International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 575-592 www.ijprajournal.com ISSN: 2456-4494

Formulation and Evluation of Hydrogel of Meloxicam for the Management of Rheumatoid Arthritis

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Date of Submission: 09-11-2023 Date of Acceptance: 24-11-2023

Abstract

The aim of the present study was to develop, evaluate the hydrogel containing an Oxicam derivative.

Method: Hydrogel were prepared by using Carbopol and poloxamer and mixing them by using water and alcohol as solvent. The preparation was kept for 12 hrs by using magnetic stirrer. The resulted formulations were subjected for further evaluation. **Results**: The formulations were passed for evaluation in terms of drug content, Spreadability, extrudability, viscosity, *In-vitro* diffusion study. The result of the formulation was found to be satisfactory. Drug content was within acceptable range

Conclusion:

Based on the results it can be concluded that the Hydrogel formed had good physical stability. The evaluation parameter data were within the range. FT-IR peaks showed that the drug polymer was compatible to each other. *In-vitro* release study showed that by using polymer with various concentration hydrogel van be used for sustained release of meloxicam. With DoE design optimized formulation was obtained. The prepared hydrogel using meloxicam may hold promise as an effective formulation through transdermal drug delivery

KEY-WORDS: Hydrogel, oxicam derivative, meloxicam, Rheumatoid arthritis.

I. INTRODUCTION:

Transdermal Drug Delivery System (TDDS) are self-contained, discrete dosage forms which when applied to the intact skin, deliver the drug at a controlled rate to the systemic circulation with minimal inter and intra patient variation. Currently transdermal delivery is one of the most Promising methods for drug application as it reduces the load that the oral route commonly places on the digestive tract and liver. Hence bypasses first pass metabolism, enhancement of Therapeutic efficacy and maintenance of steady plasma level of drug.[1]

HYDROGEL

The term hydrogel describes 3D network structures obtained from a class of synthetic and/or Natural polymers which can absorb and retain significant amount of water.

1.8.1 CLASSIFICATION OF HYDROGEL

Hydrogel is classified into two categories

a. Chemical/permanent hydrogel: They form covalently cross linked (Replacing hydrogel bond by a stronger and stable covalent bond) networks, they attain an equilibrium swelling State which depends on the polymer water interaction parameter and the cross link density.

b. Physical/reversible hydrogel: Networks are held together by molecular entanglements and or Secondary forces including ionic, hydrogen bonding or hydrophobic interaction. In physically Cross-linked gels dissolution is prevented by physical interactions. [2]

1.11 Hydrogel in transdermal delivery[3,4,5]

Transdermal Delivery Drug delivery to the skin has been generally used to treat skin diseases. In recent years, however a transdermal route for the delivery of drugs has been investigated. Swollen hydrogels can be delivered for long duration and can be easily removed. These hydrogels can also bypass hepatic first-class metabolism, and are more comfortable for the patient.

- Hydrogel-based formulations are being looked at for transdermal iontophoresis to obtain enhanced permeation of drug and other products like hormones and nicotine. Current research in this field is now focused on electrically-assisted delivery using iontophoresis and electroporation.

These hydrogels can be used as controlled release devices in the field of wound dressing

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Rheumatoid arthritis [6]

Rheumatoid arthritis (RA) is a chronic autoimmune disease accompanied by infiltration of inflammatory cells and proliferation of synovial fibroblasts, which can lead to synovial damage, cartilage damage, and joint deformities. The incidence rate of RA is about 1% of the total population, and it is higher in females than in males. RA is accompanied by a trend from mild injury to severe disability, which can reduce the life expectancy of patients from 10 to 15 years. The physical and chemical properties, genetic factors, and environmental factors involved in RA are complicated, so the specific pathogenesis of RA is still not completely clear. However, the pathogenic inflammatory factors of RA have been extensively studied. The etiology of RA includes the complex role of genetic factors, external environmental factors and specific risk factors (smoking, periodontitis, gut microbiome) on individuals.

Meloxicam (MLX) classified as a BCS class II drug (high permeability and poor solubility) is a potent non-steroidal anti-inflammatory (NSAID) drug used orally to alleviate the symptoms of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis. Arthritis, an inflammatory disorder is the most common cause of functional disability. Currently, no curative treatments of arthritis exist and the therapeutic objectives are mainly focused on the symptomatic treatment to relieve pain, inflammation and stiffness Q2 of joints. Following oral administration, MLX is well absorbed from the gastrointestinal tract with a high absolute bioavailability of 89%. In clinical trials, MLX has shown a better gastrointestinal safety profile at therapeutic oral doses of 7.5 and 15 mg once daily in comparison to other NSAID.

Carbopol (0.5-2%) and poloxamer (15-20%) were the main polymer used as a gelling agent.

Hydroxypropyl-beta-Cyclodextrin (4-8%) used as a solubilizing agent because Meloxicam has low solubility in water.

Hydrogel contain large amount of water and to maintain the moisture of formulation Propylene glycol (15-20%) used as a humectant.

Transdermal delivery system needs the permeation enhancer to permit from the skin barrier and systemic circulation on this case Oleic acid (1-3%) was used as the permeation enhancer.

Triethanolamine (0.5-2%) is the surfactant that helps to form the gel by adding drop by drop and it also helps to reduce the surface tension of oleic acid.

II. Materials And Methods

Materials

Meloxicam was obtained as gift sample from Apex Healthcare., Gujrat, India. Carbopol 934, Poloxamer 40, polyethylene glycol, and triethanolamine, Oleic acid, Ethanol, Hydroxypropyl-beta-Cyclodextrin were purchased from Yarrow Chem, Mumbai, India. All other chemicals were of the analytical grade and used as received.

Preformulation studies

Solubility

The solubility of drug was observed in different solvents such as water, ethanol, methanol, dimethylformamide.

Melting point Determination

Melting point of the drug was determined by melting point apparatus.

Standardization method of estimation of meloxicam

a) Preparation of reagents and solutions:

Standard solutions preparation: [Ethanol] [7]

Standard solution of Meloxicam was prepared by dissolving 50 mg of Meloxicam with ethanol in 50 ml volumetric flask, then diluting with ethanol up to the mark. Pipette out 5ml of stock solution and transfer into a 50 ml volumetric flask to dilute with ethanol 50 ml up to the mark.

Determination of Absorbance spectrum of Meloxicam:

Transfer 1 ml of standard solution into ethanol in 10 ml volumetric flask and dilute up to the mark. The resulted 10 µg/ml solution was measured at range (200- 400nm) using ethanol as blank, show the absorbance spectrum and λ max at 365nm.

Preparation of Calibration curve:

From the sample solution, 100µg/ml resulting solution was prepared. From this 100 µg/ml solution (0.2- 2.0 ml) was transferred to 10ml volumetric flasks and dilute with ethanol up to the mark. The method was determined at different concentration levels ranging (2-20µg/ml)

for Meloxicam, the calibration curve was constructed by plotting absorbance versus concentration of Meloxicam (µg/ml)

Preparation of pH 7.4 Phosphate Buffer [8]

Prepare 800 mL of distilled water in a suitable container. Add 20.214 g of Sodium Phosphate Dibasic Heptahydrate to the solution. Add 3.394 g of Sodium Phosphate Monobasic Monohydrate to the solution. Adjust solution to final desired pH using

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HCl or NaOH.Add distilled water until the volume is 1 L.

Standardization of meloxicam in 7.4 Phosphate Buffer:

a) Estimation of Meloxicam: Spectrophotometric method is mainly used for estimation of meloxicam by using U.V spectroscopy.

b) Preparation of Standard Stock Solution: Dissolve 50 mg of pure drug in 50ml of pH 7.4 Phosphate Buffer, this is stock 1. 5ml of solution pipette out from the stock 2 and placed in 100ml of volumetric flask. Then prepare serial dilutions by taking 2ml, 4ml, 6ml, 8ml, 10ml and dilute it to 10 ml with the same buffer. The absorbance of the resulting solution was measured spectrophotometrically at 363 nm.

c) Standardisation of Meloxicam: In this spectroscopic method serial dilutions were prepared (Conc: 20, 40, 60, 80, 100 µg/ml) by using phosphate buffer. Then the absorbance was recorded at 363 nm by using UV Spectrophotometer.

Standardization of meloxicam in 6.8 pH Phosphate buffer: [9]

a) Preparation of pH 6.8

Dissolve13.872 g of potassium dihydrogen phosphate, 35.08 g of disodium hydrogen phosphate and add sufficient water to produce 1000mL.Adjust the pH, if necessary

b) Estimation of Meloxicam: Spectrophotometric method is mainly used for estimation of meloxicam by using U.V spectroscopy.

c) Preparation of Standard Stock Solution: Dissolve 10mg of pure drug in 100ml of pH 6.8 pH Phosphate Buffer, this is stock 1. 10ml of solution pipette out from the stock 2 and placed in 100ml of volumetric flask. Make up the volume up to the mark with same buffer Then prepare serial dilutions by taking 2,4, 6, 8 and 10 ml and diluting it to 10 ml with the same buffer. The absorbance of the resulting solution was measured spectrophotometrically at 362 nm.

PREPARATION OF MELOXICAM HYDROGEL

Preparation of hydrogels Carbopol 934 was gradually dispersed in water or a mixture of water and ethanol in the case of hydroalcoholic gel. MLX (1 % w/w) was added to the mixtures and kept under magnetic stirring for 12 h. The gel was spontaneously formed by the addition of few drops of triethanolamine.

Poloxamer was slowly added to water or to a mixture of water and ethanol with gentle mixing. The mixture was left in refrigerator (4 °C) overnight for complete dissolution of the polymer. After formation of a clear viscous solution, the drug was added, stirred gently at room temperature until a clear gel was formed [10].

Table:1 formulation table

Formulation code	Drug (%)	Carbopol 934 (%)	Poloxamer 407 (%)	Hydroxypropyl-beta-Cyclodextrin (%)	Propylene glycol (%)	Oleic acid(%)	Triethanolamine (%)	Alcohol (%)	Water (%)
F1	1	0.5	15	4	15	1	0.5	23	40
F2	1	1.25	15	4	15	1	0.5	23	40
F3	1	2	15	4	15	1	0.5	23	40
F4	1	0.5	17	4	15	1	0.5	22	39
F5	1	1.25	17	4	15	1	0.5	20	40
F6	1	2	17	4	15	1	0.5	20	40
F7	1	0.5	20	4	15	1	0.5	20	38
F8	1	1.25	20	4	15	1	0.5	20	38

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F9	1	2	20	4	15	1	0.5	20	38

EVALUATION OFTHE MELOXICAM HYDROGEL

DRUG CONTENT ANALYSIS

The drug content of **Meloxicam hydrogel** formulation was measured using UV spectroscopic method. 10 µg/ml of aliquot was prepared using hydrogel formulation using methanol as a solvent. The samples were measured as 210 nm using UV spectroscopic method.[11]

$$\text{Drug content} = \frac{\text{absorbance} \times \text{dilution factor}}{\text{Slope}}$$
$$= \text{concentration} \times \text{dilution factor}$$

$$\%\ \text{Drug content} = \frac{\text{drug content} \times 100}{\text{Label claim}}$$

***In-vitro* DIFFUSION STUDIES:**

Franz diffusion cells (area 3.4618 cm^2) with a cellulose membrane were used to determine the release rate of Meloxicam hydrogel for all the formulations. The cellulose membrane was first hydrated in distilled water at 25 ºC for 24 hours. The membrane was then clamped between the donor and receptor compartments of the cells. Each Diffusion cell was filled with 130 ml of phosphate buffer pH 6.8. The receptor fluid was constantly stirred by externally driven magnetic bars at 300 rpm throughout the experiment. At 1,2,3,4,5,6,7 and 8hr time intervals, 5ml sample was removed from receptor for spectrophotometric determination and replaced immediately with an equal volume of fresh receptor medium. Samples were analysed by UV visible spectrophotometer at 240nm. [12]

Physical appearance:

The physical appearance (i.e., light yellow colour, clarity, and smoothness) and homogeneity of the prepared transdermal hydrogel tested by visual observations[13].

pH determination

The pH of the hydrogel measured by directly dipping pH meter rod into hydrogel.

Readings were taken in triplicate manner[14].

Determination of viscosity:

The viscosity of the Hydrogel formulations was determined using Brookfield viscometer with spindle no. 6 at 10 rpm at the temperature of 25^0C[15].

Spreadability test

Spreadability (gm.cm/sec) is expressed in terms of time taken in seconds by two slides to slip off from the hydrogel placed between them, under certain load. The standardized weight tied on the upper plate was 20 g and length of the glass slide was 7.5 cm. Spreadability was calculated by using the following formula.[16]

Spreadability = (Weight × Length) /Time

Swelling index

In order to measure swelling index of hydrogel, gravimetric method was used. hydrogel with cross-linker was dipped in buffer of pH 7.4. The swollen hydrogels were removed from medium and weighed at specific time interval of 0.5, 1, 1.5, 2, 2.5, 3, 3.5, 4, 4.5 hours until the weight of swelled hydrogel became constant. Extra water was separated from hydrogel surface by slight tapping of surface with filter paper. Percentage swelling was measured using formula given below[17].

$$\text{Swelling\%} = \frac{w_2 - w_1}{w_1} * 100$$

where

W1= Initial weight of hydrogel

Extrudability Study:

It is a test to determine the force required to extrude the gel from the tube. The Hydrogel extruded should be at least 0.5 cm ribbon in 10s. The higher the quantity of gel extruded, the better is the extrudability. The extrudability of each formulation was measured, in triplicate, and calculated by using the formula:

E = M/A

Where E- Extrudability, M- Applied weight to extrude gel from tube, A-Area

Stability studies

Stability studies were carried out to detect any changes in pH, globule size, transmittance, and drug content. Results of temperature stability studies on the optimized Hydrogel. Results obtained indicated that the Meloxicam based hydrogel was stable for one month.

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Accelerated stability studies of hydrogel were carried out at temperature of $40^0C \pm 2^0C$ and relative humidity of 75% ± 5% for a period of 1 month (15 and 30 days). Hydrogel was evaluated for physicochemical properties.

III. RESULTS

Solubility

Table: 2

Drug	Solubility	Mg/ml
Water	Insoluble	0.1779
Methanol	Very slightly soluble	0.2328
Ethanol	Very slightly soluble	0.2425
Dimethylformamide	Soluble	0.3012

Melting point

Table:3

SL No.	Temperature (˚C)
1	253
2	255
3	253

Standardization method of estimation of Meloxicam in ethanol

Table:4

Sl. no	Concentration µg/mL	Absorbance
1	2	0.1020
2	4	0.1859
3	6	0.2815
4	8	0.3593
5	10	0.4673

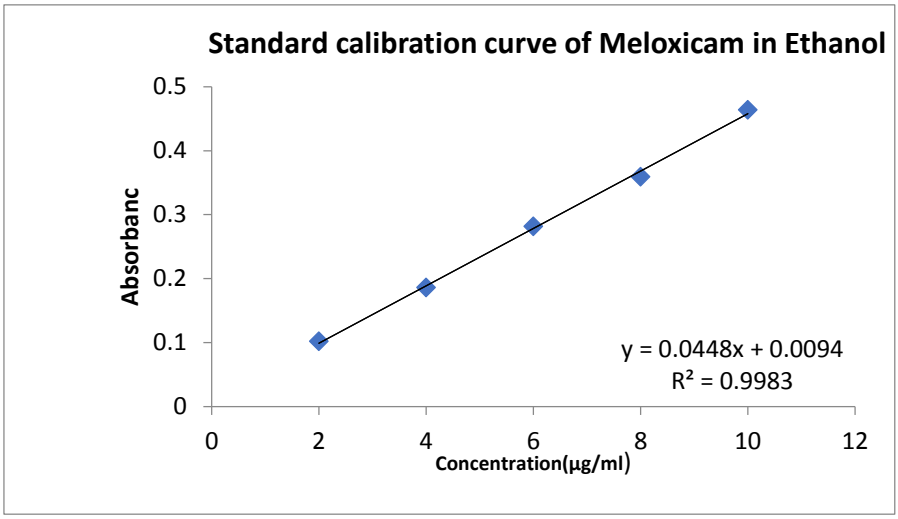

Figure:1 Calibration curve of Meloxicam in Ethanol

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Standardization method of estimation of Meloxicam in Phosphate Buffer 7.4

Table:5

Sl. no	Concentration µg/ml	Absorbance
1	2	0.1006
2	4	0.1945
3	6	0.2872
4	8	0.3758
5	10	0.4660

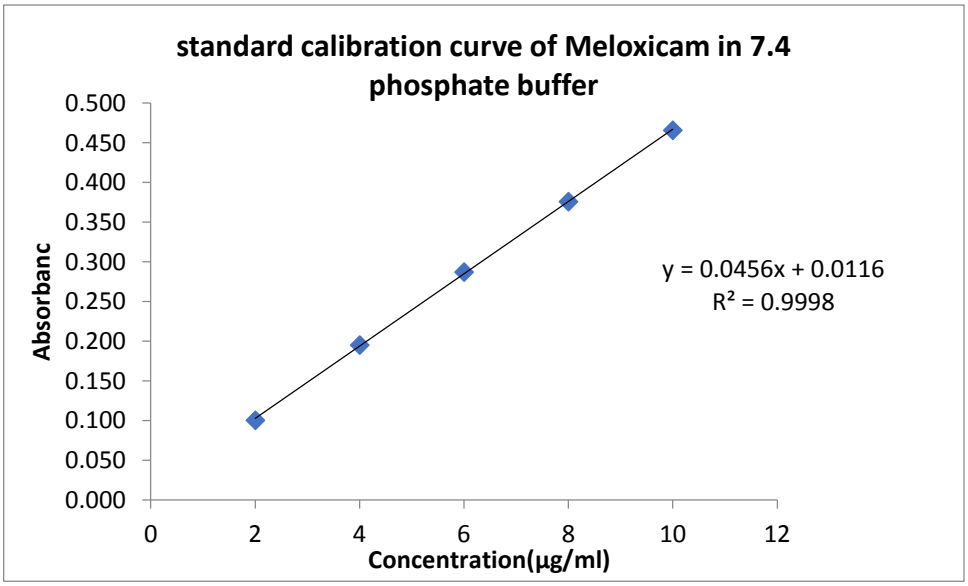

Figure:2 Calibration curve of Meloxicam in Phosphate buffer 7.4 pH

Calibration curve of Meloxicam in Phosphate buffer 6.8 pH

Table: 6

SL. No	Concentration µg/ml	Absorbance
1	2	0.123
2	4	0.216
3	6	0.329
4	8	0.431
5	10	0.553

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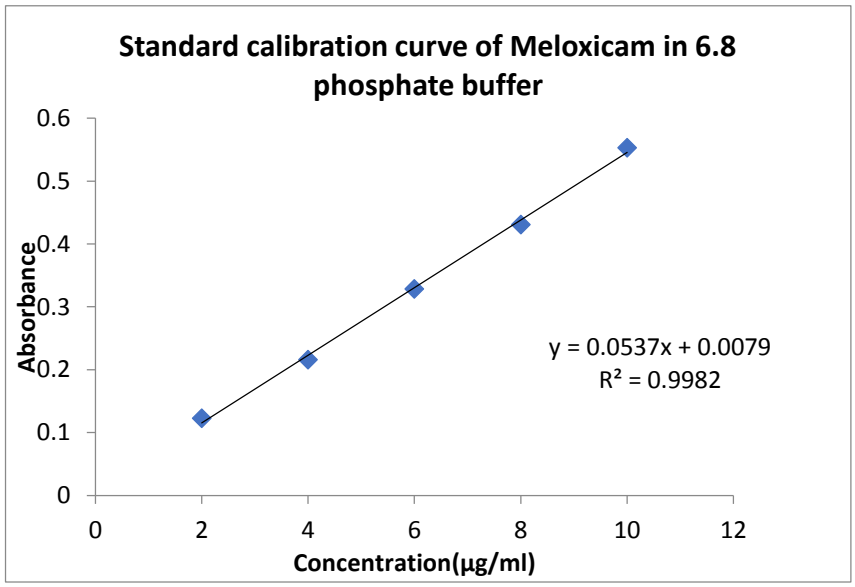

Figure:3 Calibration curve of Meloxicam in phosphate buffer 6.8

FT-IR ANALYSIS

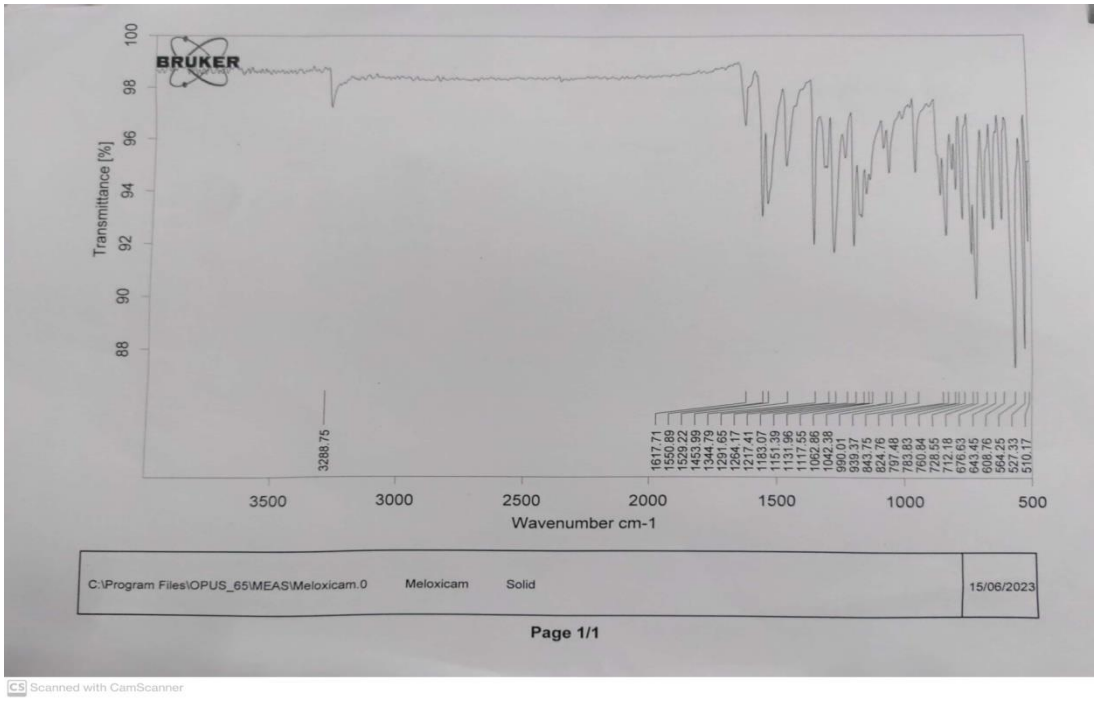

Figure:4 FT-IR of pure drug

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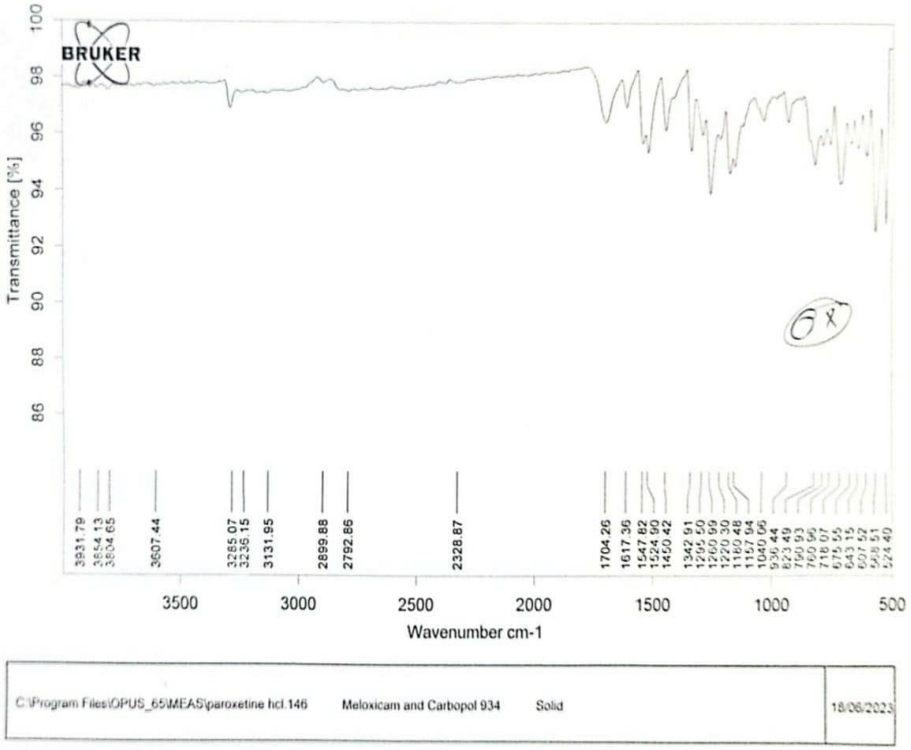

Figure:5 FT-IR of Meloxicam & Carbopol 934

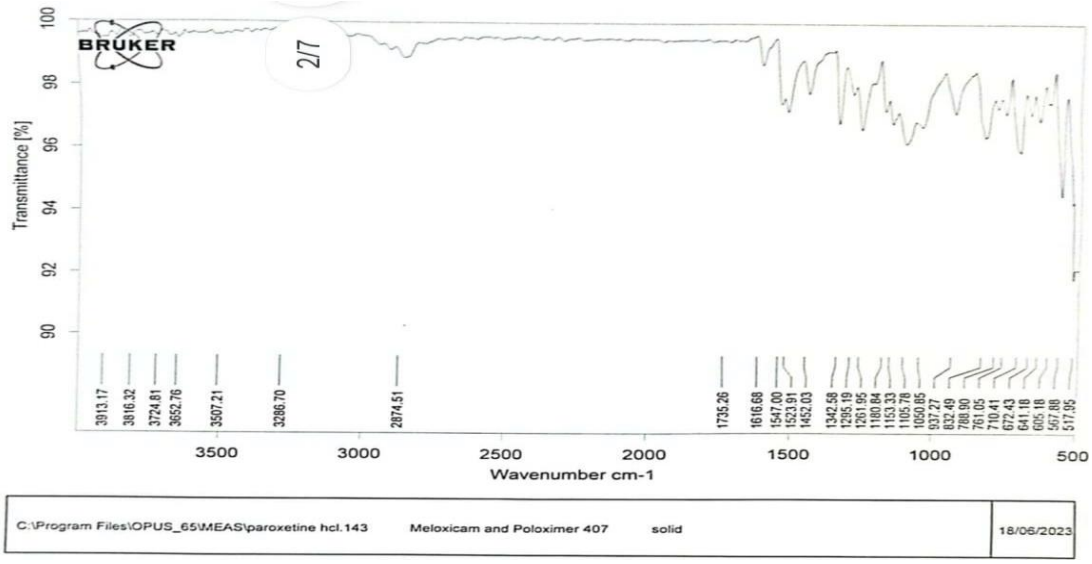

Figure:6 FT-IR of Meloxicam & Poloxamer 407

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EVALUATION

8.3.1 Physicochemical evaluation of Hydrogel

Table:7

Formulation code	Physical appearance	pH	Viscosity (cps)	Spreadability (g.cm/sec)	Swelling index (%)	Drug Content (%)
F1	Light yellow	6.83	7844± 2	18.6 ± 0.3	89.21	80±0.12
F2	Light yellow	6.98	7980± 1.5	19.5 ±0.11	91.46	80±11
F3	Light yellow	6.33	8342± 2.5	11.8 ±0.6	89.98	84±0.3
F4	Light yellow	6.47	8380± 1.5	15.3 ±0.4	90.89	90±0.8
F5	Light yellow	6.42	8636± 1.5	14.9 ±0.9	90.87	98±0.7
F6	Light yellow	6.85	8736± 1.5	15.5 ±0.6	86.84	96±0.1
F7	Light yellow	6.82	8980± 1.5	13.5 ± 0.7	90.88	96±0.6
F8	Light yellow	6.36	9242± 2.5	10.9 ±0.5	90.9	98±0.5
F9	Light yellow	6.34	9436± 1.5	17.4± 0.2	95.94	96±0.11

In-vitro DIFFUSION STUDIES:

Table:8 *In-vitro* drug release data of Meloxicam loaded Hydrogel

Formulation code	Drug Release %
F1	53± 0.13
F2	47±0.18
F3	46±0.17
F4	43±0.34
F5	44.6±0.24
F6	46±0.16
F7	39±0.11
F8	41±0.16
F9	38±0.13

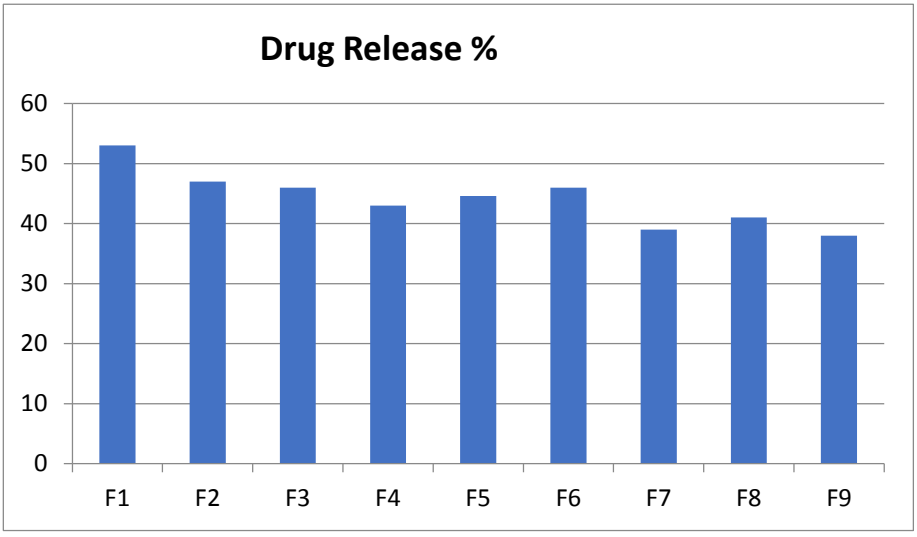

Figure:7 Comparative drug release profile for prepared formulation from F1-F9

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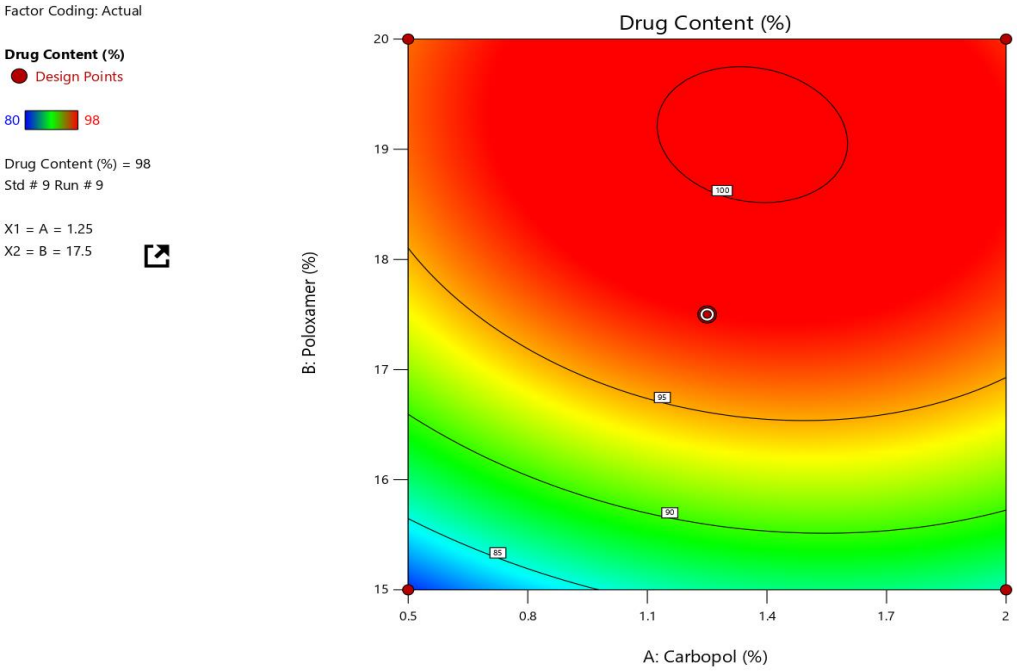

Figure:8 Contour plot of Drug content

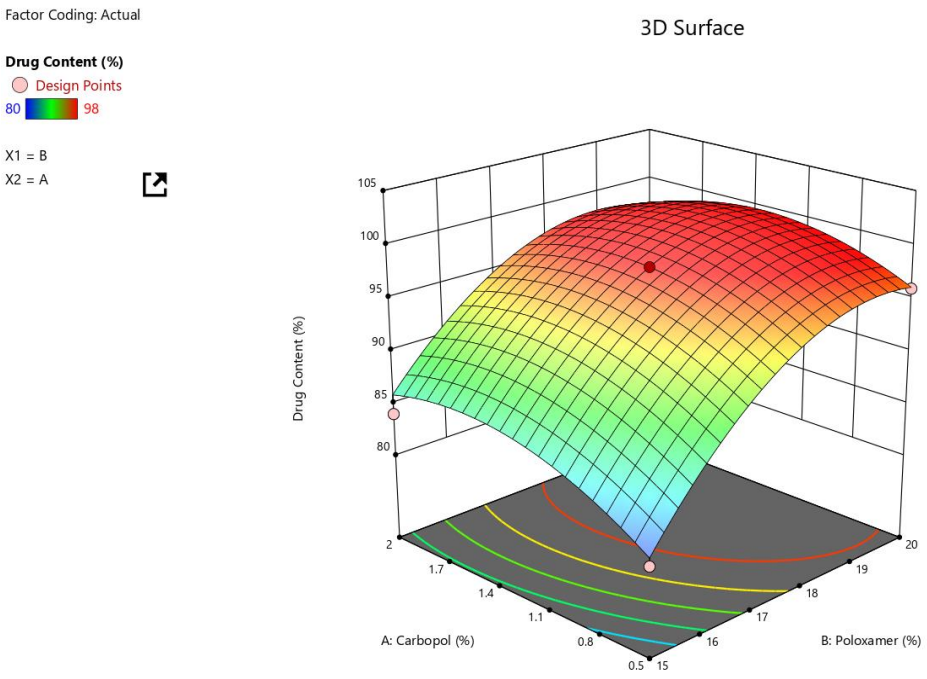

Figure:9 3D Surface Graph of Drug Content

Fit Summary

**Response 2: *In-vitro drug* release **

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Table no :9

Source	Sequential p-value	Lack of Fit p-value	Adjusted R^2	Predicted R^2	
Linear	**0.0220**		**0.6263**	**0.3155**	**Suggested**
2FI	0.3970		0.6172	-0.0783	
Quadratic	0.9766		0.3719		
Cubic	0.1181		0.9737		**Aliased**

ANOVA for Linear model
**Response 2: *In-vitro drug* release **

Table no :10

Source	Sum of Squares	df	Mean Square	F-value	p-value	
Model	109.62	2	54.81	7.70	0.0220	Significant
A-Carbopol	0.9504	1	0.9504	0.1336	0.7273	
B-Poloxamer	108.67	1	108.67	15.27	0.0079	
Residual	42.70	6	7.12			
Cor Total	152.32	8				

Factor coding is **Coded**.
Sum of squares is **Type III - Partial**
The **Model F-value** of 7.70 implies the model is significant. There is only a 2.20% chance that an F-value this large could occur due to noise.
P-values less than 0.0500 indicate model terms are significant.

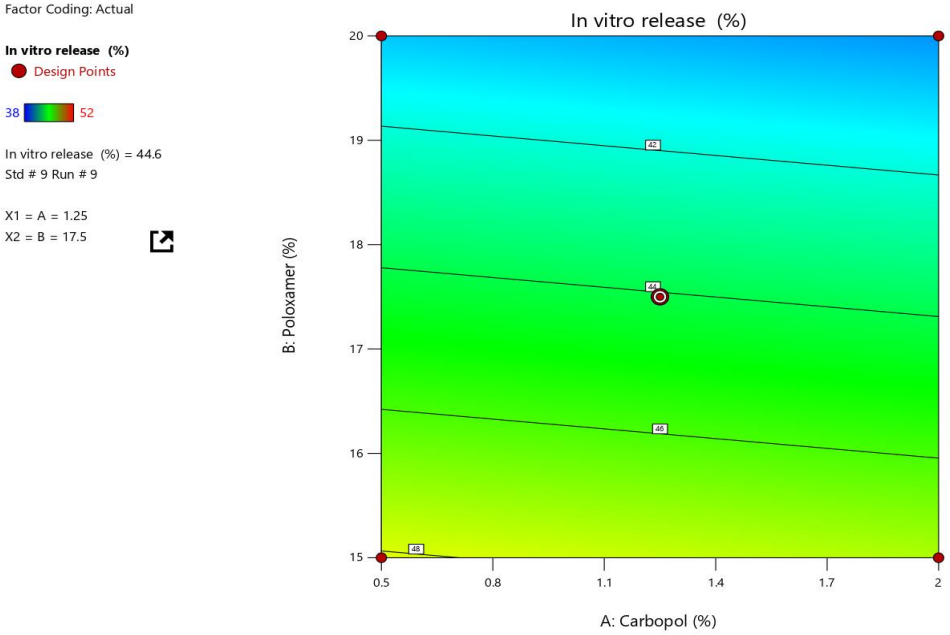

Figure:10 Contour Plot of *In-vitro* Drug Release

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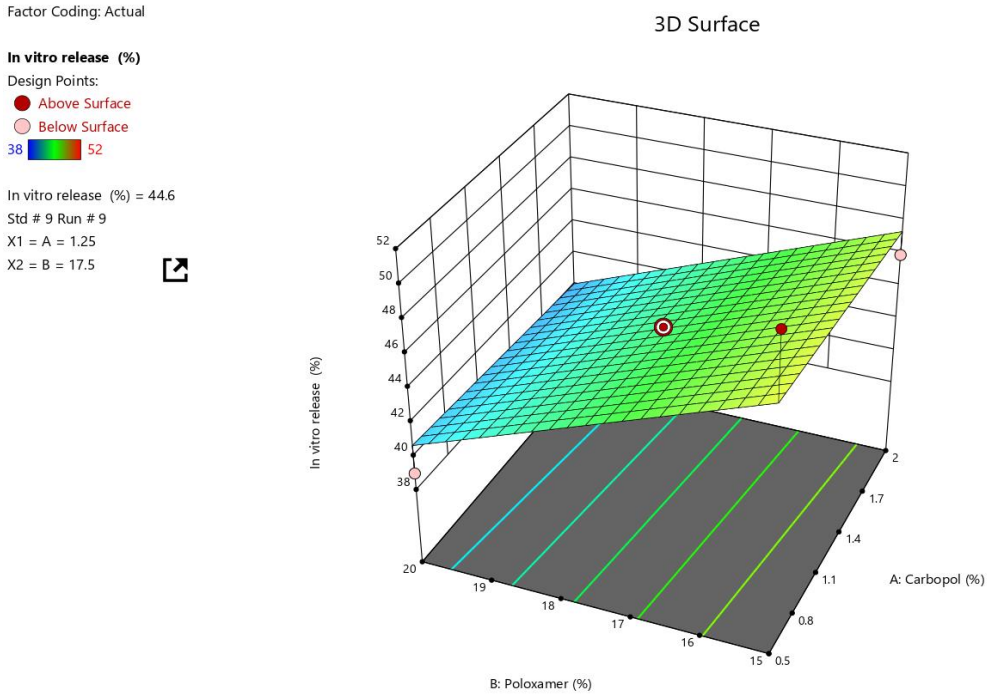

Figure:11 3D Graph of *In-vitro* Drug Release

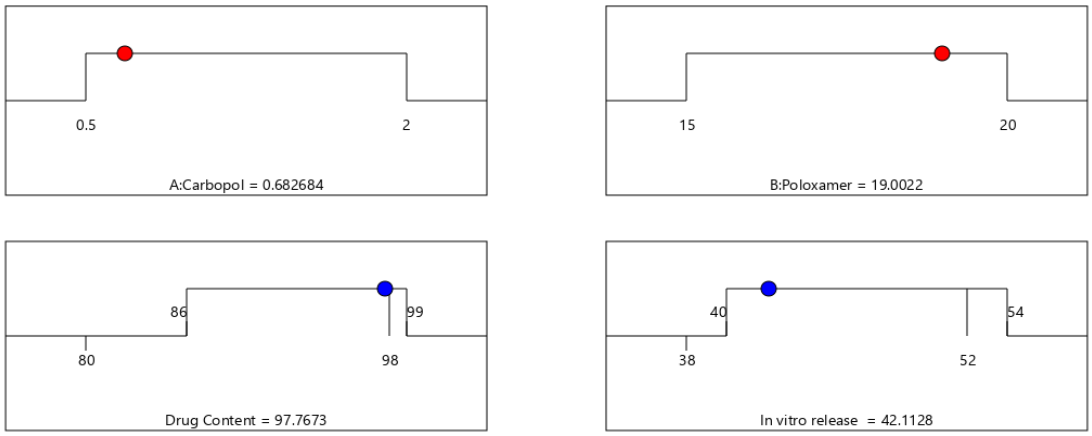

Figure:12 Ramp Model

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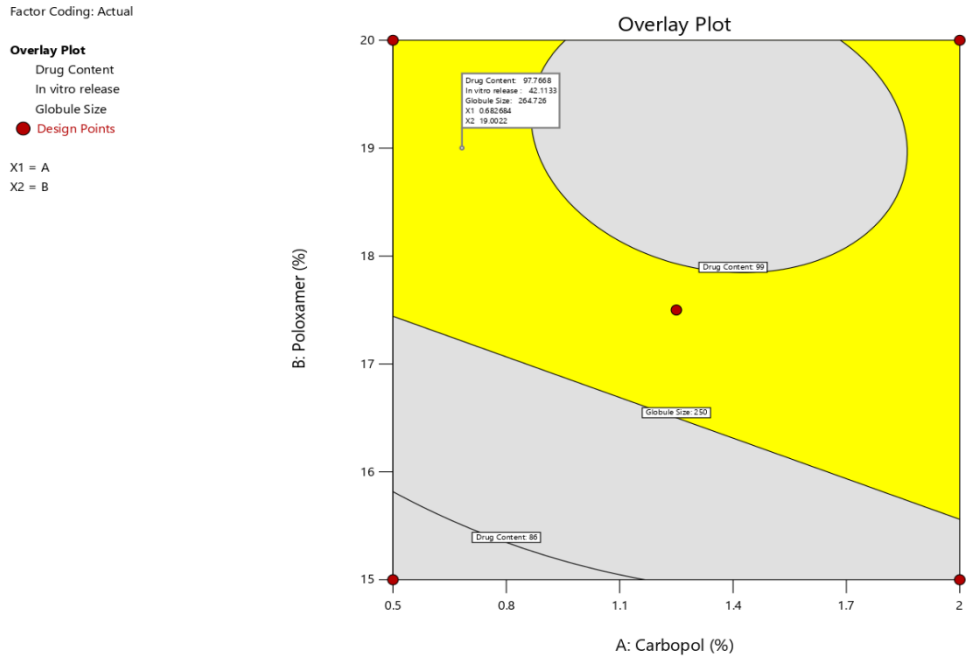

Figure:13 Overlay Plot

8.6 OPTIMIZED FORMULATION

Table no. 11: Optimized Formulation F9 of Meloxicam hydrogel

F. code	Drug	Carbopol 934	Poloxamer 407	Hydroxypropyl-beta-Cyclodextrin	Propylene glycol	Oleic acid	Triethanolamine	alcohol	Water
F9	1	2	20	4	15	1	0.5	20	38

Table no: 12: *In-vitro* Drug release studies of optimized formulation

Time(h)	% CDR
0	0
1	10.72635
2	13.77544
3	22.68241
4	27.58381
5	29.1253
6	34.14739
7	36.11415
8	38.081

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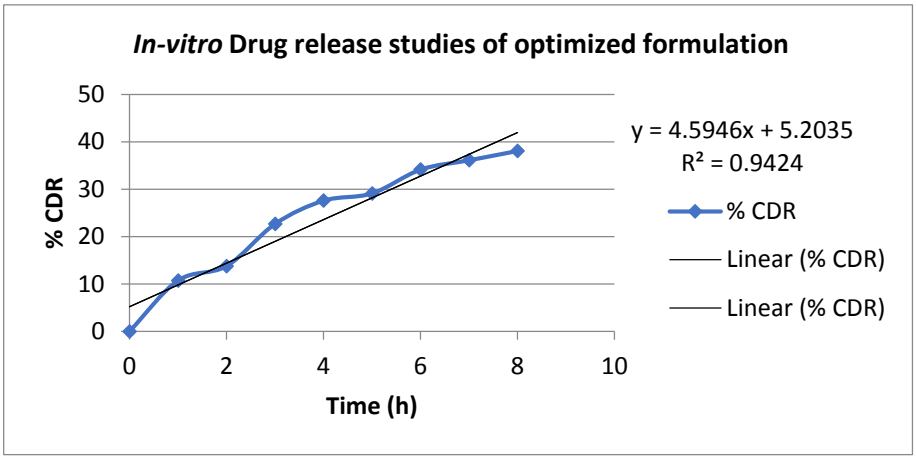

Figure: 14 *In-vitro* Drug release studies of optimized formulation

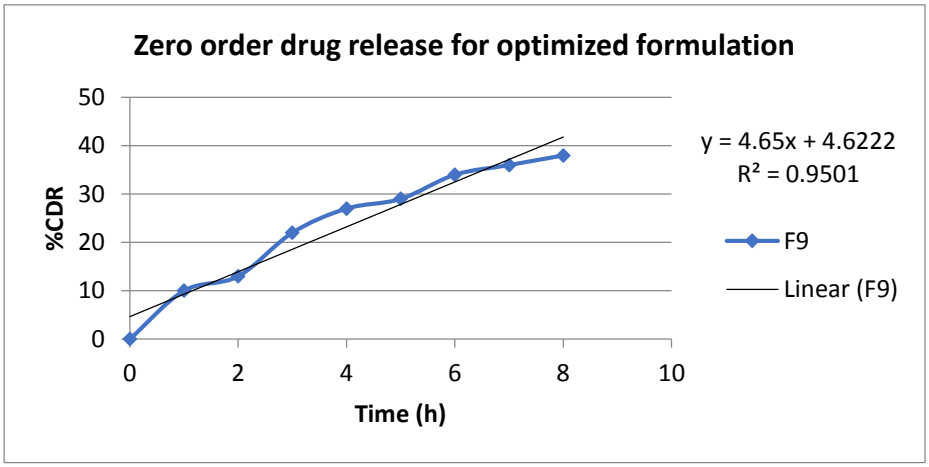

Figure:15 Zero Order for Drug Release Optimized Formulation

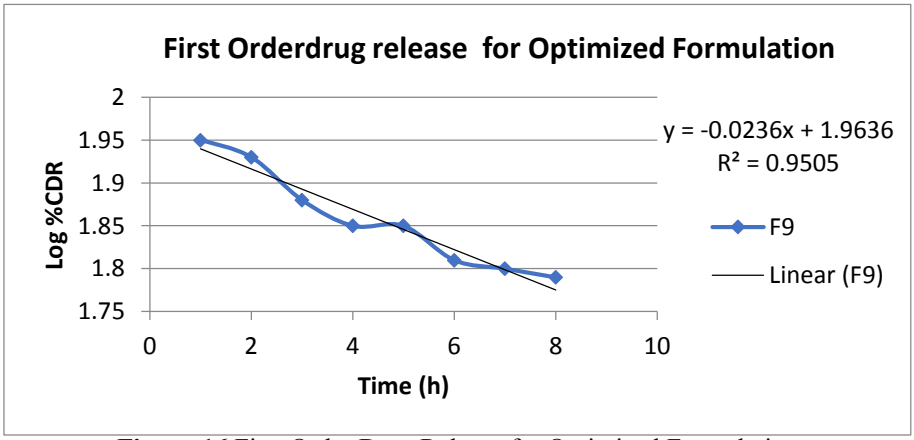

Figure:16 First Order Drug Release for Optimized Formulation

International Journal of Pharmaceutical research and Applications
Volume 8, Issue 6, Nov.-Dec. 2023, pp: 575-592 www.ijprajournal.com ISSN: 2456-4494

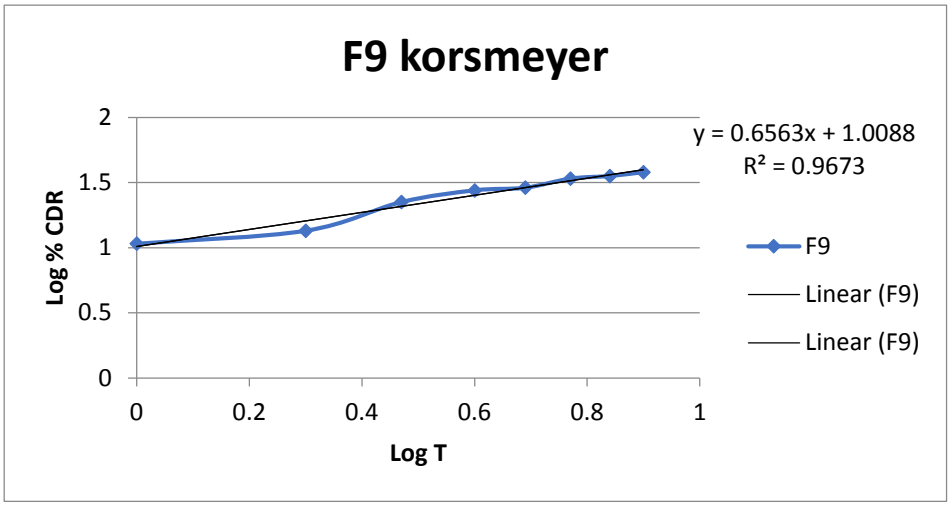

Figure:17 Korsmeyer-Peppas Graph for Optimized Formulation

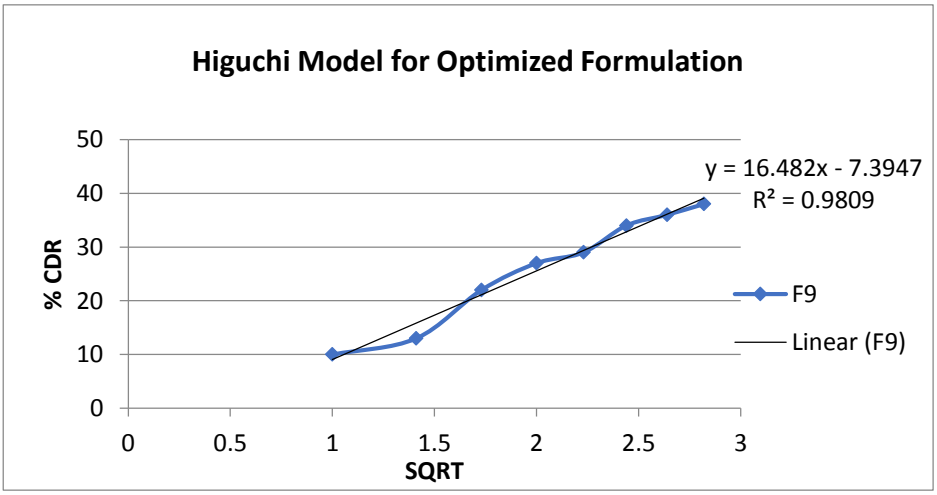

Figure:18 Higuchi Model for Optimized Formulation

IV. Discussion

In the present study, an attempt has been made to formulate Hydrogel by simple mixing method. The prepared Hydrogel were systematically subjected to physicochemical evaluation, *in-vitro* drug release and several characterizations.

Standard Calibration Curve in Ethanol:

Standard calibration curve was carried out in Ethanol and the spectrophotometric data are given in the Table No.07 The R^2 value showed nearly 1 which signifies linearity respectively. The maximum absorbance was taken in 365 nm.

Standard Calibration Curve of Meloxicam in pH 7.4 Phosphate Buffer Solution:

Standard calibration curve was carried out in pH 7.4 Phosphate Buffer Solution and the spectrophotometric data are given in the (Table No. 8) The R^2 value in pH 7.4 Phosphate Buffer Solution showed nearly 1 (Figure No. 08) which signifies linearity respectively. The maximum absorbance was taken in 362 nm.

Standard Calibration Curve of Meloxicam in pH 6.8 Phosphate Buffer Solution:

Standard calibration curve was carried out in pH 6.8 Phosphate Buffer Solution and the

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spectrophotometric data are given in the (Table No.9) The R^2 value in pH 6.8 Phosphate Buffer Solution showed nearly 1 (Figure No. 9) which signifies linearity respectively. The maximum absorbance was taken in 363 nm.

Pre-formulation studies:

Pre-formulation studies were carried out by mixing the drug with various excipients in different proportions and kept for a month at different temperature and humidity conditions reveals that no significant change appear in the sample at all mentioned conditions, so no incompatibilities were observed between drug and excipients.

Solubility studies:

The result of the solubility study was carried out in different solvents. The observed the drug is practically insoluble in water, soluble in dimethylformamide, slightly soluble in ethanol.

Fourier Transform Infrared spectroscopy:

Drug and other excipients compatibility studies were carried out using IR (FTIR) to check the possible interaction of the drug and excipients in the Hydrogel formulation (Table No.07). Characteristics peaks of functional group of -C=C- stretch Alkenes, C-H, O=S=O and C-N stretch Aromatic amines were observed with pure drug as well as combination of Carbopol and poloxamer. It was found that there were no interaction between the drug, polymer or excipients in their individual form as well as in the combination form and the obtained spectra.

Drug Content Estimation

The percentage of drug content of all the formulations varied from 80±0.12- 98±0.7% as shown in the Table no.10. This result indicates that there was uniform distribution of the drug throughout the batch (Figure No. 18).

pH determination

The result pH of various transdermal hydrogels is shown in table No.10.The pH of the formulations F1 to F9 ranged from 6.33 to 6.98. The result results were found to be satisfactory and in the range **o**f 6-7.4. It can be concluded that the prepared hydrogels fulfilled the requirement of gel-based formulations for dermatological use

Determination of viscosity

Viscosity of the developed formulations F1 to F9 varied from 7844±2 to 9436±1.5 cps and was which is given in table No.10 found to be uniform. The optimized formulation F10 shows 9436±1.5 cps. Which is helpful in retaining moisture and helps in enhancing the hydration of skin. This viscosity range gives good flow property and adherence to the skin as transdermal hydrogel as to deliver the drug thorough the skin give effect. The viscosity increased with increase in (polymer) Poloxamer and Carbopol concentration.

Spreadability

Spreadability of Meloxicam hydrogels decreased by increasing the Polymer (Carbopol, Poloxamer) concentration and the formulation F1 to F9 values were in the range of 10.9±0.5 to 19.5±0.11 gm.cm/sec and is give in the table No. 10 The formulation F2 shows the maximum Spreadability compared to others due to low concentration of polymer (Poloxamer, Carbopol), F8 has low spread ability due to high concentration of drug polymer ratio concentration**.** It can be concluded that the prepared hydrogels fulfilled the requirement of gel-based formulations for dermatological use which should have several favourable properties such as lack of grease and ease of spread ability.

Swelling index

Swelling rages of hydrogel formulations F1 to F9 was shown in table No. 10 among them F10 shows maximum swelling 95.94% and F7 shows minimum swelling 86.84%. The optimized formulation F10 showed 95.94% swelling. From the result it can conclude that more the swelling more is the drug release. Swelling is the main property of hydrogel in which hydrogel can hold large amount of water which helps maintain moisture, helps in adhering to skin and in drug holding.

Extrudability

The hydrogel extruded was a 0.5 cm ribbon in 10s. The higher the quantity of gel extruded, the better is the extrudability.

***In-vitro* drug release study**

In-vitro drug release test results indicate diffusion of drug from all its within 1 to 8 h which is depicted in Table No.12; All the formulation were observed to have similar pattern of drug release were it was found initial burst release within 1 hours and then after 8 hours the release were found to be between 38±0.13 to 53±0.13%. The release studies of the formulation were analysed on the basis of zero order, First order, and Korsmeyer-Peppas kinetics. The R^2, k, n values are shown in table. All the formulations were best fitted to kinetic models.

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V. CONCLUSION

The present investigation focused on formulation, evaluation, characterisation and optimization of Meloxicam loaded hydrogel by simple mixing method.

The developed spectrophotometric method for the estimation of Meloxicam by UV method was significant. Compatibility study by FTIR revealed that there was no interaction of drug. The preparation of Meloxicam Hydrogel by simple mixing method was found to be feasible & economical.

The evaluation parameters of the formulated Meloxicam Hydrogel show significant result. The Drug content was found to be near to 90%. Also, the *In-vitro* drug release for various formulations were found to be near 53% within 8h.

DOE by using Response Surface method was carried out by using Poloxamer (15-20%) and Carbopol (0.5-2%) as two variables using their higher and lower limits. Three responses were noted that includes, drug content and drug release. The results showed the optimized formulation was found to be effective.

It is concluded from the present studies that Meloxicam Hydrogel show a potential drug delivery system with good stability and release profile. All the other formulations were also equally good in their physicochemical characteristics.

Further animal study, skin irritation study to be done to prove the safe and effective use of the hydrogel of Meloxicam

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