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FORMULATION AND EVALUTION OF DICLOFENAC SUSTAINED RELEASED TABLET

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ABSTRACT

Diclofenac is a Non-steroidal Anti Inflammatory drug (NSAIDS). It can shows Anti-inflammatory, Antipyretic, and analgesic activity and Diclofenac is important to Inhibition of Cyclooxygenase (COX I, COX II) Enzyme is responsible for Inhibition of Prostaglandins Synthesis. The Authentication and Preformulation studies associated to pure drug diclofenac is conducted for maintaining their standard and stability. The formulation of Diclofenac Sustained release Tablet is important to give prolonged activity in prolonged drug release in Extended Period of Time for the Long Term Therapeutic activity. The Formulation of Sustained Released Tablet by using Suitable Excipients such as HPMC K 100, Ethyl Cellulose, Talc, Magnesium Stearate. This Diclofenac Sustained released tablet is from by Wet Granulation Method. The Prepared sustained released Tablet is Evaluated In terms of bulk density, tapped density, angle of repose, carr's Index and, hardness test, weight variation test, friability test and *in vitro* study. The result associated in Optimized batch is good to Satisfactory and having a good free flowing property. The hardness, weight variation, and friability these values are within the pharmacopeia limit. The in vitro Dissolution studies shows Maximum percentage of release of drug (90.52) with in 190 min.

KEYWORDS

Diclofenac, Sustained Release, anti-inflammatory drug, extended release, prolonged released.

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INTRODUCTION

Diclofenac is a Non-steroidal Anti Inflammatory drug (NSAIDS)[1]. It is an Anti-inflammatory, Antipyretic drug is important to prevent the inflammation and it is also important to give analgesic activity[2]. Diclofenac is important for treatment of inflammatory disorders may include musculoskeletal complaints, especially arthritis, rheumatoid arthritis, polymyositis, dermatomyositis, osteoarthritis, dental pain, TMJ pain, spondylarthritis, ankylosing spondylitis, gout attacks and pain management in cases of kidney stones and

gallstones[3]. The Chemical name Diclofenac is 2-(2,6-dichloranilino) phenyl acetic acid[4]. The Primary Mechanism of Diclofenac is Anti-inflammatory, Antipyretic, and analgesic action and Diclofenac is important to Inhibition of Cyclooxygenase (COX I, COX II) Enzyme is responsible for Inhibition of Prostaglandins Synthesis[5]. It is important for Bacterial DNA synthesis activity. Diclofenac is Drug is used to treat mild to moderate postoperative or posttraumatic pain, in particular when inflammation and is effective against menstrual pain and endometriosis[6].

MATERIALS AND METHOD

MATERIALS

Diclofenac and all Formulation Excipient (HPMC K100M, ethyl cellulose, Talc and Magnesium Stearate) were obtained from Pharmaceutics Laboratory of R. C. Patel Institute of Pharmaceutical Education and Research, Shirpur 425405, Maharashtra State, India.

METHOD

The parameters of Authentication and Preformulation are carried out by pure drug Diclofenac for Maintaining their Quality and Standard.

AUTHENTICATION PARAMETERS[7-9]

Melting Point Method

Melting Point determination is one of the preformulation property in which the temperature at which it changes state from solid to liquid at atmospheric pressure. At the melting process the solid and liquid can exist equilibrium. The Melting point of diclofenac pure drug is determine by using two types of method one is Conventional method and another is Digital method.

Log P Value

Log p value is determined by using Partition Coefficient Phenomenon. In which The 1 gm of drug is added in separating funnel containing equal portion of 25 ml of Octanol and 25 ml of Water. The separating funnel is shake 20–25 min. and stabilized the mixture. After stabilizing the mixture to remove water phase from separating funnel and filter it. Take Absorbance of Filtrate and calculate the log p value.

Solubility Studies

The Term Solubility is defined as maximum amount of solute that can be dissolved in a given amount of solvent to form a homogenous system at specified temperature and Specific Pressure to from Saturated Solution.

Procedure

- To Prepare a different solutions Water, PH 1.2 Acidic Buffer, PH 6.8 Phosphate Buffer, PH 7.4 Phosphate Buffer.
- The drug material is added in to above solutions till Supersaturated Solution is from.
- The Mixture can Placed in Orbital Shaker for 24 hrs. After 24 hrs. Filter the mixture Take Filtrate and Give Absorbance.
- To detect the Concentration of Drug is Soluble in Different Solutions.

Calibration Curve of Diclofenac

Calibration Curve is determined by using UV Spectrophotometric methods. In which 10 mg drug is added in 100 ml of water (100 µg/ml Solution). To Prepared different Dilutions (0, 2, 4, 6, 8, 10, 12) of above solution (100 µg/ml Solution). Take Absorbance in respective λmax 275 nm.

PREFORMULATION STUDIES[10-12]

Drug-Excipient Compatibility Studies

Drug is an active part of dosages form and it is mainly responsible for therapeutic value and Excipient substances which are included along with drugs being formulated in a dosage form so as to impart specific qualities to them. It is important for determination of Stability of the dosage and its helps to avoid the surprise problems by performing DECS we can know the possible reaction before formulating final dosage form. It's also used for development of new drug delivery system as well as investigation of new drug Product.

Procedure

The Equal portion of Drug and Excipient (1:1 ratio) is added in Ampules and the Ampules are placed in Stability Chamber for one Weak, After One Weak the Drug Excipient Compatibility Study is

Determine by using TLC (Thin Layer Chromatography) and IR (Infrared Spectroscopy).

METHOD OF PREPARATION OR METHOD OF FORMULATION[13]

The diclofenac sustained release tablet is prepared by Wet Granulation Process. The formulation ingredients of tablet is given in Table No.1.The Required Quantities of Preparation of Diclofenac Tablet is HPMC K100M and ethyl cellulose are mixed thoroughly in dry Mortar and Pestle By using a Geometric Dilution Technique. After mixing the ingredients to add solvent Isopropyl alcohol to from dough mass. The Prepared wet mass is pressed through mesh no 12 to obtained wet granules. The obtained wet granules are dried at 20 - 40˚c Temperature. The dried Granules are passed through mesh no. 16 and Aggregates are break. At last The Lubricants such as Talc and Magnesium Stearate were passed through mesh no. 60. After Preparation of dry Granules are packed in Dry and clean Polyethylene bag. The Prepared Granules of Tablet is compressed on the 9-Staton Tablet Punching Machine. Having a Hardness 9 - 11 Kg/cm2.

EVALUTION PARAMETERS[14-16]

Bulk density

It is a ratio of Bulk mass and Bulk Volume is known as Bulk Density. Amount of Powder is Weighed Separately and transferred into 100 ml of measuring cylinder, initial volume of Powder Material is measured and calculated bulk density according to following formula.

Bulk density=Mass / Volume

Tapped Density

It is a Ratio of Bulk Mass and Tapped Volume is known as Tapped Density. Tapped density is Important Evaluation Parameter is determined by placing a graduated cylinder containing a known mass of powder Undergoes Tapping in Manually (100 Tapes) as well As Using a Mechanical apparatus under powder bed volume has reached a minimum volume. The Tapped Density is calculated by following Formula.

Tapped density =Weight of Powder/ tapped volume of Powder

Compressibility Index or Carr's Index

The Calculation of Compressibility index is based on the Tapped density and Bulk density. It is a ratio of Tapped density and Bulk Density i.e. Compressibility Index. The Following formula for determination of Compressibility Index.

$$CI = \frac{(TD-BD)}{TD} \times 100$$

Where,

TD = Tapped density

BD =Bulk density.

Carr's Index is less than or equal to <10 indicates free flowing properties and Carr's Index is greater than >10 indicates poor flowing Properties.

Angle of Repose

It defines as the Pile surface of Powder is known as Angle of Repose. In this method of determination of angle of repose in which the angle of repose is to pour the powder a conical on a level, flat surface and measure the included angle. The Following Formula for determination of angle of repose.

$$\theta = Tan^{-1} (h/r)$$

Where,

θ = Angle of repose,

h = Height of the powder cone,

r =Radius of the powder cone.

The Angle of repose is less than or equal to 40° indicates free flowing properties. The angle of repose is greater than 40° indicates poor flow of material.

Hardness or Crushing strength

Hardness of Tablet is determined by using Conventional Hardness Tester and Digital Hardness Tester. The Standard range of the hardness of Sustained release tablet is 10 -20 kg.

Friability Test

The friability of 20 tablets was determined Using Friability Tester. 20 tablets from each formulation were weighed and tested at a speed of 25 rpm for 4 min. After removing of dusts, tablets were re-weighed and friability percentage was calculated using the following Formula.

$$\text{Friability index} = \frac{I - F}{I} \times 100$$

Where,

I - Initial weight

F - Final weight

Weight variation test

Weight variation was carried out to ensure that, each of tablets contains the proper amount of drug. The test was carried out by weighing the 20 tablets individually using analytical balance, then calculating the average weight, and comparing the individual tablet weights to the average. The percentage of weight variation is calculated by using the following formula.

Weight variation =[X*/ X] × 100

X = Actual weight of the tablet

X =Average weight of the tablet

In vitro drug release studies

It is a Process in which Solid Material Dissolved in Liquid Medium per Unit Time Period. It is mainly based on Sink Condition. Dissolution of Sustained Release Tablet is determined by Paddle Type of Dissolution Apparatus. The tablet was added into cylindrical vessel containing 900 ml PH 1.2 Acidic media having 75 rpm for next two hours and tem. 37±0.5˚C. Dissolution media was changes tablet was added in to PH 6.8 Phosphate buffer for next one hour for 10, 20, 30, 40, 50, 60 min of interval. After every 10 min 5 ml sample was Withdrawn and appropriate quantity of sample take absorbance by using U.V. spectroscopy technique and determine rate of dissolution of tablet.

RESULTS AND DISSCUSION

AUTHENTICATION PARAMETERS

Melting Point Method

The Melting Point of Diclofenac is determined by Conventional and Digital Method and Melting Point of Diclofenac is Reported in Table No.2.

Log P Value

Log P Value is determined by Partition Coefficient Phenomenon and Log P Value of Diclofenac is reported in Table No.2.

Solubility Studies

The Solubility of Diclofenac in Given Solution. (Water, PH 1.2 Acidic Buffer, PH 6.8 Phosphate Buffer, PH 7.4 Phosphate Buffer) is Reported in Table No.3.

Calibration Curve of Diclofenac in water

The Calibration Curve of Diclofenac is determined by using U.V. Spectroscopic Method. In which the Absorbance of Diclofenac in Different Concentration (0, 2, 4, 6, 8, 10, and 12) is reported in Table No.4. And The Calibration Curve is shown in Figure No.1.

PREFORMULATION STUDIES

The Drug and Excipient Compatibility studies determined by TLC (Thin Layer Chromatography) and IR (Infrared Spectroscopy) Method In which The TLC of Drug, Drug and Excipient before Stability Chamber and After Stability Chamber is reported in Table No.5. And the IR of Drug, Drug and Excipient Spectra is taken. The IR Spectra of Diclofenac is shown in Figure No.2. The Drug and Excipient such as Diclofenac and HPMC K100M is Shown in Figure No.3. Diclofenac and Ethyl Cellulose is Shown in Figure No.4. Diclofenac and Talc is Shown in Figure No.5. Diclofenac and Magnesium Stearate is Shown in Figure No.6.

EVALUTION PARAMETERS

Bulk density

It is important parameter for determination of Flow characteristic in which the Bulk Density of Diclofenac is reported in Table No.6.

Tapped Density

It is important parameter for determination of Flow characteristic in which the Tapped Density of Diclofenac is reported in Table No.6.

Compressibility Index or Carr's Index

The compressibility index is determined on the basis of Tapped density and bulk density and it is important for determination of flow characteristic in which the Compressibility Index or Carr's Index of Diclofenac is reported in Table No.6.

Angle of Repose

It is important flow property for determination of flow of material and the value associated in angle of repose is less than 40° is indicate good flow property in which angle of repose of Diclofenac tablet is reported in Table No.6.

Hardness or Crushing strength

The hardness is determined by using a conventional or digital hardness tester in which the hardness of Diclofenac tablet is reported in Table No.6.

Friability Test

The Friability of Tablet is always less than 1% and the Friability of Diclofenac is reported in Table No.6.

Weight variation test

All 20 Sustained released tablet is passed the weight variation test as per pharmacopoeial limits. The weights of all 20 tablets are uniform and the weight variation of diclofenac is reported in Table No.6

***In vitro* drug release studies**

The *In vitro* drug release studies of Sustained released tablet is determined in PH 6.8 Buffer, the absorbance of diclofenac in PH 6.8 Buffer is reported in Table No.7., Calibration curve of Diclofenac in PH 6.8 Buffer shown in Figure No.7. The absorbance of concentration of diclofenac soluble in dissolution medium in different time of interval and % CDR of diclofenac is reported in Table No.8. And the *in vitro* drug released of diclofenac is shown in Figure No.8.

Table No.1: Formulation of different batches of Diclofenac Tablets

S.No	Ingredient (mg / tablet)	Formulation Batch (F_1)	Formulation Batch (F_2)	Formulation Batch (F_{op})
1	Diclofenac Sodium	100	100	100
2	HPMC K 100 M	4.0	50	50
3	Ethyl Cellulose	1.2	4.3	5.49
4	Talc	2.0	2.2	2.26
5	Magnesium Stearate	2.0	2.2	2.24
	Total weight (mg)	109	158	160

Table No.2: Melting point and Log P Value

S.No	Parameters	Result	Std.
1	**Melting Point (˚c)**	283 – 285˚c	284 -285˚c
2	**Log p Value**	4.49	4.51

Table No.3: Solubility Studies

S.No	Medium	Concentration of drug Soluble (mg /ml)
1	Water	1.36
2	PH 1.2 Acidic Buffer	2.96
3	PH 6.8 Phosphate Buffer	3.69
4	PH 7.4 Phosphate Buffer	5.20
Result	**Class of drug**	**BCS Class II**

Table No.4: Calibration Curve of Diclofenac in Water

S.No	Concentration	Absorbance
1	0	0
2	2	0.087
3	4	0.161
4	6	0.238
5	8	0.298
6	10	0.388
7	12	0.481

Table No.5: The TLC of Drug, Drug and Excipient before Stability Chamber and After Stability Chamber

S.No	Samples (Pure From of Drug material) (Drug + Excipient Mixture)	Retention factor of drug Before the Stability Chamber	Retention factor of drug After the Stability Chamber
1	Pure Drug Diclofenac	0.76	0.80
2	Diclofenac + HPMC K 100 M	0.79	0.79
3	Diclofenac + Ethyl Cellulose	0.73	0.75
4	Diclofenac + Talc	0.71	0.73
5	Diclofenac + Magnesium Stearate	0.73	0.76

Table No.6: Evaluation Parameters

S.No	Parameters	Result (F_{op})	Conclusion (F_{op})
1	Bulk Density (gm/cm3)	0.68	Pass
2	Tapped Density (gm/cm3)	0.71	Pass
3	Angle of Repose (θ)	24.12	Pass
4	Carr's Index (%)	1.58	Pass
5	Hardness Test (kg/cm)	9.1	Pass
6	Friability Test (%)	0.8	Pass
7	% of Weight variation test	99.84	Pass

Table No.7: The absorbance of diclofenac in PH 6.8 Buffer (*In vitro* drug release studies)

S.No	Concentration	Absorbance
1	0	0
2	2	0.183
3	4	0.332
4	6	0.497
5	8	0.643
6	10	0.793
7	12	0.964

Table No.8: % CDR of diclofenac (*Invitro* drug release studies)

S.No	Time	Abs	Con^c µg/ml	DF	Con^c µg/ml	Con^c mg/ml	Con^c mg/5ml	Con^c mg/900ml	CDR	%CDR
1	0	0	0	0	0	0	0	0	0	0
2	30	0.028	0.18	10	1.83	0.0018	0.009	1.65	1.65	9.705882
3	60	0.03	0.2	10	2.08	0.002	0.01	1.87	1.88	11.05882
4	90	0.032	0.23	10	2.34	0.0023	0.011	2.1	2.11	12.41176
5	120	0.033	0.24	10	2.46	0.0024	0.012	2.22	2.23	13.11765
6	130	0.052	0.48	10	4.87	0.0048	0.024	4.38	4.39	25.82353
7	140	0.069	0.7	10	7.02	0.007	0.035	6.32	6.34	37.29412
8	150	0.075	0.77	10	7.78	0.0077	0.038	7	7.04	41.41176
9	160	0.089	0.95	10	9.55	0.0095	0.047	8.6	8.64	50.82353
10	170	0.123	1.38	10	13.86	0.013	0.069	12.47	12.52	73.64706
11	180	0.135	1.53	10	15.37	0.015	0.076	13.84	13.91	81.82353
12	190	0.148	1.7	10	17.02	0.017	0.085	15.32	15.39	90.52941

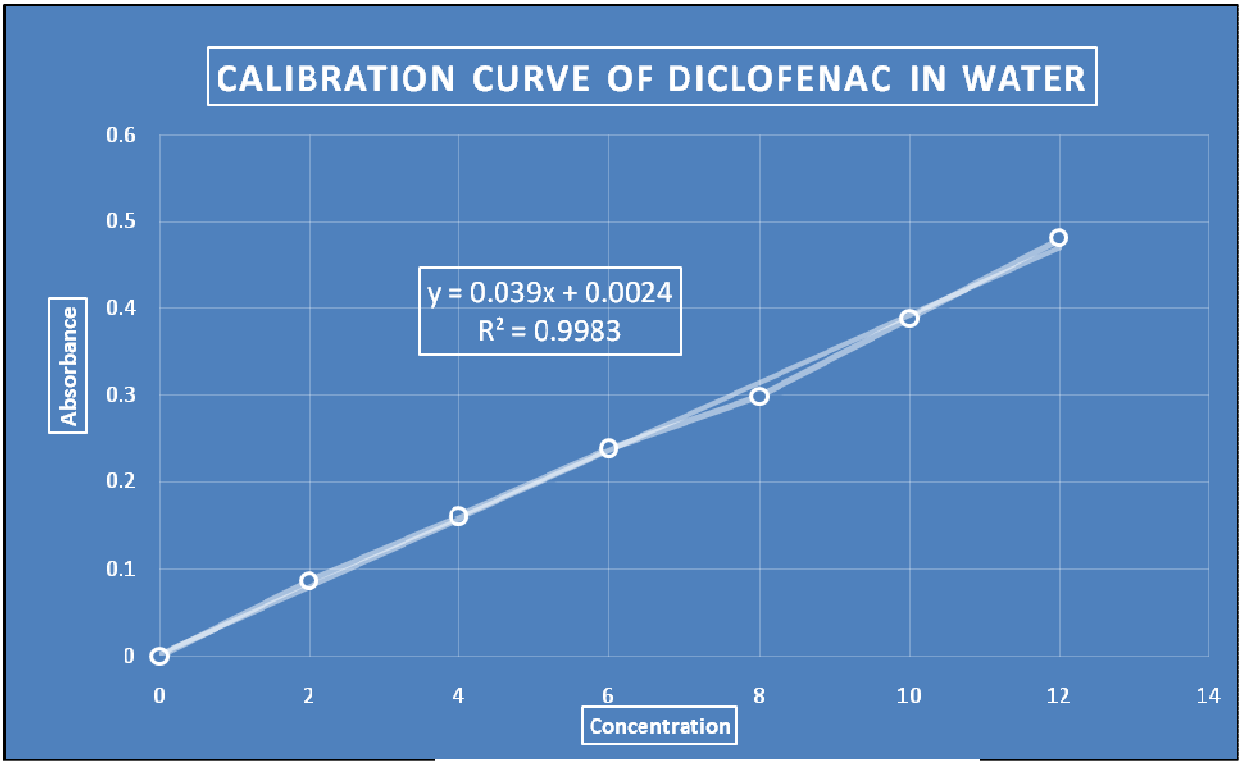

Figure No.1: Calibration Curve of Diclofenac in water

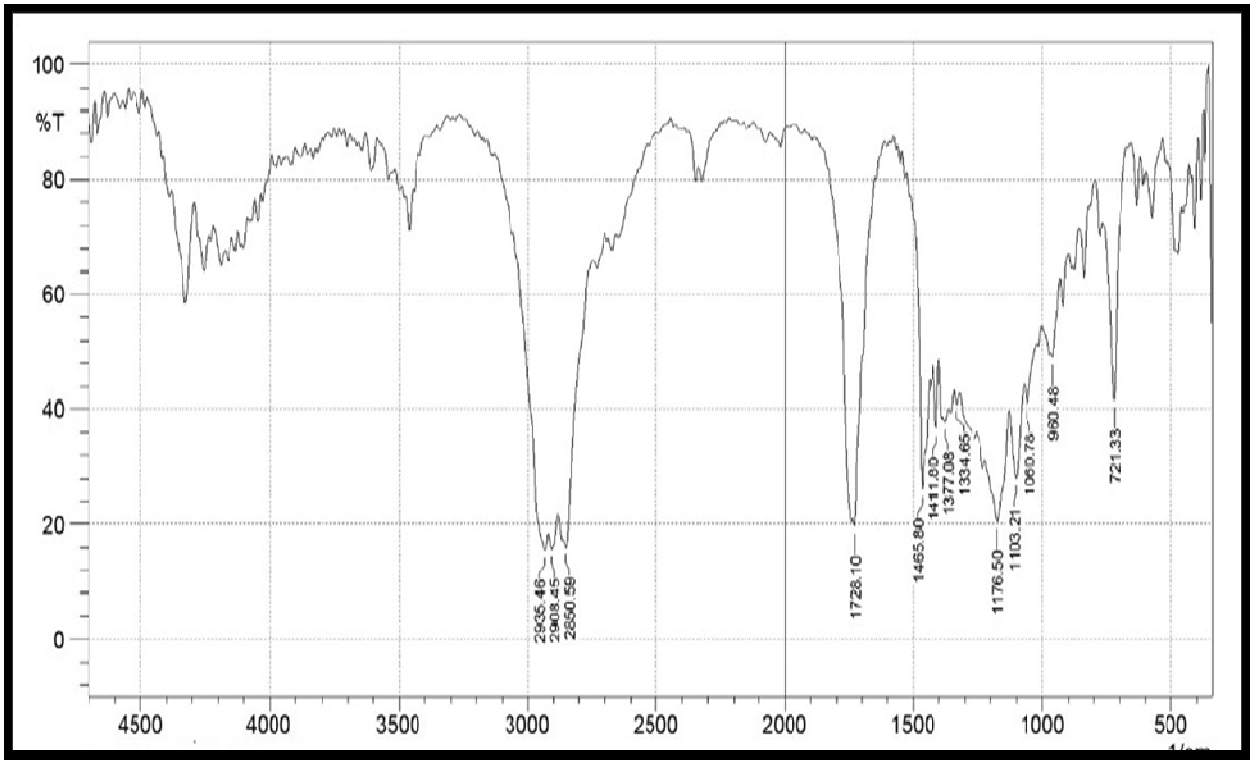

Figure No.2: The IR Spectra of Diclofenac

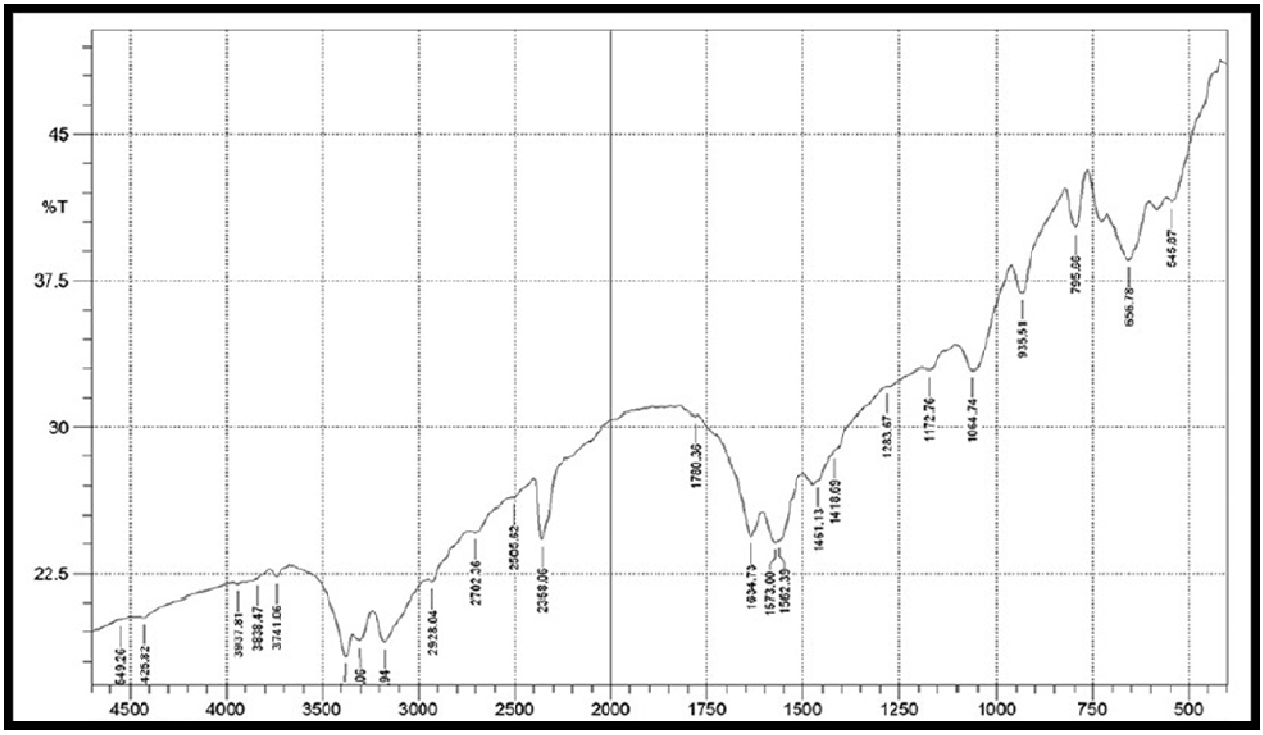

Figure No.3: Diclofenac and HPMC K100 M

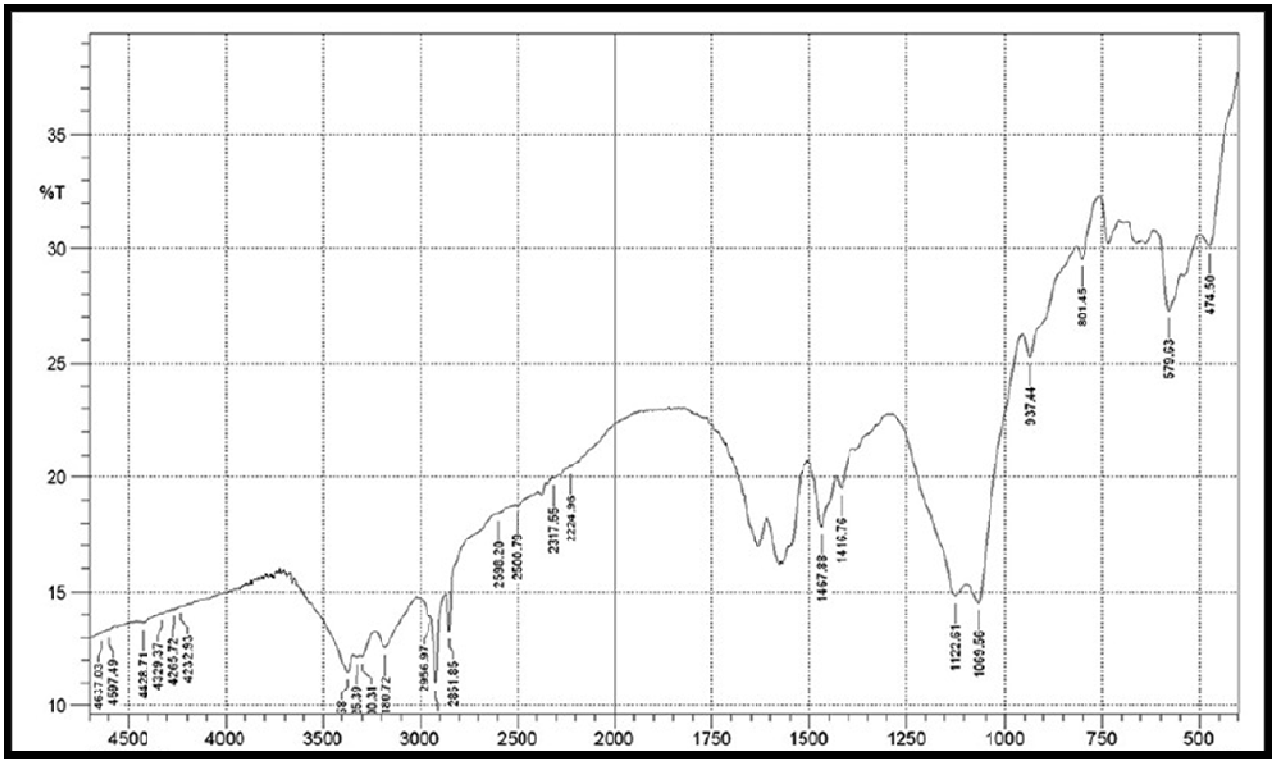

Figure No.4: Diclofenac and Ethyl Cellulose

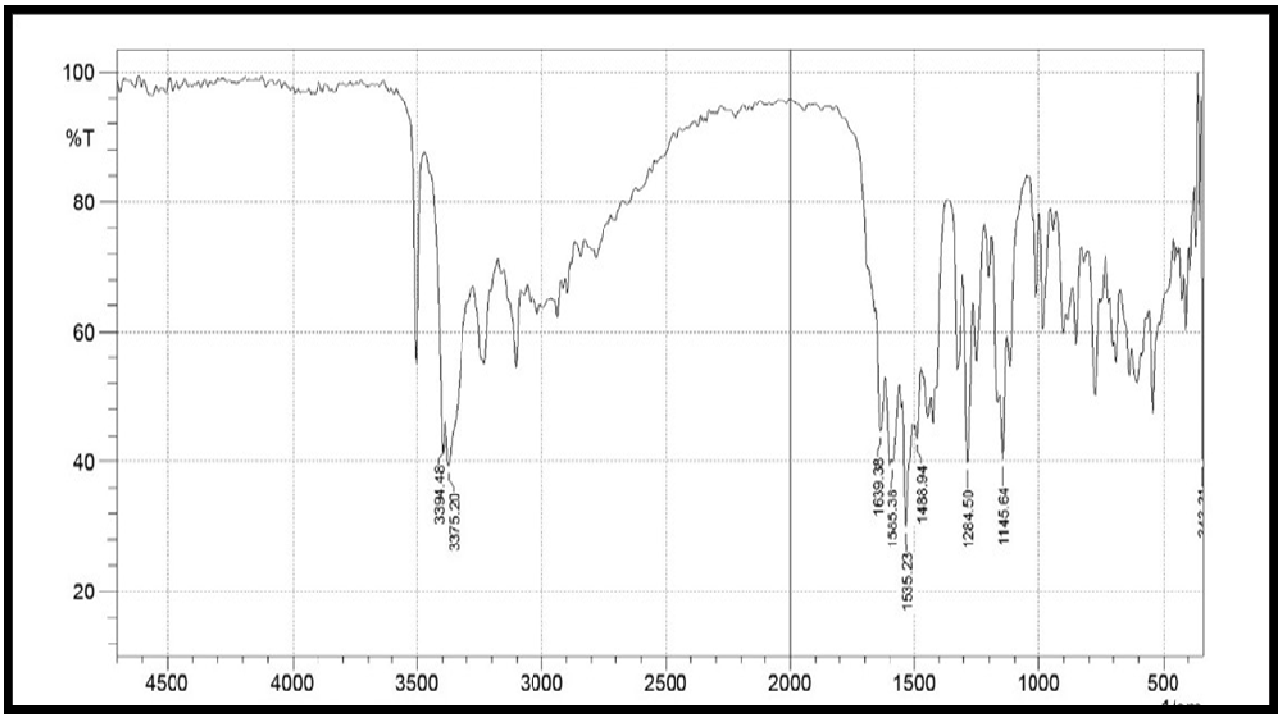

Figure No.5: Diclofenac and Talc

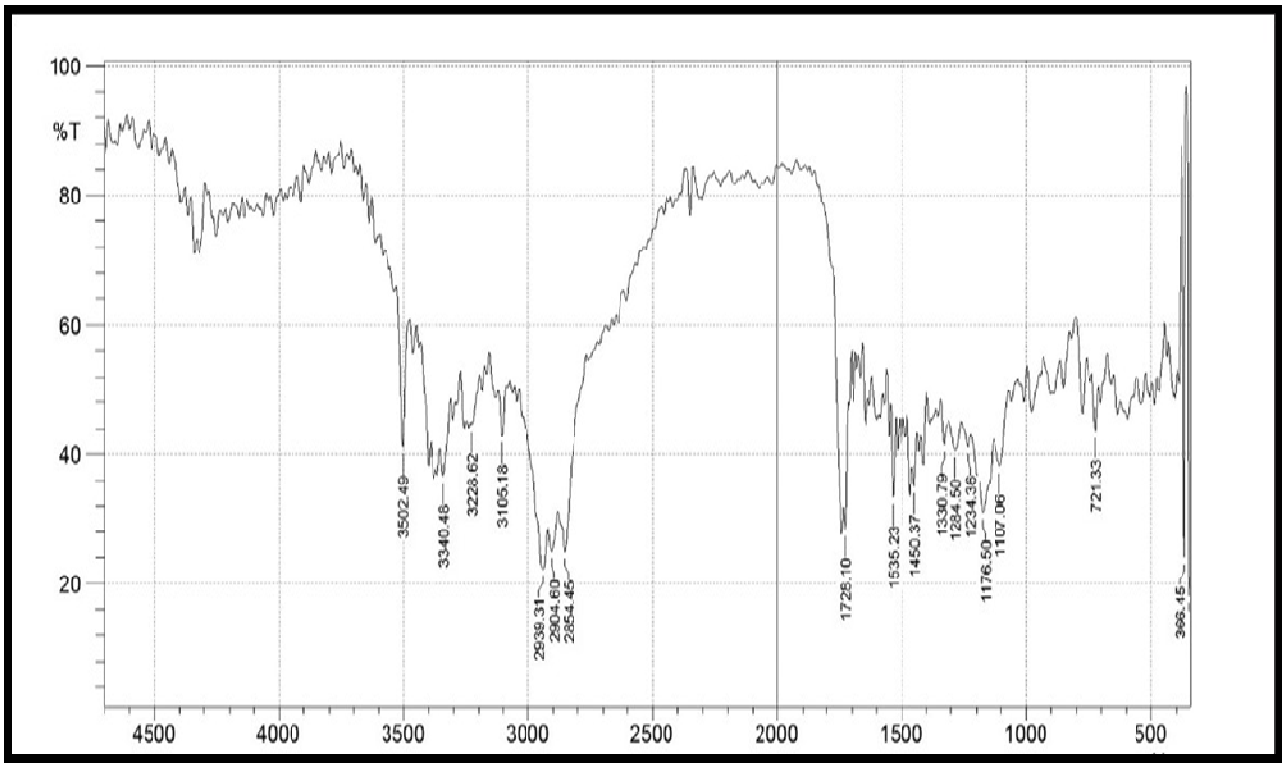

Figure No.6: Diclofenac and Magnesium Stearate

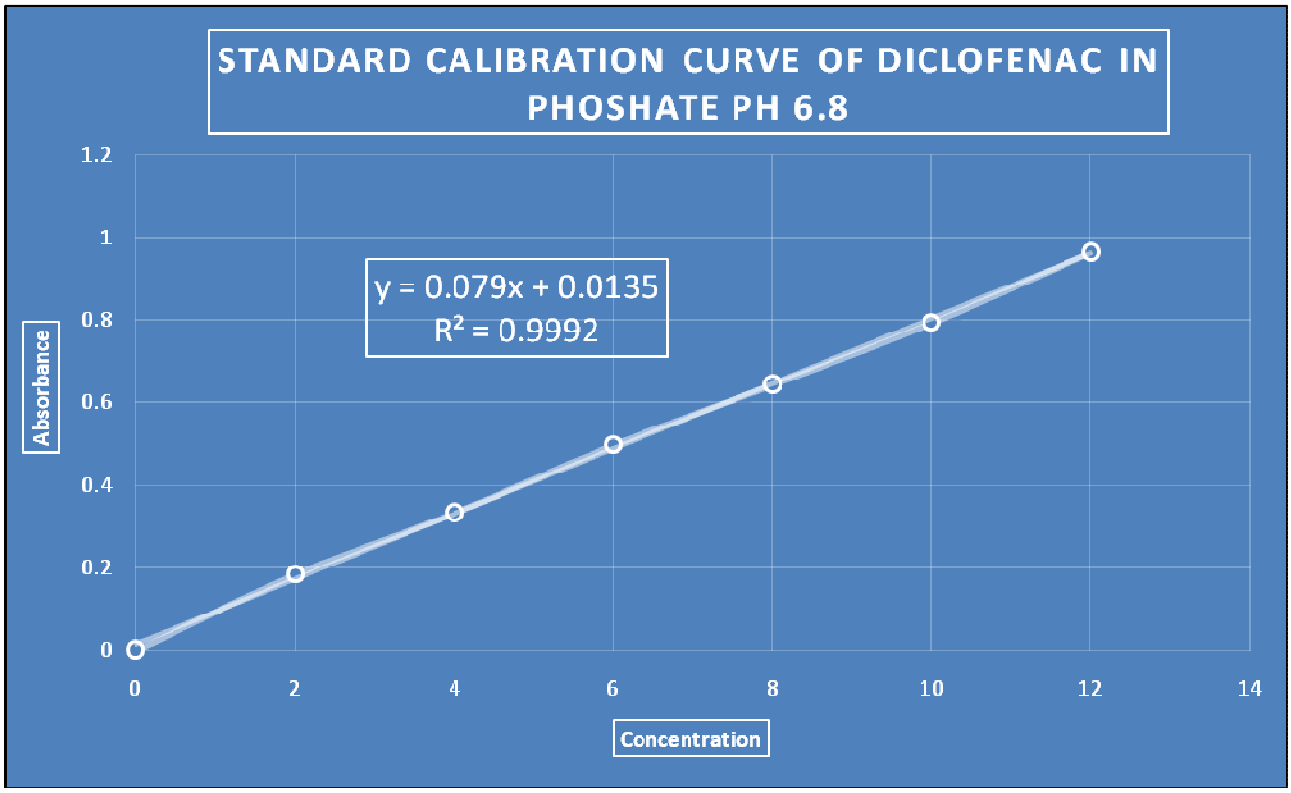

Figure No.7: Calibration curve of Diclofenac in PH 6.8 Buffer

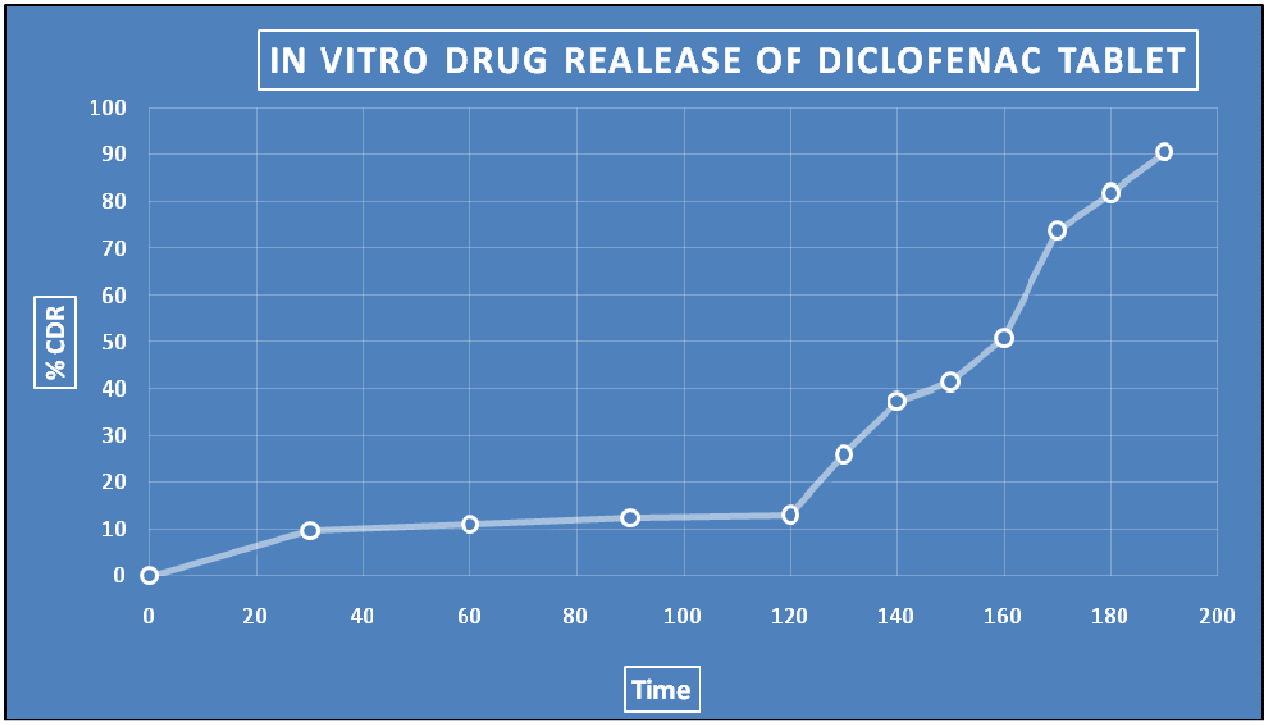

Figure No.8: *In vitro* drug released of diclofenac

CONCLUSION

Diclofenac Sustained release Tablet is made by Wet Granulation Method by employing a HPMC K 100 M is responsible for the slow release of drug and spared over longer period of time up to 12 hrs. The release is mainly depended on the composition of tablet Formulation Material. The result associated in Optimized batch is good to Satisfactory and having a good free flowing property. The hardness, weight variation, and friability these values are within the pharmacopeia limit. The *in vitro* Dissolution studies show Maximum percentage of release of drug. The sustained released formulation of Diclofenac is helpful to overcome the problem associated in patient compliance as well as efficiency of dosage form in eliciting desired therapeutic response related problems associated with the conventional dosage forms. Cost effectiveness and once-daily dose are the plus points along with other benefits. Hence, The Formulation of sustained-release tablet dosage forms for drug therapy.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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