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FORMULATION AND EVALUATION OF THE MELOXICAM MOUTH DISSOLVING TABLETS

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ABSTRACT
Formulation, development, in vitro characterization of the Meloxicam mouth dissolving tablets. For development of the tablets different excipients are used. The used various excipients such as theccs, Mg.sterate,Talc,,MCC, pvpk30used as the diluents The formulation is developed by the using direct compression method. The formulation is prepared by using different excipients. The excipients are ccs, in various compositions for drug to release prolong time. The pre compression parameters are done such as the bulk density, tap density, compressibility index, Hauners ratio, Angle of repose. The all parameters are come under within range goof flow. The post compression parameters are done such as the harness, thickness, weight variation, friability, disintegration. The evaluation parameters of the optimized formulation F9 values:The weight variation of orodispersable tablets, 199mg.The hardness of the orodispersable tablets, 3.7(Kg/cm^2)Thickness of the orodispersable tablets, 2. .42mm. Disintegration of the orodispersable tablets, 3min. Drug content of the orodispersable tablets, 97.86%. Friability of the orodispersable tablets, 0.56%. In-vitro drug dissolution studies of the orodispersable tablets,96.23%. The all parameters come under acceptable criteria within range of limits. The In-vitro drug release studies are done by USP-II apparatus paddle method. The optimized formulation F9 gives the prolong release up to 30mins the drug release 96.23%

KEYWORDS: Meloxicam, Mouth dissolving tablets, Mg.sterate, Talc,, MCC, pvpk30.

INTRODUCTION
Orally administered doesage form e.g. tablet computers, pills are convenient dosage kind for lots of medications--however they are testing to the develop if the energetic substances has inadequate dissolution or low bioavailability. Polymer finishing allows the solution of mouth dissolving and also preference masking of bitter taste drugs-thereby giving far better client conformity[1] Tablets that are quick disintegrate or liquify rapidly in the patient's mouth, are convenient for children, aged and clients with ingesting difficulties[2] For these formulations, the tiny volume of saliva is normally enough to lead to tablet disintegration in the oral cavity[3] The medicine then be taken in partially or entirely right into the systemic flow from blood. vessels in the sublingual mucosa, or it can be swallowed as an option to be soaked up from the intestinal tract (GIT)[4] The bioavailability of some drugs may be boost as a result of absorption of drugs in oral cavity and additionally due to pregastric absorption of saliva including spread medicines that give into the tummy. The amount of medicine that is subject to first pass metabolic process is minimized as contrasted to mouth dissolving tablet computers[5] By mouth disintegrating tablets have wide variety of pharmaceutical active components covering lots of restorative classifications. The moment for fragmentation of by mouth degenerating tablets are typically thought about less than one min. Orally degenerating tablet computers are identified by high porosity, low thickness and also reduced solidity. When administered, an in-situ suspension is created in the mouth as the tablet computer degenerates and is consequently swallowed[6] Lately, the Classification and Identifying board at USP has accepted the Orally Degenerating Tablet computers terminology. Meloxicam is a nonsteroidal anti-inflammatory drug of the oxicam class, used to soothe the signs and symptoms of joint inflammation, main dysmenorrhea, fever and as an analgesic, specifically where there is an inflammatory component[7] Meloxicam hinders cyclooxygenase (COX) synthesis. This enzyme is in charge of converting arachidonic acid into prostaglandin H2. This is the first step in the synthesis of prostaglandins, which are moderators of swelling. Meloxicam has actually been revealed, particularly at its reduced restorative dose, uniquely to prevent COX-2 over COX-1[8] A key benefit of the oxicam family members of medications is their long half-life which permits once-day application[9] In

gastric condition, reduced dose of meloxicam is called for 7.5 mg/day. Meloxicam is much safer then other NSAID's[10] The essential technique utilized in the development of the fast-dissolving or mouth dissolving tablet computer is using a super disintegrants. Sodium starch glycolate, and also crospovidone were evaluated in the present study. A various strategy utilized in creating Mouth liquifying tablet computers is making the most of the pore arrangement of the tablets[11] I Suspended animation as well as II vacuumdrying techniques have been attempted by researchers to take full advantage of the pore framework of tablet computer matrix. Freeze drying out is challenging as well as it yields brittle as well as hygroscopic products. Consequently, it was identified to approve the vacuum-drying method in the here and now research[12-14] Vacuum cleaner drying was adopted after including of a subliming representative to increase porosity of the tablet computers. It is feasible that a porous hydrophilic matrix will quickly pick up the disintegrating medium and also break swiftly. NSAIDs are the most regularly prescribed by medical professionals for inflammatory disorders. NSAIDs apply their effect via restraint of cyclooxygenase II, the primary type of isozyme related to inflammation however the simultaneous restraint of cyclooxygenase-I and also the resulting gastric and also renal dysfunction limit their constant usage.[15-17]

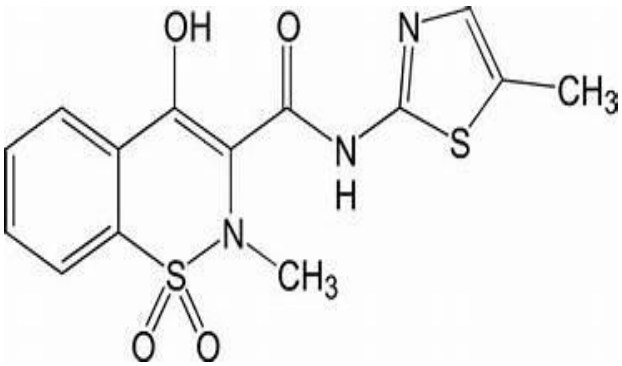

Fig no1: Chemical structure of Meloxicam.

MATERIALS

Meloxicam was a gift sample from Sun pharma, Hyderabad, India, ccs, Pvpk30 are from Colorcon Asia Pvt. Ltd., Goa, Standard chemical reagents from SD fine chemical Ltd, Hyderabad. Methanol was of high performance liquid chromatography (HPLC) grade. All other reagents and solvents were of analytical reagent grade

METHODOLOGY

Preformulation Studies

It is one of the important prerequisite in development of any drug delivery system. Preformulation studies were performed on the drug, which included organoleptic character's, determination, solubility and compatibility studies

Solubility: Solubility of meloxicam was determined in water, acetone, methanol, practically insoluble in ethanol (95%), chloroform and ether.

Compatibility Studies: Compatibility with excipients was confirmed by carried out I R studies. The pure drug and its formulations along with excipients were subjected to IR studies

PREPARATION OF STANDARD CALIBRATION CURVE OF MELOXICAM

METHOD

10mg meloxicam was accurately weighed and transferred into 10ml volumetric flask. It was dissolved and diluted to volume with acetone to give stock solution containing 1000µg/mlThe standard stock solution was then serially taken 1ml of solution from 1st stock solution diluted with acetone to get 1 to 100µg/ml or secondary stock solution. From secondary stock solution take 1ml of the solution to get 10µg/ml or tertiary stock solution. The absorbances of the solution were measured against acetone as blank at 281 nm using UV spectrophotometer. The absorbance values were plotted against concentration (µg/ml) to obtain the standard calibration curve.

FORMULATION TABLE OF MELOXICAM TABLETS

Table.no:1 formulation table for Meloxicam tablets

Ingredient's	F1	F2	F3	F4	F5	F6	F7	F8	F9
Meloxicam	2	2	2	2	2	2	2	2	2
ccs	10	20	30	40	50	60	70	80	90
Pvpk30	10	20	20	20	20	20	20	20	20
MCC	174	154	144	134	124	114	104	94	84
Mg. Stearate	2	2	2	2	2	2	2	2	2
IPA	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S	Q.S
Talc	2	2	2	2	2	2	2	2	2
Total wt	200	200	200	200	200	200	200	200	200

MELOXICAM TABLETS PREPARED BY USING DIRECT COMPRESSION METHOD

Dispensing: The drug and all ingredients are dispensed above mentioned in table.

Mixing: All ingredients are mixing with by adding IPA this is undergo formation of the lump except adding mg.sterate and talc

Seiving: The lump under kept for sieving in sieve no:40 the granules will farm.

Drying: The formed granules under kept for the drying at room temperature.
Mixing: The dried granules are mixed along with the talc and magnesium stearate
Punching: After mixing the mixed granules are under kept for the punching under multi compression mission.

EVALUATION OF POWDER BLEND FOR PRE-COMPRESSION PARAMETERS

ANGLE OF REPOSE

The angle of repose of powder blend was determined by the funnel method. The accurately weight powder blend were taken in the funnel. The height of the funnel was adjusted in such a way the tip of the funnel just touched the apex of the powder blend. The powder blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

$$\tan\theta = h/r$$

Where, h and r are the height and radius of the powder cone.

BULK DENSITY

Both loose bulk density (LBD) and tapped bulk density (TBD) was determined. A quantity of 2 gm of powder blend from each formula, previously shaken to break any agglomerates formed, was introduced in to 10 ml measuring cylinder. After that the initial volume was noted and the cylinder was allowed to fall under its own weight on to a hard surface from the height of 2.5 cm at second intervals. Tapping was continued until no further change in volume was noted. LBD and TDB were calculated using the following equations.
LBD= Weight of the powder blend/Untapped Volume of the packing
TBD=Weight of the powder blend/Tapped Volume of the packing

COMPRESSIBILITY INDEX

The Compressibility Index of the powder blend was determined by Carr's compressibility index. It is a simple test to evaluate the LBD and TBD of a powder and the rate at which it packed down. The formula for Carr's Index is as below:
Carr's Index (%) = [(TD-BD) x100]/TBD

HAUSSNERS RATIO

The haussners ration is determined by using fallowing formula, i.e

$$\text{Haussners ration} = TD/BD$$

EVALUATION OF TABLETS FOR POST COMPRESSION PARAMETERS

Weight Variation Test

To study weight variation twenty tablets of the formulation were weighed using a Sartorius electronic balance and the test was performed according to the official method. Twenty tablets were selected randomly from each batch and weighed individually to check for weight variation.

Drug Content

Five tablets were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in 30 ml of the 6.8 buffer solution, from that solution 1 ml is taken in 10 ml of the volumetric flask. the drug content was determined measuring the absorbance at 281 nm after suitable dilution using a Lab india 2000 UV/Vis double beam spectrophotometer.

$$\text{Drug content} = \text{Test Abs}/\text{StdAbs} \times \text{Std.conc}/\text{sample conc} \times 100$$

Hardness

Hardness indicates the ability of a tablet to withstand mechanical shocks while handling. The hardness of the tablets was determined using Monsanto hardness tester. It is expressed in kg/cm^2. Three tablets were randomly picked and hardness of the tablets were determined.

Thickness

The thickness of the tablets was determined by using vernier calipers. Five tablets were used, and average values were calculated.

Friability Test

The friability of tablets was determined using Roche Friabilator. It is expressed in percentage (%). Ten tablets were initially weighed ($W_{initial}$) and transferred into friabilator. The friabilator was operated at 25rpm for 4 minutes or run up to 100 revolutions. The tablets were weighed again (W_{final}). The % friability was then calculated by –

$$\%F = 100\ (1\text{-}W_0/W)$$

% Friability of tablets less than 1% are considered acceptable.

IN VITRO DISSOLUTION STUDIES

The release rate of meloxicam from controlled release tablets was determined using *The United States Pharmacopoeia* (USP) dissolution testing apparatus II (paddle method lab India 800plus). The dissolution test was performed using 900 ml of 6.8 buffer solution at 37 ± 0.5°C and 50 rpm A sample (5 ml) of the solution was withdrawn from the dissolution apparatus for 30mins, and the samples were replaced with fresh dissolution medium. The samples diluted to a suitable concentration with 6.8 buffer solution. Absorbance of these solutions was measured at 281nm using a Labindia 2000 UV double beam spectrophotometer. Cumulative percentage of drug release was calculated using the equation obtained from a standard curve.

RESULTS

API CHARECTERIZATION

ORGANOLEPTIC CHARACTERS

Table.No:2 Table showing organoleptic characters of the active pharmaceutical ingredient.

Properties	Results
Description	White solid powder
Taste	Taste less
Odour	Odour less
Colour	Colour less

SOLUBILITY STUDIES

SOLUBILITY OF THE MELOXICAM IN VARIOUS SOLVENTS:

Table No: 3 Table showing solubility studies of the active pharmaceutical ingredient.

Solvent	Solubility properties of drug (1gm)
Acetone	Freely Soluble
Ethanol	In Soluble
Methanol	In Soluble
Water	Sparingly soluble

CALIBRATION CURVE IN ACETONE

Table. No: 4: Table showing values of the calibration studies in the acetone.

Concentration (µg/ml)	Absorbance in acetone
0	0
10	0.166
20	0.324
30	0.445
40	0.598
50	0.78

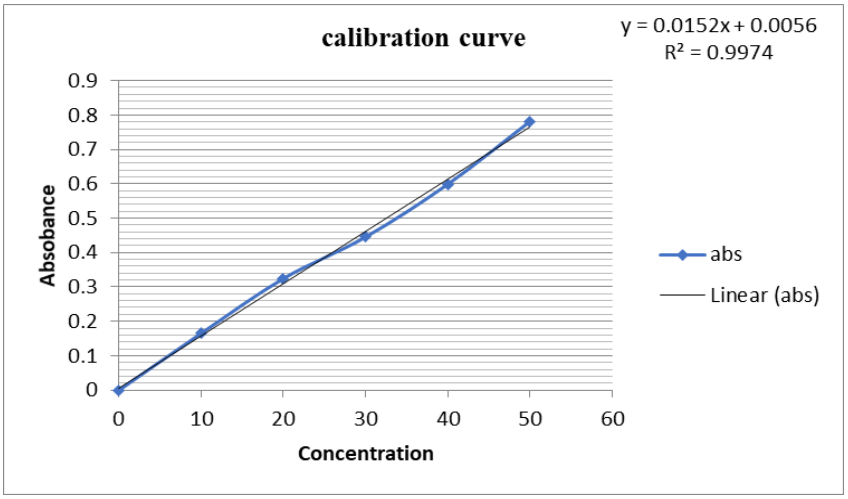

Fig. No: 2 Picture showing standard plot.

FTIR STUDIES

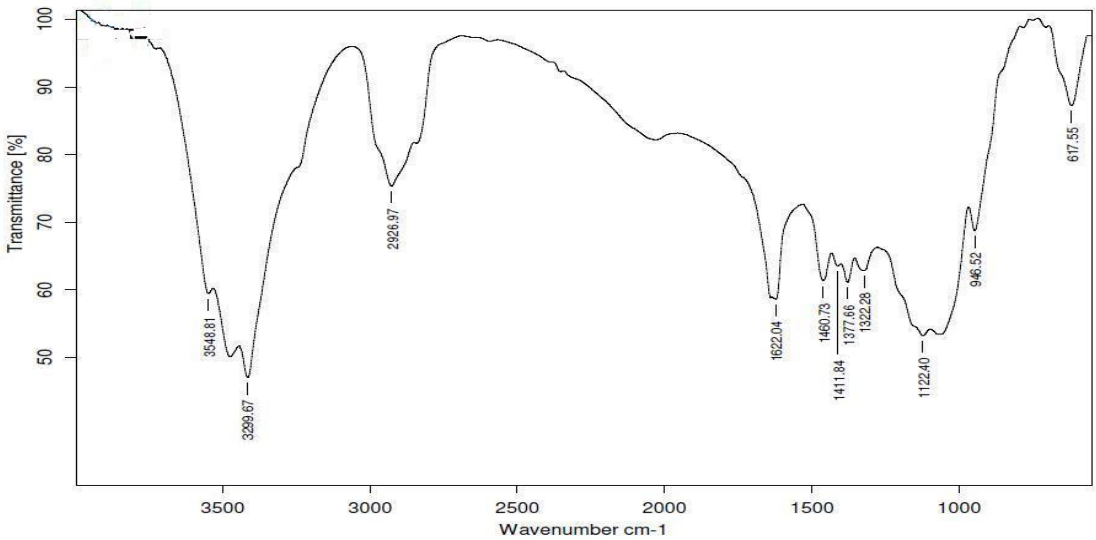

Fig. No: 3: FTIR Spectra of the pure drug Meloxicam.

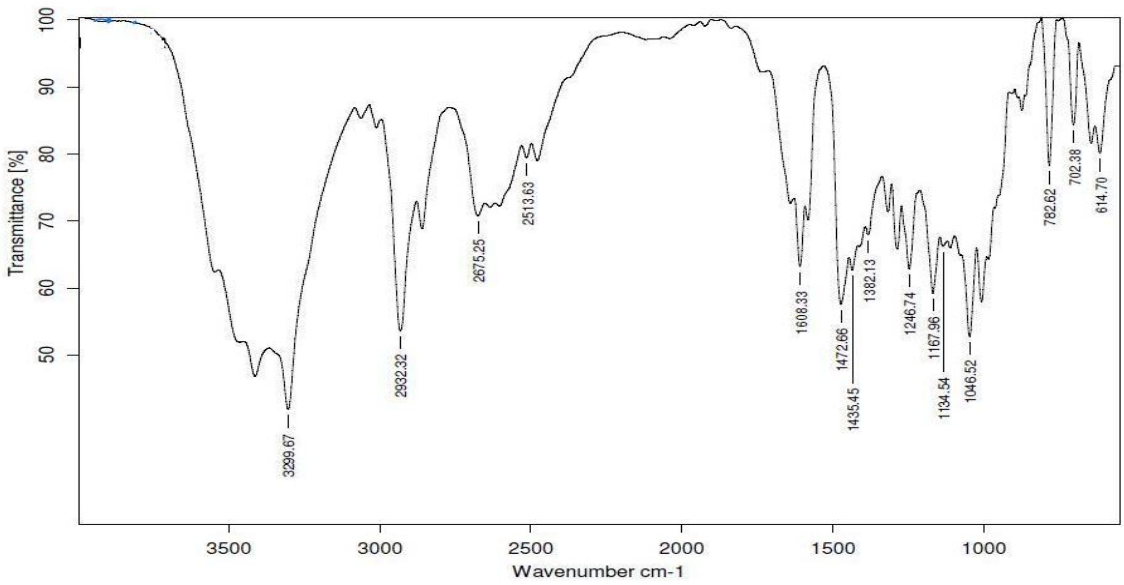

Fig.No: 4: FTIR Spectra of the optimized formulation.

Table No 5: Showing spectra of pure drug substance stretch bonds values.

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	OH stretching	3600-3500	3299.67
2	OH Bending	1100-1600	1411.56
3	C-N stretching	1350-1700	1622.25

Table No 6: Showing spectra of the optimized formulation stretch bond values.

S.No.	Characteristic Peaks	Frequency range (cm-1)	Frequency (cm-1)
1	C-N stretching	1350-1700	1608
3	OH bending	3150-3400	3299.0

Discussion: The drug and excipients are compatible with each other there is no presents of other inactive substances.

PRE-COMPRESSION PARAMETERS OF THE F1-F5

Table No: 7: The table showing pre-compression values of the F1-F5.

Formulation	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F1	22.38±0.13	0.36±0.02	0.44±0.02	18.56±0.13	1.22±0.01
F2	23.52±0.28	0.37±0.02	0.45±0.03	17.74±0.13	1.21±0.01
F3	23.19±0.19	0.36±0.02	0.44±0.03	18.18±0.13	1.22±0.02
F4	24.51±0.16	0.38±0.01	0.45±0.01	15.53±0.15	1.18±0.01
F5	23.60.21	0.40±0.01	0.45±0.00	15.25±0.05	1.12±0.02

Discussion: The all the F1-F5 formulations pre compression parameters such as the angle of repose, bulk density, tap density, husners ratio, compressability index all comes under the within range of limits. All the formulations fallow the good flow.

Table.no 8: The table showing pre-compression values of the F6-F9 .

Formulation	Angle of repose (θ)	Bulk density (gm/ml)	Tapped density (gm/ml)	Carr's index (%)	Hausner's ratio
F6	23.52±0.28	0.37±0.02	0.45±0.03	17.74±0.13	1.21±0.01
F7	23.19±0.19	0.36±0.02	0.44±0.03	18.18±0.13	1.21±0.01
F8	22.67±0.19	0.38±0.01	0.45±0.01	15.53±0.15	1.22±0.02
F9	22.89±0.18	0.40±0.01	0.45±0.00	15.25±0.05	1.18±0.01

POST COMPRESSION PARAMETERS FOR F1-F5 FORMULATIONS

Table.no 9: The table showing post-compression values of the F1-F5.

Formulation	Weight variation	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Drug content (%)	Disintegration (min)
F1	198±1.02	2.50±0.01	2.5±0.06	0.632	97.24±0.22	4
F2	198±0.08	2.65±0.00	2.6±0.06	0.646	96.57±0.42	3
F3	199.002	2.7±0.01	2.5±0.00	0.686	97.43±0.13	3
F4	198±0.003	2.58±0.01	2.85±0.06	0.526	97.83±0.42	3
F5	199±0.08	2.42±0.01	2.7 ±0.10	0.546	97.86±0.32	3

Table.no 10: The table showing post-compression values of the F6-F9.

Formulation	Weight variation	Thickness (mm)	Hardness (Kg/cm^2)	Friability (%)	Drug content (%)	Disintegration (min)
F6	198±1.02	2.50±0.01	2.5±0.06	0.632	98.24±0.22	4
F7	198±0.08	2.65±0.00	2.6±0.06	0.646	98.57±0.42	3
F8	199.002	2.7±0.01	2.5±0.00	0.686	97.43±0.13	3
F9	198±0.003	2.58±0.01	2.85±0.06	0.526	99.83±0.42	3

***IN –VITRO* DRUG RELEASE STUDIES FOR ALL FORMULATIONS**

Table No. 11: Table showing *In-vitro* drug release studies of the all formulations.

Time in hrs	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5min	9.32	12.23	19.85	21.56	23.54	34.52	37.32	40.52	45.65
10min	25.62	29.56	35.56	41.87	45.89	47.52	49.52	53.53	65.62
15min	35.31	39.54	42.17	46.52	52.51	56.12	58.13	65.72	74.56
20min	41.61	48.56	52.65	58.98	65.35	69.46	70.25	76.62	80.62
25min	45.65	47.21	51.12	62.45	70.25	74.65	76.56	78.65	90.65
30min	57.32	60.78	62.32	65.23	75.98	81.32	84.32	89.35	96.23

ALL COMPARATIVE GRAPH FOR F1-F5

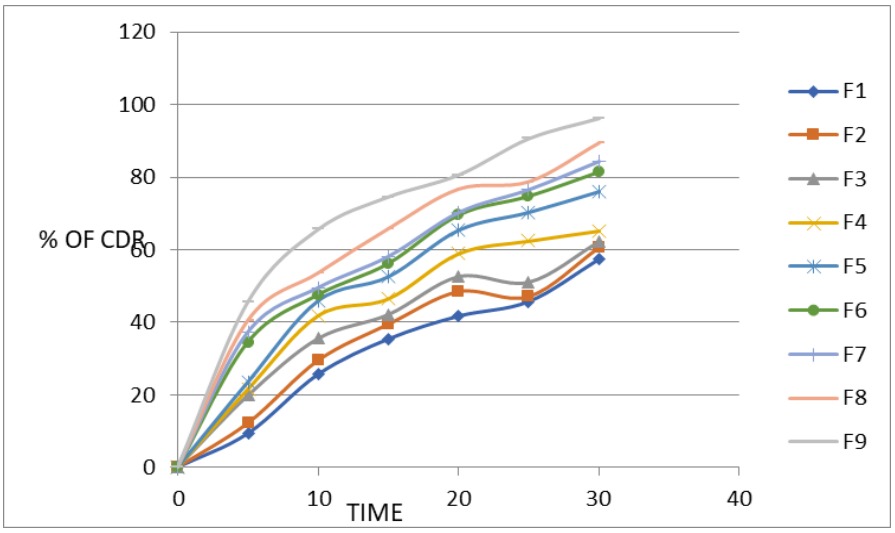

Fig.No. 5: Ficture showing all comparative studies of the F1-F9.

Table. No: 12 comparative drug release studies of f1-f3.

Time in hrs	F1	F2	F3
0	0	0	0
5min	9.32	12.23	19.85
10min	25.62	29.56	35.56
15min	35.31	39.54	42.17
20min	41.61	48.56	52.65
25min	45.65	47.21	51.12
30min	57.32	60.78	62.32

COMPARATIVE DRUG RELEASE STUDIES OF F1-F3

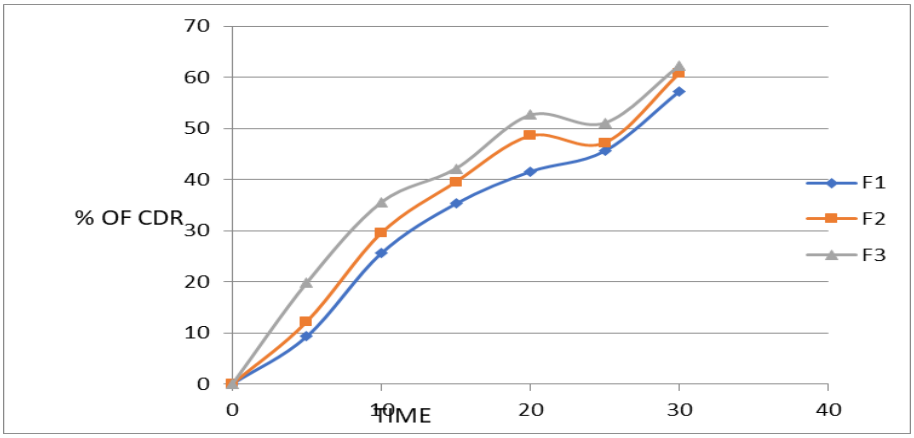

Fig. No. 6: Ficture showing drug release studies of the F1-F3.

Table. No: 6 comparative drug release studies of f4-f6.

Time in hrs	F4	F5	F6
0	0	0	0
5min	21.56	23.54	34.52
10min	41.87	45.89	47.52
15min	46.52	52.51	56.12
20min	58.98	65.35	69.46
25min	62.45	70.25	74.65
30min	65.23	75.98	81.32

COMPARATIVE DRUG RELEASE STUDIES OF F4-F6

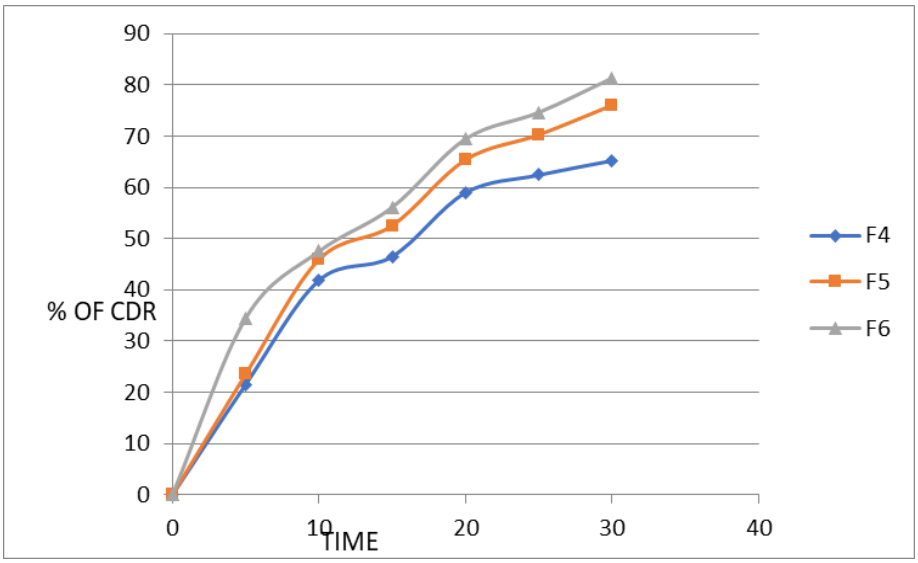

Fig. No. 7: Ficture showing drug release studies of the F4-F6.

Table. No 13: Comparative drug release studies of f7-f9.

Time in hrs	F7	F8	F9
0	0	0	0
5min	37.32	40.52	45.65
10min	49.52	53.53	65.62
15min	58.13	65.72	74.56
20min	70.25	76.62	80.62
25min	76.56	78.65	90.65
30min	84.32	89.35	96.23

COMPARATIVE DRUG RELEASE STUDIES OF F7-F9

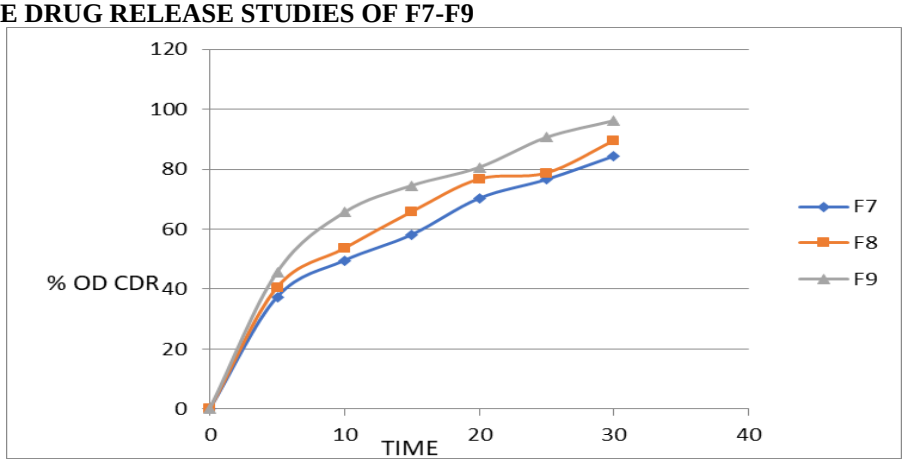

Fig. No. 8: Ficture showing drug release studies of the F7-F9.

STABILITY RESULTS

STABILITY SAMPLES ARE STORED AT

- Accelerated: 40±2^{0}C/75±5% RH
- Intermediate: 30±2^{0}C/65±5% RH
- Long term: 25±2^{0}C/60±5% RH

Testing Intervals

- Accelerated: Initial,1 month.

Table no: 14 Results of stability studies of optimized formulation F-9.

Formulation Code	Parameters	Initial	1st month
F-9	25^{0}C/60%RH % Release	96.23	95.89

Discussion

It was concluded that stability studies of the optimized F5 was carried out using the samples at temperatures 40^{0}C ± 2^{0}C/ 75% ± 5%RH for a period 1 month, the Meloxicam hcl immediate release tablets are observed and there is no significant change in the release characteristics and physicochemical properties.

Kinetic profile data

Table no: 15: kinetic profile data.

Time	%cdr	Log T	√T	Log%cdr	ARA	Log%ARA
0	0	1	0	1	100	2
5	45.65	0.69897	2.23606798	1.345373731	77.85	1.891258617
10	65.62	1	3.16227766	1.682596291	51.85	1.714748761
15	74.56	1.17609126	3.87298335	1.779812863	39.77	1.599555591
20	80.62	1.30103	4.47213595	1.905526048	19.55	1.291146762
25	90.65	1.39794001	5	1.957846634	9.25	0.966141733
30	96.23	1.47712125	5.47722558	1.984662306	3.47	0.540329475

ZERO ORDER PLOT

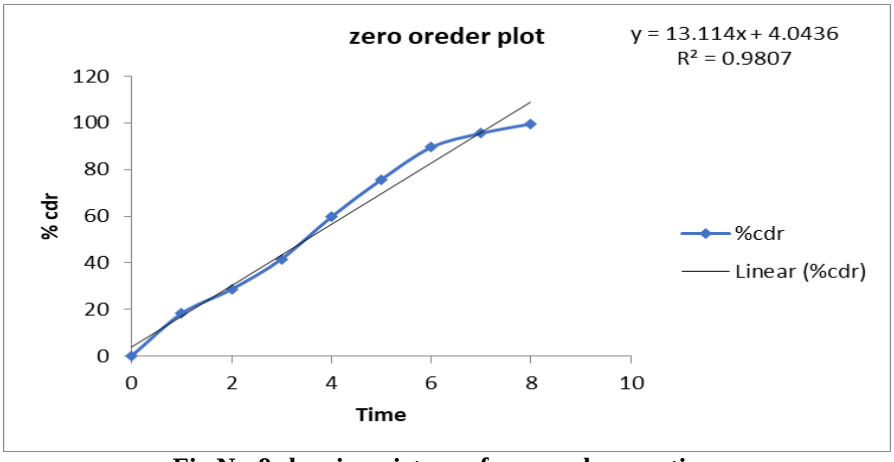

Fig.No:9 showing picture of zero order reaction.

FIRST ORDER PLOT

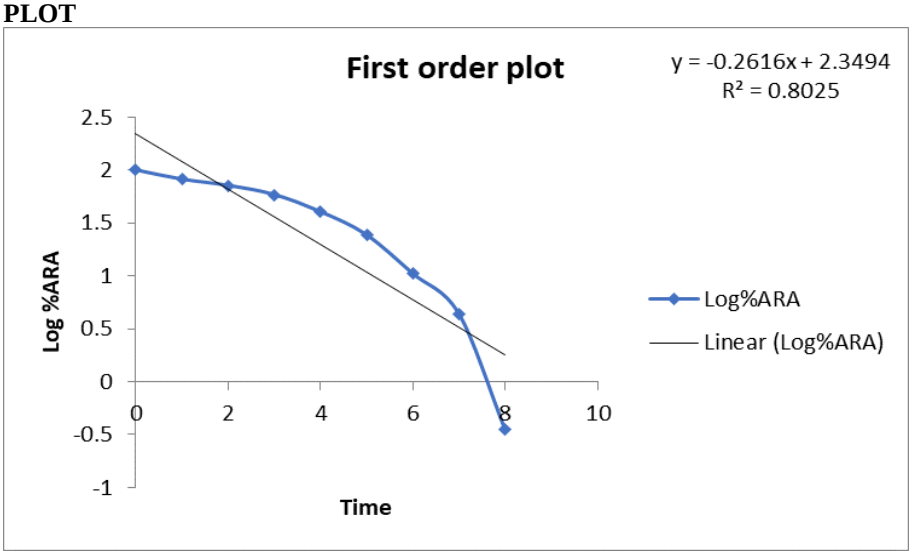

Fig.No:10 showing picture of First order reaction.

HIGUCHI PLOT

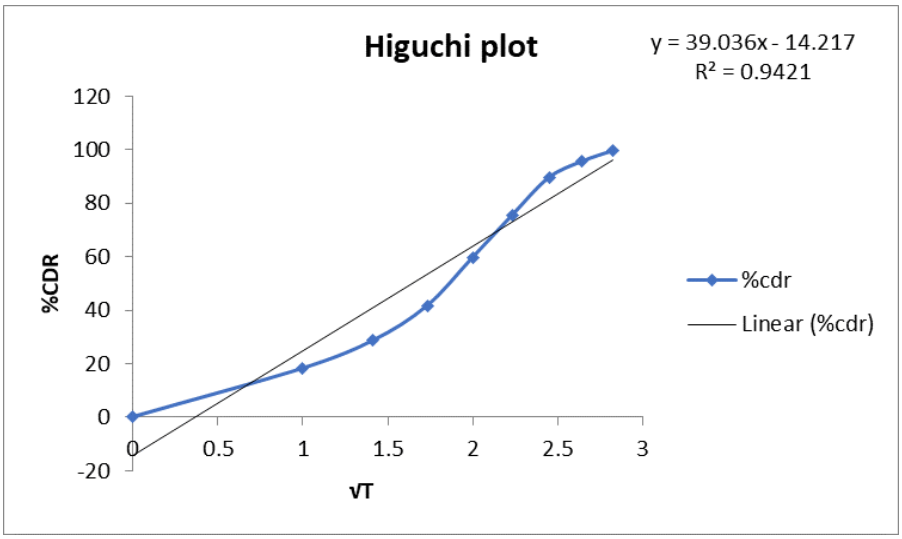

Fig.No 11: Showing picture of higuchi reaction.

KROSS MAYER PEPPAS

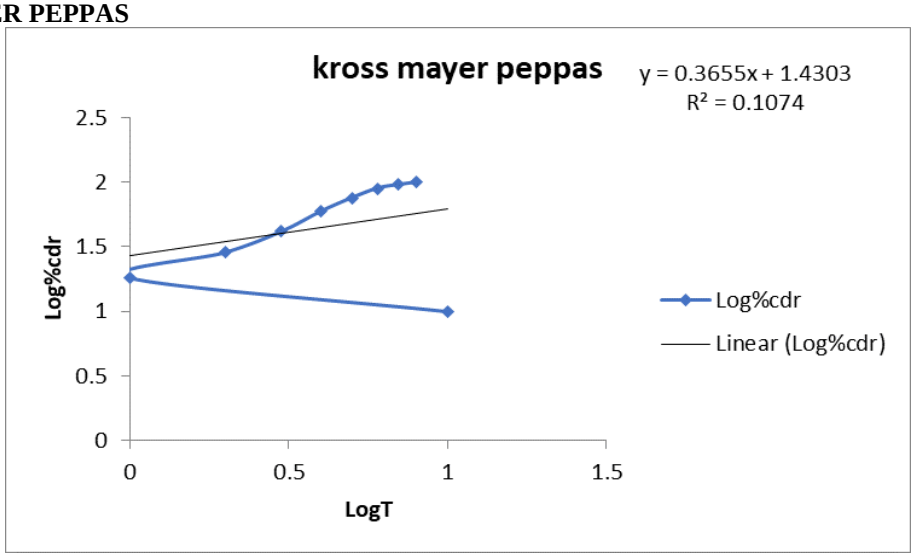

Fig.No:12 showing picture of kross mayer peppas reaction.

Table.no:16 showing table kinetic values of the stavudine patch optimized F7.

S.no	Zero oreder	First order	Higuchi	Krossmayerpeppas
Code	R^2	R^2	R^2	R^2
F9	0.9807	0.8025	0.9421	0.1074

It was concluded that the optimized formulation F9, followed zero order release where the regression value was found to be 0.9807It was also found that the drug was released by diffusion as the regression in Higuchi's plot was 0.9421

SUMMARY

Formulation, development, in vitro characterization of the Meloxicam mouth dissolving tablets. For development of the tablets different excipients are used. The used various excipients such as theccs, Mg.sterate,Talc,,MCC, pvpk30used as the diluents Mg. sterate used as the lubricants,

For formulation design the literature review is carried out. The drugs selection and the excipients selection is based on the collection of review literature. The excipients such as the super disintegrant's choosing also carried out by the review literature.

Before going to development the pre formulation studies are done such as the color, odor, taste, solubility studies. The drug and the excipient compatibility studies are done by using the FTIR studies.

The formulation is developed by the using direct compression method. The formulation is prepared by using different excipients. The excipients are ccs, in various compositions for drug to release prolong time. The pre compression parameters are done such as the bulk density, tap density, compressibility index, Hauners ratio, Angle of repose. The all parameters are come under within range goof flow. The post compression parameters are done such as the harness, thickness, weight variation, friability, disintegration.

The evaluation parameters of the optimized formulation F9 values:

The weight variation of orodispersable tablets, 199mg
The hardness of the orodispersable tablets, 3.7(Kg/cm^2)
Thickness of the orodispersable tablets, 2.42mm
Disintegration of the orodispersable tablets, 3min
Drug content of the orodispersable tablets, 97.86%
Friability of the orodispersable tablets, 0.56%
In-vitro drug dissolution studies of the orodispersable tablets,96.23%

The all parameters come under acceptable criteria within range of limits. The In-vitro drug release studies are done by USP-II apparatus paddle method. The optimized formulation F9 gives the prolong release up to 30mins the drug release96.23%

CONCLUSSION

Formulation, development, In vitro characterization of the meloxicam mouth dissolving tablets. The before going to formulate the tablets the preformulation studies are carried out such as FTIR, calibration, organoleptic characters. The formulation is developed by using super disintegrant's such as ccs is used in different trails. The pre compression parameters such as angle of repose, burkeite, true dencity, compressibility index, these are found to be within the limits. The tablets of meloxicam hcl mouth dissolving tablets are prepared by direct compression method. The talc used as glident and lactose used as lubricant mcc used as filler. The after development of controlled release tablets of meloxicam hcl they undergo for evaluation parameters. Such as weight variation, thickness, friability, drug content, disintegration, and In vitro dissolution studies. They all are found in within range of limits.The in vitro drug release studies carried out by USP-II apparatus.The buffer medium 6.8.The optimized formulation undergo for stability studies for 30days.In stability studies the drug content and drug release studies carried out. These no degradation takes place in the drug content and drug release studies.

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