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Formulation and Evaluation of Meloxicam Fast Dissolving Tablets by Using Direct Compression Method

CH. Sathya Surya Prasad[1*], S. Chandra Sekhar[2], M. Pavani[3], M. Reshma[4], M. Sai Kiran[5], N. Mounika[6]
[1,2]*Assistant Professor, Department of Pharmaceutics, Avanthi Institute of Pharmaceutical Sciences, Bhogapuram, India*
[3,4,5,6]*Student, Department of Pharmaceutics, Avanthi Institute of Pharmaceutical Sciences, Bhogapuram, India*

***Abstract*: The purpose of this research was to develop meloxicam fast dissolving tablets. This drug is an oxicam derivative and a NSAID with anti-inflammatory, antipyretic and analgesic activities. It is usual nonselective NSAID. This is preferentially inhibited the action of cyclooxygenase II (COX-II), and the follow-on in a decrease transfer of arachidonic acid into prostaglandin precursor. Based on the result the prostaglandin synthesis is accountable for the therapeutic effects of the drug. Six formulations of meloxicam 200 mg were formulated by direct compression technique using different hydrophilic polymer grades such as PEG-400, PVP k100 as a polymers and different ingredients in different concentrations such as Micro crystalline cellulose, sodium starch glycolate, and Mannitol, Talc and Magnesium stearate. The earlier the all formulation of the granules is evaluated by pre-compression studies and after compression of tablets was evaluated with different post-compression parameters, In- vitro disintegration studies and In-vitro dissolution studies. The formulation F3 was chosen as an optimized formulation as it gives best results in terms of In - vitro drug release in a fast discharge manner. Based results the F3 formulation as followed by first order of kinetics with R value is 0.999.**

***Keywords*: Meloxicam, PEG-400, PVP K100, micro crystalline cellulose (MCC), sodium starch glycolate (SSG), mannitol and fast dissolving tablets.**

1. Introduction

The word “Drug Delivery” covers a extremely wide range of technique are used to deliver therapeutic agents into the human beings. The drugs are administered in the oral route to curing patient ailment. The Drugs are in no way applicable in raw form but are converted in a suitable dosage form. After deigning the dosage form to find out the onset of action as well as total duration of action can be checked. Along with the different routes of drug deliveries oral route is best for the drug delivery. But conventional dosage form offers a small number of boundaries which could be determined by modify the obtainable dosage form. A fast dissolving drug delivery system is the majority cases the tablets are dissolve or disintegrate in the oral route with no need for water or chewing. The fast dissolving drug delivery systems are must consist of substances to mask the flavor of the active ingredient. These drugs are dispersed by the oral spit along with the soluble and insoluble excipients. These are also called, melt in mouth tablets, rapi-melts, quick dissolving tablets, mouth dissolving tablets, orally disintegrating tablets or dispersible tablets. Their characteristic benefits like, rapid on-set of action, increased bioavailability, good stability and better patient compliance make these tablets popular as a dosage form of choice.

Even with these difference most of the existing oral dissolving drug delivery systems are in the form of solid tablets and deliberate to dissolve/disintegrate in the patient's mouth without the need to drink or chew. However, the fear of taking solid tablets and the risk of choking for assured patient populations still exist despite their short disintegration/dissolution times. Hence oral film drug delivery is a superior substitute in such cases. The oral availability of several drugs was reduced because of the pH of the stomach, the presence of enzymes, and extensive first-pass metabolism. By tradition, these drugs have been administered as parenteral drug delivery systems, which invariably lead to poor patient compliance. This has made the pharmaceutical industry look for substitute routes of drug delivery like film drug delivery. Meloxicam is exposed in particularly very less therapeutic dose and is selectively COX-2 and COX-1 inhibiters. These drug concentrations in synovial fluid vary from 40% to 50% in plasma. The free of charge part in synovial fluid is 2.5 times privileged than the plasma. Due to the minor albumin contented in synovial fluid as compare to the plasma.

2. Materials and Methods

Meloxicam (Hetero Drugs Limited, Hyderabad), PEG-400 (Finer Chemicals Gujarat), PVPK100 (Chemiloids, Vijayawada), Micro crystalline cellulose (Chemiloids,

*Corresponding author: drssp144@gmail.com

Vijayawada) Sodium Starch Glycolate (S.D. Fine-Chem. limited, Mumbai), Mannitol (S.D. Fine-Chem. limited, Mumbai) Talc (Reidel Chem. Hapur) Magnesium stearate (S.D. Fine-Chem. Mumbai).

A. Methods: Pre- formulation studies

1) Bulk Density (Db)

The proportion of the mass of powder and the volume of the bulk powder. It is calculated by weight powder and volume of the powder by a measuring cylinder and then the volume and weight was recorded and the bulk density is gm/ml.

$$Db = M/Vb$$

Where, M= weight of the powder. Vb=bulk volume of the powder.

2) Tapped density (Dt)

The proportion of the mass of powder and the volume of the tapped powder. The tapped volume was measured by tapped density apparatus and it's to maintain the constant volume. The units of tapped density is gm/ml and is given by

$$Dt = M/Vt$$

Where, M= weight of the powder. Vt = volume of the tapped powder.

3) Carr's Index (I)

It indicates the easiness of the material can be induced to flow. It is calculated in percentage and is given.

$$I= Dt- Db / Dt*100$$

Where, Dt = tapped density of the powder. Db = Bulk Density of the Powder.

4) Angle of Repose (θ)

The resistance force offense free powder be able to measure by the angle of repose θ. It is very fine and the maximum angle is possible between the surface of the pile and the flat plane.

$$\text{Tan } \theta = h/r$$

$$\theta = \text{tan-1}(h/r)$$

Where θ = angle of repose, h = height of the powder, r = radius of the powder. The combination of the powder mixture was permissible to flow through the funnel. The funnel was fixed to borate stand at exact height. The angles of repose are measuring by height and radius of the powder.

5) FT-IR Spectral studies

The FT-IR spectrum is identified by compatibility of drug and excipients data were record on Jasco FT-IR with KBr palette technique (1:100) at their explanation time of 4cm-1. The range was incorporated in transmittance form at the wave range is 400-4000 cm-1 unions were.

6) Differential scanning calorimetry

Conservative DSC and MTDSC experiment is perform using DSC Q200 (TA Instruments, NJ, USA). The frozen cool assemblage (RCS) and a modulate the ability. The DSC cell is purge with 50 ml/min in dry nitrogen and then the RCS was purge with 150 ml/min in nitrogen gas. The DSC cell was calibrated for baseline using empty pans of matched weight and for temperature using three temperature standards (cyclohexane, Tm = 279.54° K; indium, Tm = 429.61° K; tin Tm = 504.93° K). The concerning 3-5 mg of drug is exposing to the chosen heat rates as of the prefer beginning temperature to higher than the melting point of drug beneath dry nitrogen gas. It is removal (50 ml/min) in hermetically sealed aluminum pans. The sequence is analyzed by ordinary Analysis Software.

B. Analytical method for estimation of Meloxicam:

1) U. V Spectrophotometer

Calibration curve of the pure drug Meloxicam was prepared in the concentration range from 2-10 µg/ml at the wavelength of 346 nm by using 0.1N HCL buffer solutions. A graph was plotted between the absorbance vs. concentration. Based on the graphical representation data this is obey the Beer's law. The calibration curve showed good linearity and regression coefficient (r2) value is 0.999, and intercept 0.006.

2) Preparation of standard Stock solution of Meloxicam

100 mg of API (Meloxicam) was dissolved in 100 ml of 0.1N HCL buffer into a 100 ml volumetric flask and prepared up to the volume by 0.1N HCL buffer. To tack the 1 ml of solution and it was made up of to 100 ml with 0.1N HCL buffer.

3) Method

For the assessment of Meloxicam in 0.1N HCL buffer the stock solution has to be dilute consequently with the 0.1N HCL. The buffer to find a series of dilutions contain 2, 4, 6, 8, 10 µg/ml of solution. The absorbance of the solution was measured at 346 nm against blank. The calibration curve was constructed.

4) Formulation of Meloxicam Fast dissolving tablets

Meloxicam fast Dissolving tablets are prepared by direct compression technique. We are deigned four formulas each formula containing 200 mg of Meloxicam. To be prepared in dissimilar concentration of different excipients shown in given below. Meloxicam and polymers such as PEG-400, PVP K100M and SSG were accurately weighed, mixed uniformly and passed through # 40 meshes. Microcrystalline Cellulose and Mannitol is used as diluents were weighed accurately and passed through #40 meshes. Both were mixed properly and the mixture of Talc and magnesium stearate was added and mix for few minutes. Then the above mixture was compressed in to tablets by using station rotary compressed machine with punch size of 8 mm.

Table 1
Formulation of Meloxicam Fast dissolving tablets Table title

Ingredients mg/tab	**Formulation**			
	F1	**F2**	**F3**	**F4**
API (Meloxicam)	7.5	7.5	7.5	7.5
PEG-400	10	20	-	-
PVPK100	-	-	10	20
SSG	10	10	10	10
MCC	118.5	108.5	118.5	108.5
Mannitol	50	50	50	50
Magnesium Stearate	2	2	2	2
Talc	2	2	2	2
Total weight (mg)	200	200	200	200

C. Evaluation of Meloxicam Fast dissolving tablets

1) Physical appearance

The Physical form of a tablet is identity the size, shape, colour, odour, taste, surface texture and recognition symbols on the tablet.

2) Weight variation test

The weight variation examination is performing by electronic balance. In this experiment to take 20 tablets from

each batch and measure the weighing the individual tablets recorded. The average weight was calculated as given formula.

% Weight difference = (WA- WI) ×100/ WI

Where,

WI = Individual weight of the tablets

WA = Average weight of the tablet

Table 2
Weight variation specifications (B.P)

Average weight of tablet	Maximum difference allowed
Less than 130	5
130-324	7.5
More than 324	10

Table 3
Weight variation specifications (I.P)

Average weight of tablet(mg)	Percentage deviation
130 or less	10
130 to 324	7.5
More than 324	5

3) Thickness

The thickness of the tablet is resolute by using vernier calipers. Each batch contains five tablets are randomly selected calculate the average value.

4) Hardness (kg/cm^2)

The Hardness of the tablet was determined by using Monsanto hardness tester. Each batch contains five tablets are randomly selected and then calculate the hardness each tablet.

5) % Friability

The Friability was resolute in a Roche friabilator. Ten tablets are selected and measure the weigh in initially (w1) and maintain the speed at 25 RPM. The tablets are dipping in the friabilator and maintain the 100 revolutions per min. After end of these rotations the tablets were dedusted and weighed (w2). The percent defeat in mass or friability (f) is calculated by using the given formula.

% Friability = (Initial wt- Final wt) / Initial wt × 100

6) In-vitro disintegration studies

In -vitro disintegration point in time be perform by equipment particular in USP. The water was used as disintegration medium and the temperature was maintained at 37±2°C and the time in seconds taken for the complete disintegration of the tablet.

7) In-vitro dissolution studies

In-vitro dissolution test was performing the USP type II dissolution test apparatus (paddle type) [Lab, India (DS-8000, Mumbai)]. In this experiment the RPM was maintained at 75 RPM and 900ml of 0.1N HCL buffer was used as dissolution medium. The temperature was maintained at 37±0.5ºC. The sample be reserved at exact time intervals (10, 20, 30, 40, 50 and 60min) and filtered with 0.45 micron filters. The amount of drug was dissolved in the medium and calculates the % of drug release by using UV spectrophotometer at 346 nm.

3. Results and Discussion

Formulations of Meloxicam fast dissolving tablets are prepared by using hydrophilic polymers like PEG-400 and PVP K100 was impact on In- Vitro dissolution rate.

1) Pre-formulation studies

The Active pharmaceutical ingredient (Meloxicam) and excipients were blended and evaluated for different parameters as clarified before. Bulk density was found in the limit of 0.501 g/cm3 and the tapped density between 0.623 g/cm^3. Based on density data Carr's index was resolute. The Carr's index was found to 18.24 % and the Hausner's ratio was found to be 1.142. The result shows good flow properties of blend. The good flow properties of powder were also evident from angle of repose that range from 23.91°. In the current test was indicating outstanding flow property of powders.

Table 4
Micromeritic properties of the granules of Meloxicam formulation

Formulation code	Bulk density (g/ml)	Tapped density (g/ml)	Hausner's ratio	Angle of repose (ɵ)	Compressibility Index (%)
F1	0.510	0.634	1.31	23.01	18.20
F2	0.491	0.626	1.32	24.18	18.30
F3	0.500	0.622	1.29	25.11	20.57
F4	0.510	0.632	1.28	23.23	21.42

2) Pre – compression parameters

B. FT-IR Spectral studies

1) FT-IR studies

The FT-IR studies are concluded the related typical peak by small dissimilarity intended for drug and excipients. Therefore, it appears no chemical communication flanked by the drugs and excipients. The FT-IR Spectra of with, PEG-400 and PVP K 100 shown. The following peaks were observed in as well as Meloxicam with excipients.

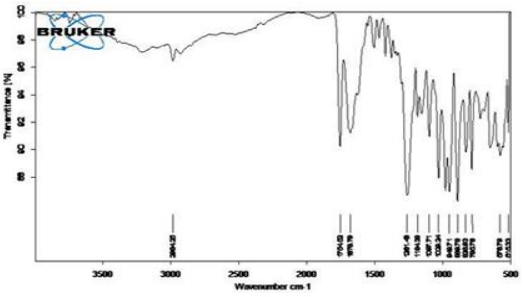

Fig. 1. FT-IR Reports of Meloxicam

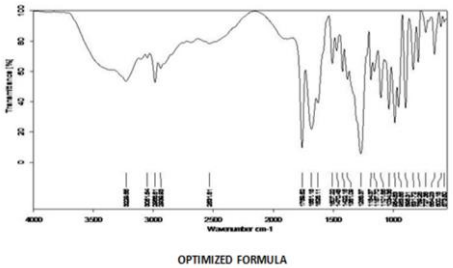

Fig. 2. FT-IR Reports for Meloxicam Optimized formula

2) Differential scanning calorimetry

DSC indicates the improved drug constancy occurrence of water loving polymers. A stronger drug amorphization and entrapment in hydrophilic polymers was observed.

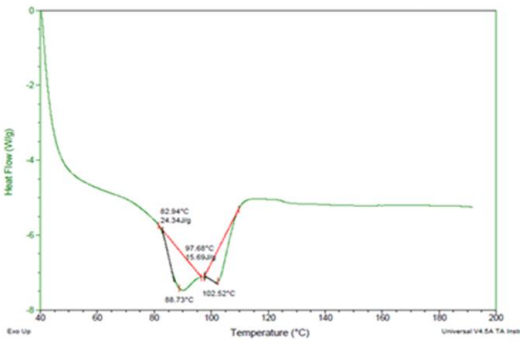

Fig. 3. DSC Reports for Meloxicam

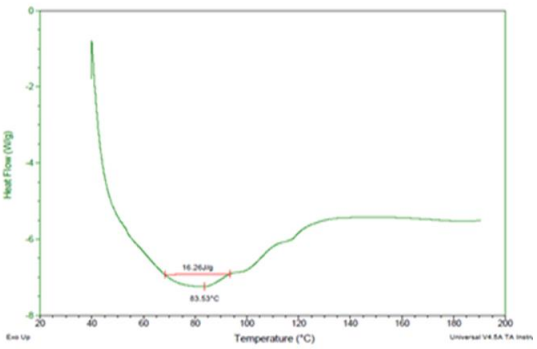

Fig. 4. DSC Reports for Meloxicam Optimized Formula

3) Analytical method development

Meloxicam was estimation using UV/VIS spectrophotometer method. It was found that under UV/VIS spectrophotometer standard absorbance of the peak of Meloxicam was 0.719 µg/ml,

Table 5
Standard Calibration Data of Meloxicam in 0.1N HCl

Concentration (µg/ml)	Absorbance
0	0
2 (µg/ml)	0.259
4 (µg/ml)	0.501
6 (µg/ml)	0.719
8 (µg/ml)	0.971
10 (µg/ml)	1.226

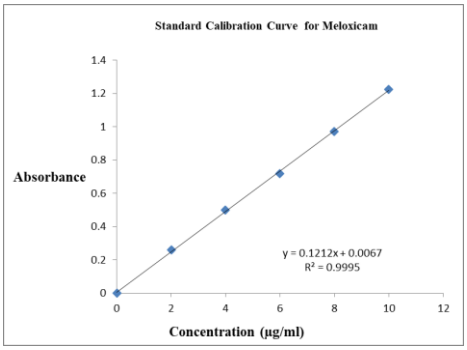

Fig. 5. Standard Calibration Data of Meloxicam in 0.1N HCl.

4) Evaluation of post-compression parameters Meloxicam fast dissolving tablets

The beginning study is accepted by prepare different formulations by different procedure. The changeable and subjecting the formulation to everyone post-compression parameters have satisfied according to IP standard.

5) Weight variation

Average weight of 20 tablets of Meloxicam was calculated for each formulation which varied from 234.4 ±1 to 241.5 ±3 mg.

6) Tablet thickness

The thickness of the Meloxicam formulation varied from 2.00±0.06 mm to 2.35 ±0.06mm

7) Tablet hardness (kg/cm^2)

The hardness for optimized formula was show 4.1 ±1.0 kg/cm^2 to 4.5±1.0 kg/cm^2.

8) %Friability

The friability of the optimized formula different as of loss which is less than 1% as per IP. In-Vitro Disintegration studies

9) Meloxicam Fast dissolving tablets

In-vitro disintegration study was performed by using USP disintegration test apparatus [Lab, India] 900ml of water was used as the disintegration medium which was maintained at 37±0.5^{o}C. The tablet breakup time was originated to be 105.47 to 120.1 sec.

10) Post – compression parameters

11) In-Vitro Dissolution studies of Meloxicam Fast dissolving tablets

In-vitro dissolution test was performing the USP type II dissolution test apparatus (paddle type) [Lab, India (DS-8000, Mumbai)]. In this experiment the RPM was maintained at 75 RPM and 900ml of 0.1N HCL buffer was used as dissolution medium. The temperature was maintained at 37±0.5oC. The sample be reserved at exact time intervals (10, 20, 30, 40, 50 and 60min) and filtered with 0.45 micron filters. The % of drug release was calculated by using UV spectrophotometer at 346 nm. The all four formulations are prepared by using different concentrations of polymers like PEG-400 and PVPK100. f1 and f2 contains the PEG-400 was prepared in Meloxicam Fast Dissolving tablets the drug released in formulation f1 is 98.23% in 40 min, f2 is 60.36 % in 50 min. The f3 formulation drug released is 72.36 % in 60 min; f4 formulation the drug released was 85.39 % in 60 min. The optimized formulation f1 showed 98.21% in 40 min in 0.1 N HCL.

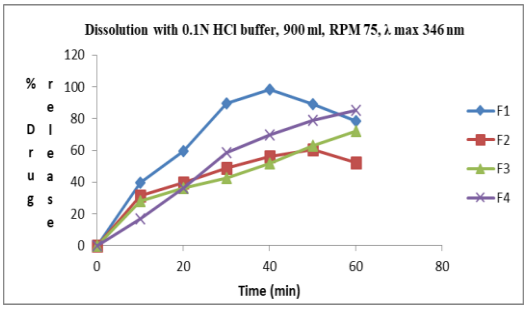

Fig. 6. %Release graph of Meloxicam fast dissolving tablets with PEG-400 (F1-F2) and PVPK100 (F3-F4)

Table 6
Post compression parameters of Meloxicam fast dissolving tablets

Formulation code	Weight Variation(mg)	Thickness (mm)	Hardness (kg/cm^2)	% Friability (% loss)	DT (sec)
F1	234.4	2.00	4.5	0.1	105.4
F2	241.5	2.10	4.1	0.1	120.1
F3	238.2	2.35	4.3	0.1	107.3
F4	239.4	2.21	4.2	0.1	117.4

Table 7
Dissolution studies for Meloxicam fast dissolving tablets.

Dissolution with 0.1N HCL buffer,900ml,RPM 75, λ max 346 nm					
% Cumulative Drug Release					
S.NO	Time (min)	F1	F2	F3	F4
1.	0	0	0	0	0
2.	10	39.56	31.55	28.14	16.8
3.	20	59.63	39.57	36.40	36.21
4	30	89.65	48.96	42.50	58.36
5	40	98.23	56.02	51.82	69.61
6	50	89.23	60.36	62.98	78.83
7	60	78.63	52.31	72.36	85.39

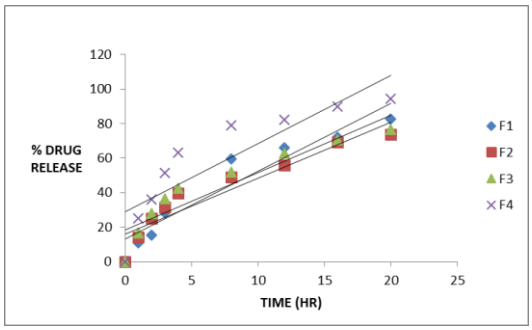

Fig. 7. Zero order release graph of Meloxicam fast dissolving tablets with PEG-400 (F1-F2) and PVPK100 (F3-F4)

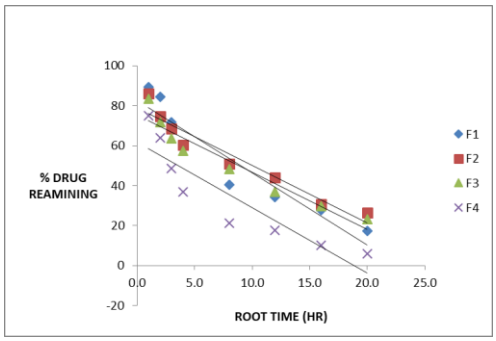

Fig. 8. First order release graph of Meloxicam fast dissolving tablets with PEG-400 (F1-F2) and PVPK100 (F3-F4)

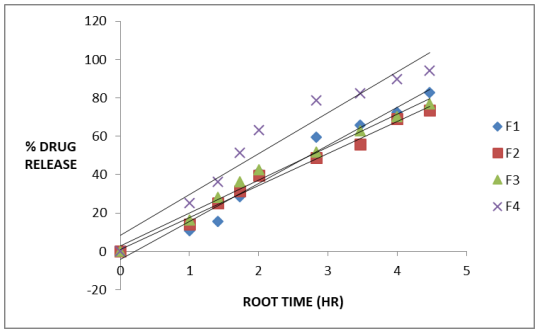

Fig. 9. Higuchi release graph of Meloxicam fast dissolving tablets with PEG-400 (F1-F2) and PVPK100 (F3-F4)

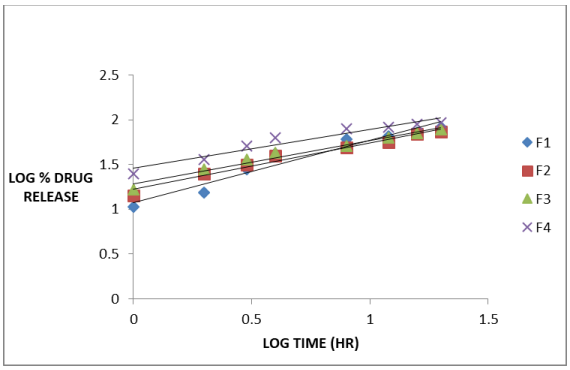

Fig. 10. Pappas release graph of Meloxicam fast dissolving tablets with PEG-400 (F1-F2) and PVPK100 (F3-F4)

12) Curve-Fitting Analysis

According to different kinetic models, the kinetics of the f1 and f4 drug release was evaluated by drug release rate models namely zero order, first order kinetics, and higuchi, papas mechanisms. The dissolution kinetics data was defected. The optimized formulation F1 showed highest r value i.e. 0.990 for first order plot indicating that release of drug follows first order kinetics, and mechanism of release was fitted to papas' equation with the r value of 0.999 indicating anomalous fickian diffusion mechanisms and may indicate that the drug release is higher by more than one process.

Table 8. Dissolution kinetics of Meloxicam fast dissolving tablets with PEG-400 and PVPK100.

Correlation co-efficient				
Formulation	Zero order	First order	Higuchi	Pappas
F1	0.924	0.990	0.971	0.999
F2	0.942	0.986	0.966	0.997
F3	0.959	0.975	0.938	0.996
F4	0.932	0.868	0.937	0.996

4. Conclusion

Meloxicam was chosen as the model candidate for this study since it possess near ideal characteristics that a drug must have in formulating a fast dissolving drug delivery system. This drug comes under BCS class –II and its low solubility and high

permeability. The successful in little plasma drug concentration and first pass effect. These formulations are prepared by direct compression method. Evaluate the physical, pre-compression, post-compression, In-vitro disintegration and dissolution studies for all formulations. Drug – excipients compatibility studies were conducted by FT-IR spectroscopy, results indicated that the Meloxicam and polymers were found to be compatible and DSC studies are also conducted. F1 formulation showed 98.23 % drug release at the end of 40min. The finally this research was concluded in all four formulations F1 formulation has successfully attained the fast release manner at 40 min. The optimized formulation F1 showed highest r value i.e. 0.990 for first order plots indicating that release of drug follows first order kinetics, and mechanism of release was fitted to papa's equation with the n value of 0.999 indicating anomalous fickian diffusion mechanisms and may indicate that the drug release is higher by more than one process.

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