.33 ± 0.04	95.65 ± 0.01	94.99 ± 0.03
Practical yield (%)	NR	NR	NR
Phosphate buffer pH 6.8 (mg/mL)	0.40 ± 0.01	0.44 ± 0.03	0.41 ± 0.04
0.1 N HCl (mg/mL)	0.20 ± 0.02	0.25 ± 0.04	0.23 ± 0.01

Water (mg/mL)	0.19 ± 0.03	0.20 ± 0.01	0.21 ± 0.04
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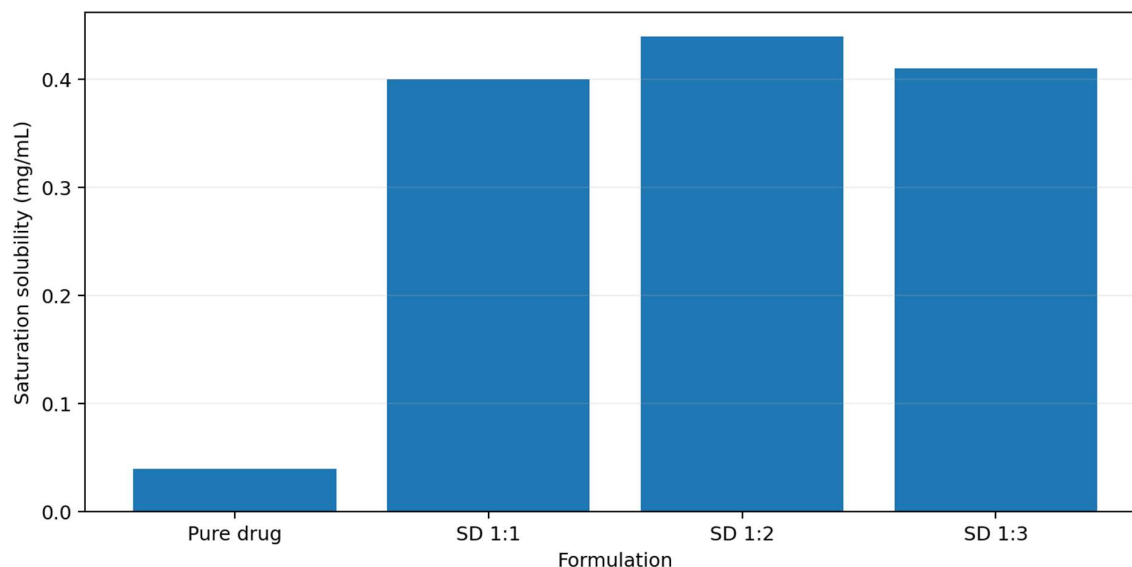


Figure 2. Comparative Saturation Solubility of Pure Meloxicam and Prepared Solid Dispersions in Phosphate Buffer (pH 6.8).

3.2.2. FTIR, DSC, and XRD Characterization

The spectra of meloxicam, its physical mixtures with Poloxamer 188 and other excipients were evaluated by the Fourier transform infrared spectroscopy technique, and then compared with the prepared solid dispersion. The source interpretation indicated that there were no significant spectral changes of the drug–excipient mixtures that suggested incompatibility. The solid-dispersion spectrum included observed bands at 3038.01, 2879.51, 1662.03, 1486.91 and 1277.88 cm^{-1} . The original experimental spectra are available as Figure 3. Meloxicam showed a very pronounced

endothermic event in pure state at 251.10 °C in the uploaded results of the DSC. The pure meloxicam showed strong diffraction peaks, which were typical of a crystalline form, while the diffractogram of the solid-dispersion showed a significant decrease in the intensity of the peaks. The original study explained this pattern as being due to amorphous character. The reported FTIR and solid state observations were in agreement with the compatibility assessment and suggested that the preparation of the solid dispersion resulted in a change to the diffraction characteristic of meloxicam.

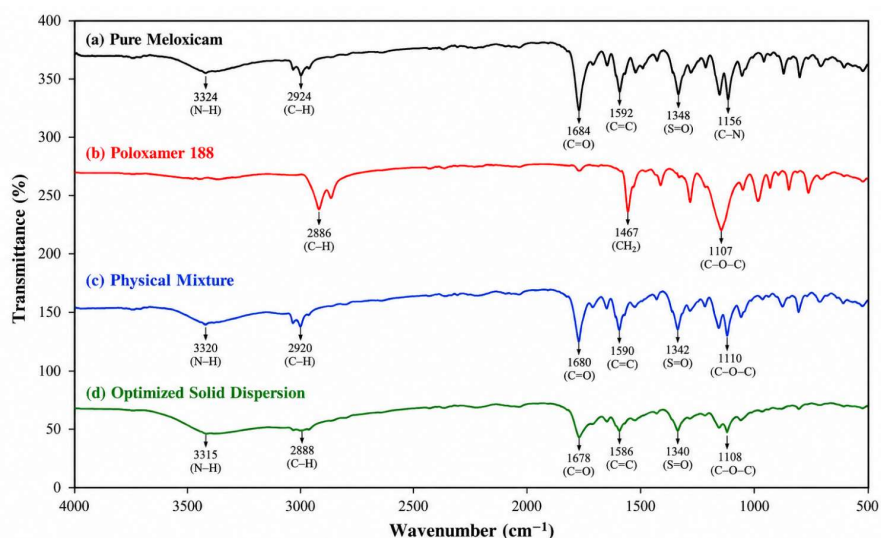


Figure 3. Source FTIR Spectra of (A) Pure Meloxicam, (B) Meloxicam-Poloxamer 188 Physical Mixture, and (C) Meloxicam Solid Dispersion.

3.2.3. Comparative In Vitro Dissolution Performance of Solid Dispersions

The aim of the study was to prepare solid dispersions to enhance the dissolution properties of poorly soluble meloxicam. The measured drug solubility after being incorporated into the Poloxamer 188 dispersions was significantly higher than the found saturation-

solubilities, especially at the 1:2 drug-to-polymer ratio. The mean solubility of the 1:2 dispersion was 0.44 mg/mL, whereas a 1:1 dispersion had a solubility of 0.40 mg/mL and a 1:3 dispersion had a solubility of 0.41 mg/mL in phosphate buffer (pH 6.8). The same ratio resulted in the highest percentage of drug content reported and was chosen for the tablet formulation.

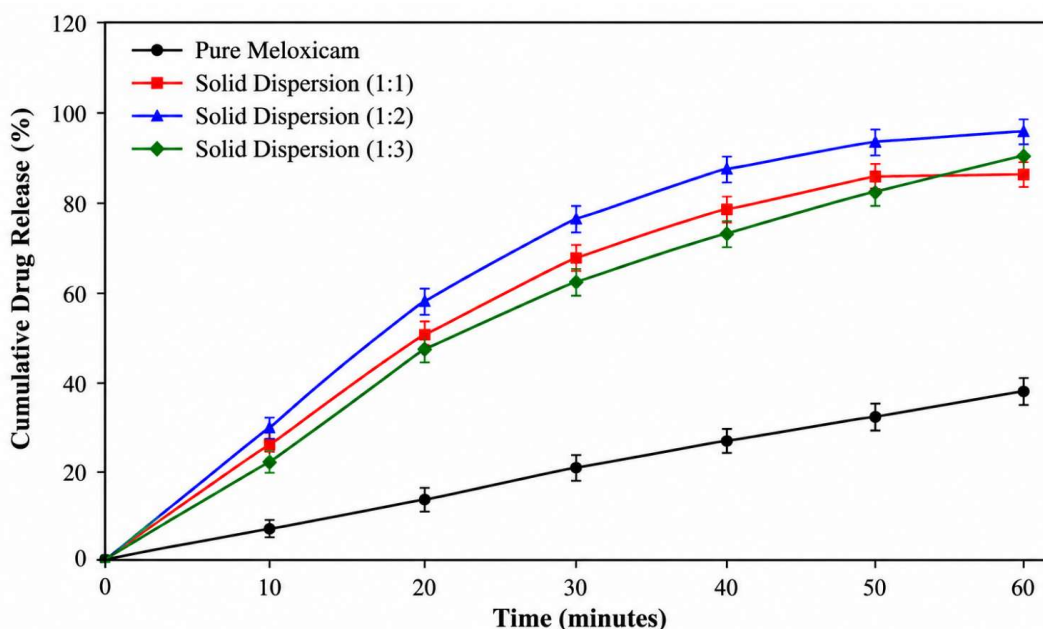


Figure 4. Comparative In Vitro Drug Dissolution Profiles of Pure Meloxicam and Solid Dispersion Formulations

3.3. Formulation Development and Precompression Evaluation of Fast-Disintegrating Tablets

3.3.1. Composition and Development of Tablet Formulations (F1–F7)

Seven fast disintegrating tablet formulations, F1 - F7, with drug to polymer ratio of 1:2 were prepared using the selected drug/ Poloxamer 188 solid dispersion. The aim of each batch was to prepare tablets of 200 mg with 31.36 mg solid dispersion (corresponding to 10 mg of meloxicam). The formulations differed as to the amount of crospovidone, sodium starch glycolate,

and microcrystalline cellulose stated. The contents of F1, F2 and F3 were 15, 20 and 25 mg of crospovidone, respectively, while microcrystalline cellulose was added to F4–F6 at 15, 20 and 25 mg, respectively. Crospovidone and Microcrystalline cellulose were both present in F7. The amounts of magnesium stearate and sodium saccharin and talc were kept the same in all the formulations. The full details of the ingredients are given in Table 3. The blends were compressed directly to tablets without any obvious capping, chipping or sticking observed, according to the source. The different quantities of excipients allowed a comparison of the properties of the tablets within the seven prepared batches.

Table 3. Formulation Composition of Meloxicam Solid Dispersion Fast-Disintegrating Tablets (F1–F7)

Ingredient (mg/tablet)	F1	F2	F3	F4	F5	F6	F7
Solid dispersion 1:2	31.36	31.36	31.36	31.36	31.36	31.36	31.36
Crospovidone	15	20	25	—	—	—	10
Sodium starch glycolate	146.64	141.64	136.64	146.64	141.64	136.64	144.64
Microcrystalline cellulose	—	—	—	15	20	25	7
Magnesium stearate	1	1	1	1	1	1	1
Sodium saccharin	5	5	5	5	5	5	5
Talc	1	1	1	1	1	1	1
Reported total (mg)	200	200	200	200	200	200	200

3.3.2. Flow Properties and Precompression Characteristics

The powder blends were evaluated with respect to bulk density, tapped density, angle of repose, Hausner ratio and Carr compressibility index. The angle of repose ranged from $24.79 \pm 1.48^\circ$ in F5 to $28.58 \pm 0.83^\circ$ in F6. The measured bulk density was in the range of 0.24-0.40 g/mL and the tapped density was in the range of 0.27-0.43 g/mL. Hausner's ratios ranged from 1.02 to 1.48, and Carr's indices ranged from

2.63% to 32.50%. The batch level observation for all batches is reported in Table 4. The powder blend for F4 had the highest Hausner's ratio and Carr's index, suggesting that it has poorer flow or packing properties than several other mixes. However, even with these differences, the original report indicated that it was possible to successfully manufacture tablets by direct compression. The data obtained from these measurements were helpful in understanding powder handling properties and the formulation conditions for fast disintegrating tablets of meloxicam.

Table 4. Precompression Evaluation Parameters of Meloxicam Tablet Formulations (F1–F7)

Batch	Angle (°)	Bulk (g/mL)	Tapped (g/mL)	Hausner	Carr (%)
F1	27.17 ± 0.20	0.37 ± 0.006	0.38 ± 0.005	1.02 ± 0.002	2.63 ± 0.82
F2	26.25 ± 2.52	0.40 ± 0.004	0.43 ± 0.005	1.07 ± 0.005	6.97 ± 0.72
F3	25.21 ± 0.54	0.36 ± 0.001	0.37 ± 0.002	1.02 ± 0.005	2.70 ± 0.31
F4	24.92 ± 1.45	0.27 ± 0.007	0.40 ± 0.004	1.48 ± 0.006	32.50 ± 0.55
F5	24.79 ± 1.48	0.31 ± 0.008	0.35 ± 0.003	1.12 ± 0.002	11.42 ± 0.47
F6	28.58 ± 0.83	0.24 ± 0.002	0.27 ± 0.006	1.12 ± 0.002	11.11 ± 1.41
F7	26.25 ± 0.50	0.25 ± 0.003	0.31 ± 0.007	1.24 ± 0.003	19.35 ± 0.41

3.4. Postcompression Evaluation and In Vitro Drug Release Performance

3.4.1. Weight Variation, Thickness, Hardness, and Friability

The seven fast disintegrating batches of tablets were subjected to post compression evaluation. Mean tablet weight ranged from 197.47 ± 1.14 mg for F7 to 198.35 ± 1.32 mg for F5. The thickness was found to be about 3.1-3.8 mm, the thickest thickness being found in the F6 variety. Tablet hardness ranged from 1.4 ± 0.023 kg/cm² for F5 to 2.8 ± 0.016 kg/cm² for F6. The friability results were between $0.39 \pm 0.023\%$ and $0.54 \pm 0.047\%$, all lower than 1%. Additional performance parameter values that are provided are summarized in Table 5. The low friability measurements suggested that the prepared tablets were not prone to abrasion under test conditions and the thickness and mass of the tested tablets were found to have a reasonable consistency between different batches. The results of the tablet quality tests did not constitute evidence of superiority, but rather justified proceeding to disintegration, drug content and dissolution testing.

3.4.2. Drug Content and Disintegration Time

Uniformity of drug content and rapid-disintegration were evaluated for F1–F7. Content uniformity was reported between $96.87 \pm 0.36\%$ for F1 and $99.12 \pm 0.12\%$ for F2. The fastest disintegration occurring in F2 was 36.63 ± 0.32 seconds, while F7 needed 62.32 ± 0.32 seconds for the fastest disintegration. Disintegration times of the remaining batches were kept within these range. The f2 formulation also yielded the lowest wetting time (23.71 ± 0.22 s) and the highest water absorption ratio ($97.89 \pm 0.59\%$). The results of the full postcompression tests are shown in Table 5 and the differences in disintegration between batches are plotted in Figure 5. In the source, the favourable performance of F2 correlated with the water uptake features and the use of crospovidone. The rapid disintegration and wetting measured in conjunction with the drug content helped to prioritize the study of F2 for further testing. Rapid disintegration and drug content were measured together, which helped to prioritize the study of F2 for further testing.

Table 5. Postcompression Evaluation Parameters of Meloxicam Fast-Disintegrating Tablets (F1–F7)

Table 5A. Physical parameters

Batch	Weight (mg)	Hardness (kg/cm ²)	Thickness (mm)	Friability (%)
F1	198.22 ± 0.12	2.3 ± 0.023	3.1 ± 0.47	0.39 ± 0.023
F2	198.11 ± 0.32	2.2 ± 0.023	3.3 ± 0.47	0.52 ± 0.020
F3	197.63 ± 0.45	2.4 ± 0.047	3.2 ± 0.48	0.47 ± 0.010
F4	197.74 ± 1.01	1.5 ± 0.041	3.2 ± 0.46	0.49 ± 0.025
F5	198.35 ± 1.32	1.4 ± 0.023	3.1 ± 0.24	0.54 ± 0.047
F6	197.89 ± 0.96	2.8 ± 0.016	3.8 ± 0.47	0.50 ± 0.040
F7	197.47 ± 1.14	1.8 ± 0.012	3.1 ± 0.23	0.51 ± 0.023

Table 5B. Disintegration, uniformity and wetting properties

Batch	Disintegration (s)	Drug content (%)	Wetting (s)	Water absorption (%)
F1	42.02 ± 0.35	96.87 ± 0.36	36.14 ± 0.14	91.34 ± 0.49
F2	36.63 ± 0.32	99.12 ± 0.12	23.71 ± 0.22	97.89 ± 0.59
F3	50.47 ± 0.14	98.10 ± 0.58	36.12 ± 0.32	94.56 ± 0.62
F4	51.21 ± 0.78	97.65 ± 0.47	32.34 ± 0.24	96.88 ± 0.75
F5	52.14 ± 0.45	98.65 ± 0.17	45.47 ± 0.32	95.67 ± 0.89
F6	43.45 ± 0.12	98.99 ± 0.96	39.45 ± 0.42	92.34 ± 1.06
F7	62.32 ± 0.32	97.63 ± 0.69	37.32 ± 0.32	93.14 ± 1.12

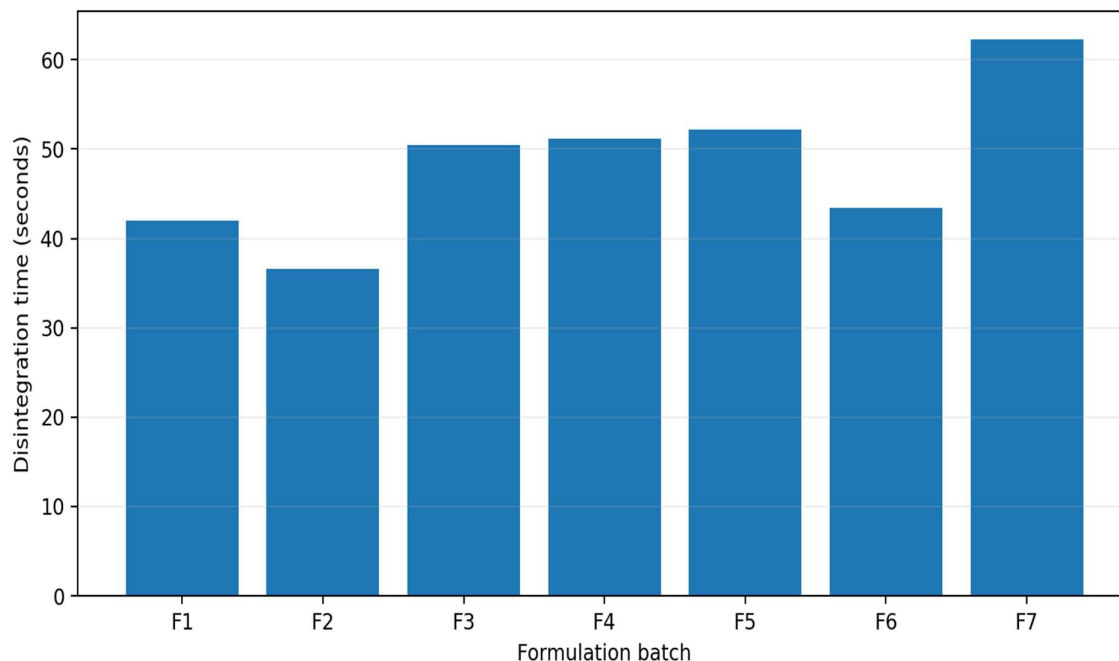


Figure 5. Comparative Disintegration Time of Meloxicam Fast-Disintegrating Tablet Formulations (F1–F7).

3.4.3. Comparative In Vitro Dissolution Profiles of Formulated Tablets

The dissolution behavior was examined in vitro in 60 minutes using phosphate buffer (pH 6.8). The cumulative drug release was found to increase with the increasing number of formulation. At 30 minutes, F2 released $69.64 \pm 2.14\%$, compared with $61.07 \pm 1.24\%$ for F1 and $68.23 \pm 1.30\%$ for F3. At the 60-

minute endpoint, F2 achieved the highest reported cumulative release, $97.18 \pm 2.84\%$, followed by F6 at $93.18 \pm 1.32\%$ and F7 at $91.72 \pm 0.97\%$. The lowest reported endpoint value was $89.03 \pm 1.01\%$ for F4. The seven mean profiles measured are shown in Figure 6. F2 also had the lowest disintegration time and both the assessments tended to prefer this formulation.

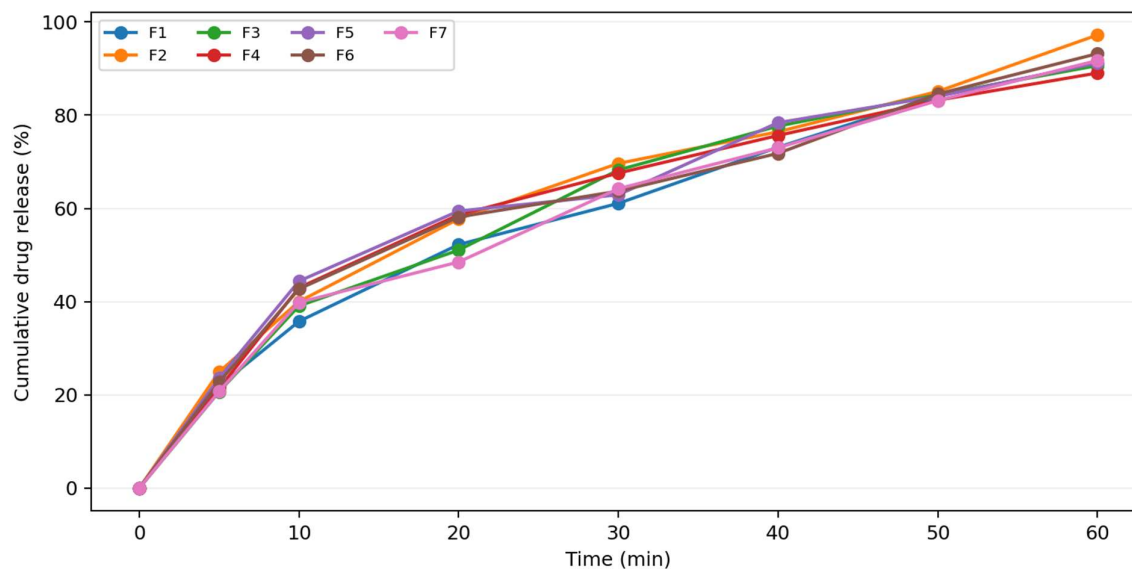


Figure 6. Comparative In Vitro Drug Release Profiles of Meloxicam Fast-Disintegrating Tablet Formulations (F1–F7).

3.5. Optimization and Stability Evaluation of the Selected Formulation

3.5.1. Selection and Performance Evaluation of the Optimized Formulation

An optimized meloxicam fast disintegrating tablet was selected, based on a combination of mechanical characteristics, uniformity, disintegration, wetting and in vitro drug release. The disintegration time recorded for F2 was 36.63 ± 0.32 seconds, which was less than that recorded for other batches, while the wetting time recorded for F2 was 23.71 ± 0.22 seconds, which was also less than that recorded for other batches. The water absorption ratio was $97.89 \pm 0.59\%$ and the postcompression drug content was $99.12 \pm 0.12\%$. Mechanical testing yielded hardness of 2.2 ± 0.023 kg/cm² and friability of $0.52 \pm 0.020\%$. The cumulative drug release of F1-F7 was the highest endpoint level at 60 minutes, $97.18 \pm 2.84\%$ (Figure

6). From these results, F2 was chosen as the best optimized preparation for the storage tests. The decision was taken due to rapid disintegration and comparatively high release of drug with good physical tablet properties.

3.5.2. Stability Assessment of the Optimized Fast-Disintegrating Tablets

An accelerated stability study of selected F2 formulation was conducted for a period of 3 months at $40 \pm 2^\circ\text{C}$ and $75 \pm 5\%$ RH. According to Table 6, hardness changed from 2.2 ± 0.023 to 2.1 ± 0.015 kg/cm² and disintegration time increased from 36.63 ± 0.32 to 38.75 ± 0.53 seconds. The source stability table showed that the values of drug content were $95.65 \pm 0.01\%$ and $94.46 \pm 0.03\%$ at the beginning and after three months respectively. In vitro cumulative drug release decreased from $97.18 \pm 2.84\%$ to $96.09 \pm 1.71\%$.

Table 6. Stability Evaluation of the Optimized Meloxicam Fast-Disintegrating Tablet Formulation (F2)

Parameter	Initial	After 3 months
Appearance	Yellow crystalline powder	Yellow crystalline powder
Hardness (kg/cm ²)	2.2 ± 0.023	2.1 ± 0.015
Disintegration time (s)	36.63 ± 0.32	38.75 ± 0.53
Drug content (%)	95.65 ± 0.01	94.46 ± 0.03
In vitro drug release (%)	97.18 ± 2.84	96.09 ± 1.71

4. DISCUSSION

The present study showed the potential of solid dispersion technology based on Poloxamer 188 for the improvement of aqueous solubility and dissolution rate of a poorly soluble drug-meloxicam in the form of fast disintegrating tablets. The results showed that pure meloxicam was poorly water soluble, with low solubility in distilled water (0.009 mg/mL), 0.1 N HCl (0.020 mg/mL) and phosphate buffer pH 6.8 (0.040 mg/mL) which highlighted formulation difficulties with this medicinal product. Saturation solubility of the drug in solid dispersions made with Poloxamer 188 showed significant improvement, especially for the 1:2 drug-to-polymer formulation, which exhibited the highest solubility in phosphate buffer (0.44 ± 0.03 mg/mL), increasing approximately 11-fold compared to the pure drug. The enhancement of wettability, dispersion of the drug and reduction in the crystallinity may be attributed to this improvement which are in accordance with the principles and mechanism of solid dispersion technology [5,6]. FTIR studies showed that the characteristic bands appeared in the same region with no significant spectral changes indicating drug-excipient incompatibility. In addition,

X-ray diffraction showed a strong crystallinity in pure meloxicam and less than strong crystallinity in the prepared solid dispersion, indicating a decrease in crystallinity. It was observed that the endothermic peak for pure meloxicam was at 251.10°C ; however, no thermal information was reported for the optimized dispersion. Seven different formulations of fast disintegrating tablets (F1 to F7) were then prepared by direct compression. The physical properties were acceptable and the friability ranged from 0.39% to 0.54%, the drug content was 96.87% to 99.12%. Tablet disintegration and drug-release characteristics were affected by the differences in the composition of superdisintegrants. The formulation F2 (20 mg crospovidone) showed the shortest disintegration time (36.63 ± 0.32 seconds), the lowest wetting time (23.71 ± 0.22 seconds) and the highest water absorption ratio ($97.89 \pm 0.59\%$). The results are in accord with the property of superdisintegrants that enable water penetration and fast tablet disintegration [7,8]. In addition, the formulation F2 showed the maximum cumulative drug release ($97.18 \pm 2.84\%$) at 60 minutes, thus it is the optimized formulation. The accelerated stability studies revealed relatively insignificant changes in hardness, disintegration time

and drug release at $40 \pm 2^\circ\text{C}$, $75 \pm 5\%\text{RH}$ for 03 months, and a cumulative release of $96.09 \pm 1.71\%$ in the end. However, in vitro characterization and accelerated stability testing for a limited period of time was conducted. There are no in vivo pharmacokinetic studies or comparative solid-dispersion dissolution profiles available nor has formal statistical testing been performed to draw conclusions about improved bioavailability or therapeutic onset. In conclusion, the results of this study provide a rationale for the potential of using Poloxamer 188 as a novel approach for the development of a fast disintegrating tablet formulation of meloxicam.

5. CONCLUSION

Based on the present study, it can be concluded that the solid dispersion technology and fast disintegrating tablet formulation is a promising approach to enhance the aqueous solubility and dissolution of meloxicam. The solvent evaporation method resulted in solid dispersions with increased saturation solubility as compared to pure meloxicam, in the presence of Poloxamer 188. The ratio of 1:2 (drug to polymer) was found to be more soluble than the other ratios with a value of $0.44 \pm 0.03 \text{ mg/mL}$ in phosphate buffer (pH 6.8), which is around 11 times higher than the pure drug. The FTIR analysis revealed no significant incompatibility between the drugs and excipients; however, the XRD results showed a decrease in crystallinity after the solid dispersion preparation. F2 formulation had a disintegration time of $36.63 \pm 0.32 \text{ s}$, drug content of $99.12 \pm 0.12\%$ and cumulative drug release of $97.18 \pm 2.84\%$ after 60 min, which was the best among the seven fast disintegrating tablet formulations tested (F1–F7). Moreover, accelerated stability testing performed for three months showed only minor alterations in the physicochemical properties with cumulative drug release of $96.09 \pm 1.71\%$. Based on these results, it can be stated that the formulation of meloxicam in fast disintegrating tablets by incorporation of solid dispersion of Poloxamer 188 is a possible approach to improve the dissolution of the drug and stability of the formulation. Further

experiments have however to be conducted on long-term stability, in vivo bioavailability and pharmacokinetic studies to confirm its clinical use and therapeutic benefits.

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