International Journal of Clinical and Experimental Medicine Research, 2022, 6(3), 222-231
https: //www.hillpublisher.com/journals/ijcemr/
ISSN Online: 2575-7970
ISSN Print: 2575-7989

Formulation and Evaluation of Orodispersible Tablets of Etoricoxib Using Hibiscus Rosa Sinesis Muscillage as Natural Super Disintegrant

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How to cite this paper: Sandeep Patel, Komal Tikariya, Jayanti Mukherjee. (2022) Formulation and Evaluation of Orodispersible Tablets of Etoricoxib Using Hibiscus Rosa Sinesis Muscillage as Natural Super Disintegrant. *International Journal of Clinical and Experimental Medicine Research*, 6(3), 222-231.
DOI: 10.26855/ijcemr.2022.07.002

Received: March 28, 2022
Accepted: April 25, 2022
Published: May 13, 2022

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Abstract

The aim of the study is to formulate orodispersible tablet of Etoricoxib for the pain management of rheumatoid arthritis and to improve the efficacy and patient compliance. In the present work, orodispersible tablets of Etoricoxib were prepared by direct compression method using Hibiscus rosasinesis leaves mucilage as natural super disintegrant with a view to enhance patient compliance and to avoid hepatic first pass metabolism and to improve its bioavailability. The prepared batches of tablets were evaluated for hardness, friability, drug content uniformity, wetting time, water-absorption ratio and in-vitro dispersion time. Addition of Drug: β-cyclodextrin inclusion complex leads to improve the dissolution characteristics and solubility of drug at optimum concentration (1:5). It was found that the formulation F5 was found to be optimized formulation from the data obtained. It is observed from the formulation F5 which shown disintegration time 30±1.25 sec. and percentage cumulative drug release shown 95.84±2.08 within 30 minute. The best formulations F5 was analyzed for short-term stability studies on the promising formulation indicated that there are no significant changes in drug content and in vitro dispersion time. The formulation was found to be stable.

Keywords

Orodispersible tablets, Etoricoxib, Natural super disintergrant, Rheumatoid arthritis, Inclusion complex, In-vitro drug release

1. Introduction

Etoricoxib is also known as Arcoxia. Belonging to the Nonsteroidal anti-inflammatory (cox 2 inhibitor) drug group. It is used for relieving moderate pain and swelling of joints associated with different forms of gout and arthritis. It belongs to class II under BCS and exhibit low and variable oral bioavailability due to its poor aqueous solubility0.00328 mg/ml. Hence, it is necessary to increase the solubility of drug in order to improve to increase bioavailability to show effective pharmacological action. The drug is having poor aqueous solubility 3.28e-03 g/l. Etoricoxib is an efficacious drug in the management of arthritis and pain. But the major drawback is its poor aqueous solubility. Etoricoxib specifically binds and inhibits the enzyme cyclooxygenase-2 (COX-2), resulting in inhibition of the conversion of arachidonic acid into prostaglandins. Inhibition of COX-2 may induce apoptosis and inhibit tumors cell proliferation and angiogenesis. Hence, it is used as nonsteroidal anti-inflammatory drug (NSAID) with antipyretic, analgesic, and potential antineoplastic properties [1].

Difficulty in swallowing (dysphagia) is a common problem of all age groups, especially the elderly and pedia-

trics, because of physiological changes associated with those groups. Other categories that experience problems in using conventional oral dosage forms include the mentally ill, uncooperative and patients suffering from nausea, motion sickness, sudden episodes of allergic attack or coughing. Sometimes it may be difficult to swallow conventional products due to non-availability of water. These problems led to the development of a novel type of solid oral dosage form called orodispersible tablets, which disintegrate/dissolve rapidly in saliva without the need of drinking water [1].

Solid dispersion of etoricoxib is used for oro dispersible tablet which can increase the solubility and bioavailability of drug. The oro dispersible tablet dissolves in oral cavity and avoid the first pass metabolism which is the main reason of low bioavailability. Improves the patient compliance. Instead of synthetic super disintegrant, the tablet will be prepared using natural super disintegrant Hibiscus Rosa Sinensis leaves mucilage which will provide rapid disintegration.

The main aim of current research is to formulate and evaluate the orodispersible tablet of Etoricoxib using hibiscus rosa sinensis leaves mucilage as natural superdisintegrant.

2. Methods

2.1. Materials

Etoricoxibwas received as a gift sample from Glenmark (Pithampur). Beta-cyclodextrin was received as a Gift sample from Alkem (Pithampur).Mannitol, Silica gel-G, Microcrystaline Cellulose, Magnesium Stearate and talc From Lobachem Pvt. Ltd (Mumbai). All other solvent and reagent are used was of analytical grade.

2.2. Experiementals

1) Extraction of Hibiscus Rosa-Senesis Leaves Mucilage:

Hibiscus rosa sinensis (China rose) was procured from the local area of Indore, India. Collected leaves was carefully washed and dried under shade for 24 h and then further dried in an oven at 30-40°C. Size was reduced with the help of grinder. Powdered leaves were passed through sieve no. #22 and then used for further evaluation.

2) Identification of Drug

By UV Spectroscopy

Identification of the drug, Etoricoxib was done by UV Spectrophotometric method using Shimadzu Spectrophotometer UV-1800 (Shimadzu Corp. Japan). About 100mg of drug was weighed and was dissolved in 100ml of phosphate buffer 7.4 pH (1000 µg/ml). 10ml of this solution was withdrawn and volume was made up to 100ml. Appropriate dilutions were made with phosphate buffer 7.4 to give concentration of 10 µg/ml, scanned in UV range from 200-400nm, which could be utilized for analysis and spectrum was recorded [2]. The UV spectra of etoricoxib drug are shown in Figure 2.

By melting point determination

Melting point determination of drug was performed using melting point apparatus (BTI-34) Melting point apparatus, Mumbai, India). In this method small amount of drug was filled in capillary tube open from both ends and it was placed along with thermometer in melting point apparatus. The temperature in the heating stand is ramped at user programmable fixed rate until the sample in the tube transition into the liquid state [2]. Melting point of drug sample was recorded in Table 3.

Preparation of standard Calibration curve of Etoricoxib

Standard stock solution of Etoricoxib was prepared by dissolving 100 mg of drug in 100 ml of phosphate buffer 7.4 (1000 µg/ml) from the above stock solution 10 ml was taken and diluted to 100 ml in phosphate buffer 7.4 (100 µg/ml). From the above solution 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, 5.0 ml was taken and diluted upto 10 ml with phosphate buffer 7.4 to get series of 5-50 µg/ml solutions in concentration. Absorbance was noted using UV-VIS Spectrophotometer at 233 nm against blank (phosphate buffer 7.4) [3]. The calibration curves of etoricoxib are shown in Figure 5.

Solubility studies of drug

Solubility of Etoricoxib was determined in distilled water and various non aqueous solvents like PEG 400, methanol, ethanol, HCl, chloroform, phosphate buffer 7.4. Qualitative solubility analysis was determined in distilled water and various non-aqueous solvents like phosphate buffer 7.4, methanol, ethanol, Hcl and chloroform. Ten mg of drug was dissolved in 10 ml of solvent taken in conical flask. For the determination of solute dissolved in each solvent. The solvents were shaken at 25^{o}C for 24 hrs. After shaking, the samples were examined for the presence of any dissolved, suspended particles and clarity [4]. Results are disclosed in Table 6.

2.3. Formulation and Optimization of Orodispersible Tablet of Etoricoxib by Using Natural Super Disintegrant

Experimental Design for Optimization

A two factor three level factorial design (3^2) was used for the formulation optimization of orodispersible tablet of Etoricoxib and experimental trials are performed at all 9 possible formulation. In which the amount of β-cyclodextrin (X_1) and Hibiscus Rosa- Senesis mucilage (X_2) were selected as independent variables(factor) varied at three different level: low(-1), medium(0), and high(+1) levels. The drug release and disintegration time used as dependent variables (response) [5].

Formulation Development Orodispersible Tablet

Table 1. Composition of Orodispersible tablet

S.No	Name ofingredients	F1 (mg)	F2 (mg)	F3 (mg)	F4 (mg)	F5 (mg)	F6 (mg)	F7 (mg)	F8 (mg)	F9 (mg)
1.	Drug(Etoricoxib)	10	10	10	10	10	10	10	10	10
2.	β-cyclodextrin	30	30	30	40	40	40	50	50	50
3.	HibiscusRosa-SenesisMucilage	4	6	8	10	12	14	16	18	20
4.	Microcrystallinecellulose	120	120	120	120	120	120	120	120	120
5.	Mannitol	40	40	40	40	40	40	40	40	40
6.	Peppermint oil	2	2	2	2	2	2	2	2	2
7.	MagnesiumStearate	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5
8.	Talc	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5	4.5

Preparation of Inclusion Complex By Kneading Method: 10mg of Etoricoxib with β-CD in different ratios (1:3, 1:4, 1:5). β-cyclodextrin and drug were taken in mortar-pestle and triturated. The trituration was continued for one hour and passed the complex through sieve no.#60.

Preparation of Orodispersible Tablet By Direct Compression: Orodispersible tablet of Etoricoxib were prepared by direct compression method. Weighed all the ingredients accurately according to Table 4. All the ingredients were mixed step by step with drug- β-cyclodextrin inclusion complex and trituration was continued for 15 minute. Then passed through sieve no. #60. Subsequently talc,magnesiumstearate mixed atlast & again mixed. The powder was compressed using multi station tablet punching machine (AidmachPvt.Ltd.) with 8 mm flat punch, B-tooling and corresponding dies.

2.4. Evaluationorodispersibletablet of Etoricoxib

Pre Compression Parameter of Orodispersible Tablet:

Bulk characterizations were estimated by Bulk density, Tapped density, Carr's index, and Hausner'sratio. The flow property was determined by Angle of repose. These properties were determined by using the following equations:

Bulk Density = Mass (g)/ bulk volume

Tapped density= Mass (g)/tapped volume

Carr's index= Tapped density- bulk density/ tapped density X 100

Hausner's ratio= tapped density/ bulk density

Angle of repose= Tan0=h/r.

The bulk characterization and flow properties were recorded in Table 12.

Evaluation of Inclusion Complex:

Solubility Determination: An excess amount of prepared Etoricoxib-β-cyclodextrin inclusion complex at different concentration (1:3, 1:4, 1:5) were separately dissolved in 5ml phosphate buffer pH 7.4 in vials and sealed properly and stirred continuously. The process was repeated until saturation solubility of inclusion complex. The solution was kept for 24hours at room temperature. Then solution was filtered. The adequately diluted with phosphate buffer pH7.4.Then solution was analyzed by using UV-visible spectrophotometer at 233 nm.

Post Compression Parameter of Orodispersible Tablet:

- **Appearance:** The tablets were visually observed for capping, chipping, and lamination.
- **Dimension (thickness and diameter):** The thickness and diameter of tablets were important for uniformity of tablet size. The thickness and diameter of the tablets was determined using a vernier caliper. Ten tablets from each type of formulation were used and average values were calculated
- **Weight variation:** For weight variation, 20 tablets of each type of formulation were weighed individually on an electronic balance, average weight was calculated and individual tablet weight was then compared with the average value to find out the deviation in weight.

Table 2. Specifications of %Weight variation allowed in tablets as per IP

S.No.	AverageWeight	%difference allowed
1	80mg or less	±10 %
2	80 mg to250mg	±7.5%
3	More than 250 mg	±5 %

- **Hardness:** For each type of formulation, the hardness value of 10 tablets was determined using Monsanto hardness tester.
- **Percentage friability:** Friability is the measure of tablet strength. This test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. A sample of pre-weighed tablets was placed in Roche friabilator which was then operated for 100 revolutions. The tablets were then deducted and reweighed [6]. A loss of less than 1 % in weight is generally considered acceptable. Percent friability (% F) was calculated as follows.

$$\%F = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} 100$$

- **Disintegration time:** The test is carried out on the 3 tablets using the apparatus specified in USP distilled water at 37 ^{0}C ± 2 ^{0}C was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds [7].
- **Drug content:** Ten tablets were taken and amount of drug present in each formulation of tablet was determined. The tablet was crushed in a mortar-pestle and equivalent to10mg of drug was dissolved in phosphate buffer pH 7.4 in a 100ml volumetric flask. Volume was made up to 100ml. The sample was filtered through filter paper. From this solution 1ml were taken in a 10 ml volumetric flask & diluted with phosphate buffer pH 7.4. Further, 1ml were taken were taken and diluted up to 10ml and analyzed for drug content by UV spectrophotometer at 233 nm using phosphate buffer and drug content calculated accordingly [8]. The drug content of various formulations is recorded in Table 10.
- **Wetting time and water absorption ratio:** A piece of tissue paper folded twice was placed in a small petridish containing 10ml of water. A tablet was put on the tissue paper and the time required for the water to diffuse from the wetted absorbent paper throughout the entire tablet was then recorded using a stopwatch [8].
- **For water absorption ratio:** The wetted tablets were the reweighed. The water absorption ratio and R was determined using following equation

  R=Wa-Wb/Wb×100

where,

Wa = Weight of the tablet after water absorption

Wb=Weight of the tablet before water absorption [9].

- **In vitro Drug release study:** In vitro drug release study was determined by dissolution test apparatus. Maintained the water level in the water bath up to the specific mark and adjusted or maintained temperature from heater knob. 900 ml of phosphate buffer pH 7.4was poured in dissolution vessel and adjusted temperature between 37±0.5°C. The shaft was positioned in such a way that its axis is within 2 mm of axis of the vessel and lower edge of blade was 23-27 mm from the inside of bottom of vessel. The paddles were lowered down. The tablet was put in each vessel and paddle was rotated at 50 rpm for 30 min. Withdrawn 5 ml sample at every 5 minutes interval and replaced by equal volume of fresh dissolution medium [10]. Filtered the samples using what man's filter paper and analyzed for drug release of the samples by UV-visible spectrophotometer at λ max

233 nm using phosphate buffer pH 7.4 as blank.

- **Stability study:** In present study the selected formulation F5 exposure up to 1 months stability studies at accelerated condition (40^0 C ± 2^0 C at 75% RH ± 5% RH) to find out the effect of aging on hardness, drug content and *in vitro* drug release. Stability studies were carried out at accelerated condition (40^0C±2^0Cat75% RH ± 5% RH) for the optimized formulation F9. The matrix tablets were stored at 40^0C±2^0Cat75%RH±5%RH for accelerated temperature in closely packed with aluminum foil for 3 months [11]. The samples were withdrawn after periods of 1st month. The samples were analyzed for its physical appearance and Rf value.

3. Result and Discussion

3.1. Identification of drug

The peak of Etoricoxib was obtained at 233nm. Which shows that drug is pure as given in the refrence. The UV spectrum of etoricoxib drug is shown in the Figure 1.

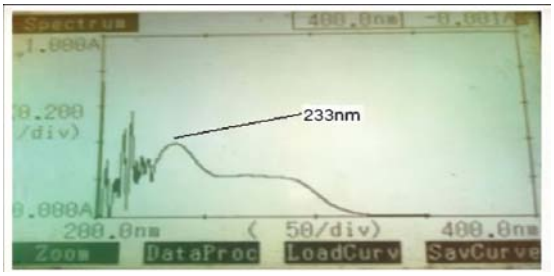

Figure 1. Spectrum of Etoricoxib by UV Spectroscopy.

Melting point:

The melting point of drug sample was determined by using melting point apparatus. As given in the reference. The melting point of etoricoxib is shown in Table 3.

Table 3. Melting Point of Etoricoxib

Drug	Observed	Refrence
Etoricoxib	138^0C	134^0-138^0C

Preparation of standard Calibration curve of Etoricoxib in Phosphate buffer pH 7.4 (λmax 233nm)

Calibration curve of Etoricoxib was prepared in phosphate buffer pH 7.4 at 233 nm. The absorbance values (mean of three determinations) with their standard deviation at different concentration in the range of 0.5-5 µg/ml for phosphate buffer pH 7.4 are tabulated. The drug obeys Beer's Lambert law in the concentration range. Linear regression analysis for all calibration curves of Etoricoxib is given in Table. So, this equation was used for the calculation of the solubility of the drug in different solvent, drug content and drug release [12].

Table 4. Data of standard calibration curve of etoricoxib in phosphate buffer 7.4

S.No.	Concentration (µg/ml)	Absorbance (nm)
1.	0	0
2.	5	0.125
3.	10	0.22
4.	15	0.317
5.	20	0.419
6.	25	0.533
7.	30	0.635
8.	35	0.746
9.	40	0.826
10.	45	0.949
11.	50	1.036

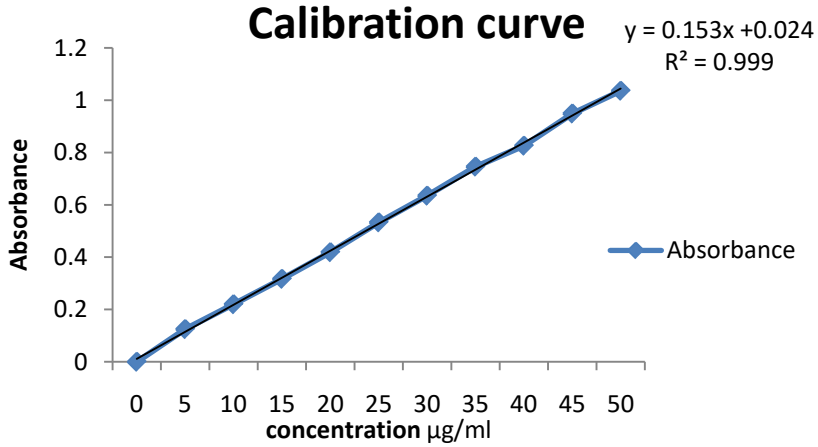

Figure 2. Calibration curve of etoricoxib in Phosphate buffer 7.4.

Determination of solubility of etoricoxib in different solvents: solubility analysis for drug etoricoxib was determined in different solvents. Results are disclosed in Table 5.

Table 5. Solubility data of Etoricoxib in different mediums

S.NO.	Solvent	Solubility(mg/ml)	Inference
1	Water	0.033	Practically in soluble
2	Phosphate buffer pH 7.4	0.119	Slightly soluble
3	Methanol	0.127	Slightly soluble
4.	Hcl	0.095	Sparingly soluble
5	Chloroform	0.093	Sparingly soluble

3.2. Evaluation Parameters

3.2.1 Determination of solubility of inclusion complex

Solubility of inclusion complex in phosphate buffer was studied. Results are disclosed in Table 7.

Table 6. Solubility data of inclusion complex

S.No.	Phosphate buffer pH7.4	Solubility(mg/ml)	Inference
1	Puredrug	0.033	Practically Insoluble
2	Drug:β-CD (1:3)	0.121	Slightly Soluble
3	Drug:β-CD (1:4)	0.123	Slightly Soluble
4	Drug:β-CD(1:5)	0.127	Slightly Soluble

3.2.2 Evaluation of Pre-Compression Parameters of Powder

The bulk density, Tapped density, Hausner's ratio, Carr's index and angle of repose of all the formulations were performed. Results are shown in Table 7.

Table 7. Evaluation of Precompression Parameters of powder

Formulation	Bulkdensity(gm/ml)	Tappeddensity(gm/ml)	Carr'sindex (%)	Angle ofrepose (^{o})	Hausner'sratio
F1	0.314	0.358	14.645	25.446	1.170
F2	0.289	0.368	14.624	29.343	1.166
F3	0.286	0.385	16.323	27.616	1.176
F4	0.335	0.365	13.937	26.946	1.16
F5	0.317	0.383	15.240	25.59	1.176
F6	0.283	0.345	17.360	27.4	1.206
F7	0.334	0.402	15.414	26.74	1.166
F8	0.346	0.356	13.354	30.6	1.15
F9	0.399	0.330	9.787	26.633	1.103

3.2.3 Evaluation of Post-Compression Parameters of Orodispersible Tablets:

The orodispersible tablets of etoricoxib like weight variation, hardness, thickness, friability, disintegration time, drug content, wetting time and water absorption ratio. The results of the studies were shown in below table.

Table 8. Weight variation, Hardness, Thickness and Friability of Formulation (F1-F9)

Formulation	Weight variation (mg)	Hardness (Kg/cm^2)	Thickness (mm)	Friability (%)
F1	210.16	2.6	3.1	0.460
F2	211.75	2.4	3.1	0.750
F3	214	3.0	3.2	0.460
F4	223	2.9	3.3	0.672
F5	232	3.0	4.06	0.346
F6	233	3.0	3.4	0.343
F7	246.58	3.0	3.13	0.349
F8	247.83	3.1	3.26	0.361
F9	251.06	3.1	3.73	0.358

Table 9. Disintegration Time, Drug Content, Wetting time & water absorption Ratio Formulation F1-F9

Formulation	Disintegration Time (sec)	Drug Content (%)	Wetting time (sec)	Water absorption Ratio (%)
F1	42	91.833	32.7	55.97
F2	38	93.36	31.37	49.01
F3	37	95.84	30.05	42.18
F4	35	92.19	32.38	46.75
F5	30	99.25	29.71	30.3
F6	33	96.85	31.06	35.90
F7	45	95.76	33.38	36.83
F8	36	95.60	34.69	40.42
F9	39	93.73	35.06	41.96

3.2.4 In vitro drug release studies:

The in vitro drug release profile of all the formulations from F1 to F9 in dissolution medium are shown in figure (11, 12, and 13). Orodispersible tablets of Etoricoxib showed a significant increase in the drug release. In the formulations F1, F2 and F3 showing 90.9%, 86.2% and 89.55 drug release, F4, F5 and F6 showing 88.13%, 95.84% and 84.6% drug release of F7, F8 and F9 showing 86.76%, 92.34% and 93.72% drug release respectively. Formulation F5 shows the highest drug release 95.84% within 30 minutes.

Table 10. Percentage cumulative drug release data of F1 to F9formulation of orodispersible tablets

Time (in min)	%Cumulative drug Release								
	F1	F2	F3	F4	F5	F6	F7	F8	F9
0	0	0	0	0	0	0	0	0	0
5	11.4	16.9	21.84	28.83	27.44	30.24	21.15	23.94	21.84
10	21.4	25.3	37.2	34.2	35.1	39.99	28.83	34.44	21.84
15	34.41	40.0	46.29	44.21	46.98	44.87	41.14	43.51	33.71
20	44.2	53.9	57.45	50.51	56.07	55.34	53.24	56.76	47
25	58.14	67.9	63.72	67.92	73.14	62.24	75.59	72.83	68.61
30	90.9	86.0	89.55	88.13	84.66	84.66	86.76	92.34	93.72

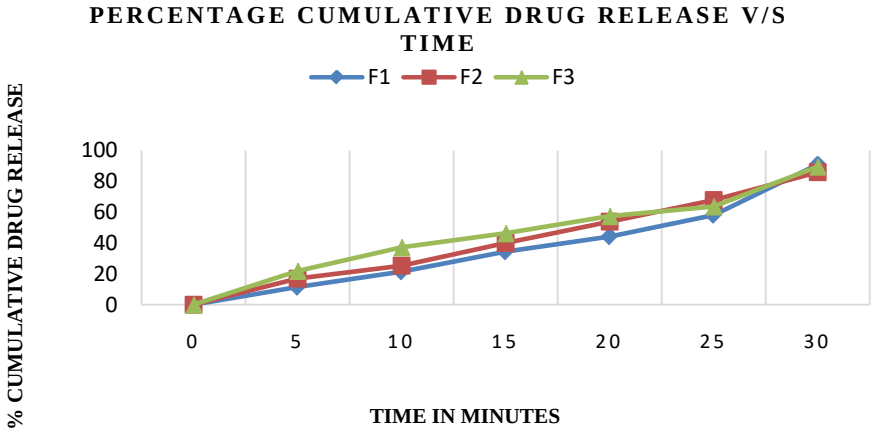

Figure 3. Cumulative drug release of formulation F1-F3.

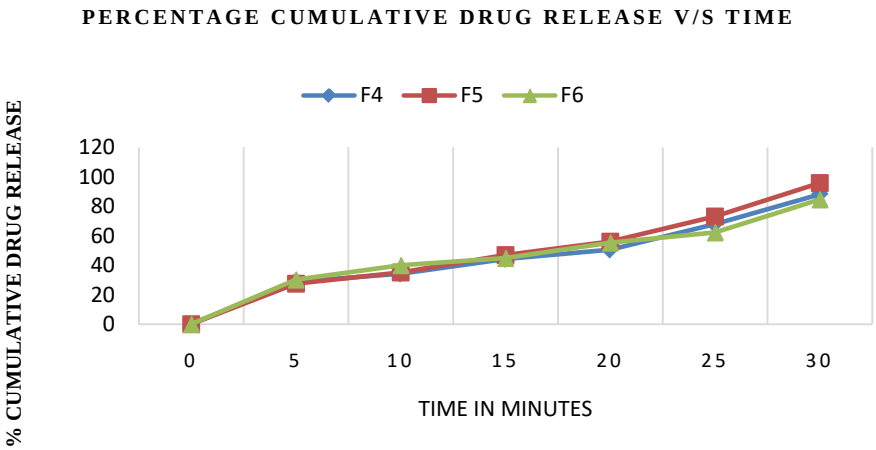

Figure 4. Cumulative drug release of formulation F4-F6.

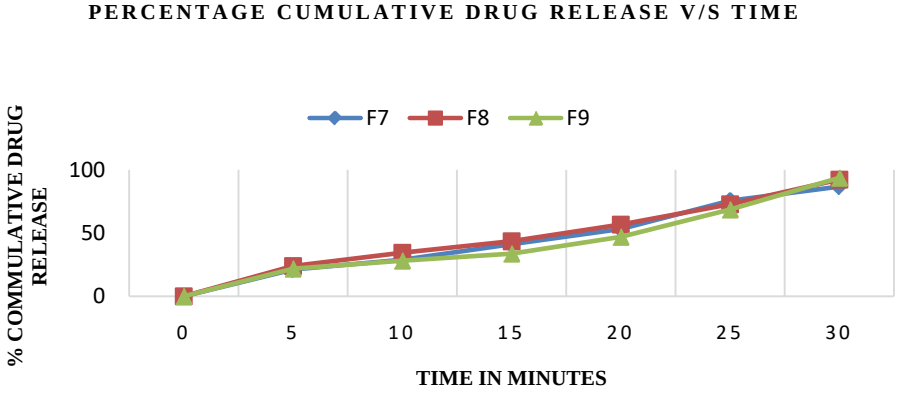

Figure 5. Cumulative drug release of formulation F7-F9.

3.2.5 Stability study:

Stability studies for two month were performed at different storage condition for optimized orodispersible tablet (F5).The optimized orodispersible tablet were found to be stable with no change in physical appearance and TLC values (Rf) were found similar at different storage condition at different time interval. It was concluded that the formulation is stable at different storage conditions.

Table 11. Stability data of optimized formulation (F5)

S.No	Time	Physical appearance	Result	Storage condition	Rf value
1	Initial Day	Off-white	No change in appearance	40°C±2°C/ 75%RH±5%RH	0.71
		Off-white	No change in appearance	Room temperature	0.70
2	1 month	Off-white	No change in appearance	40°C±2°C/ 75%RH±5%RH	0.73
		Off-white	No change in appearance	Room temperature	0.72

4. Conclusion

The study was conducted to formulate orodispersible tablet of Etoricoxib by direct compression method using hibiscus rosa sinensis leaves mucilage as natural super disintegrant by direct compression technique to enhance the bioavailability of drug and solubility be improved by preparing solid dispersion. This formulation was made to provide rapid onset of action and reduce dosing frequency. Orodispersible tablets of Etoricoxib showed a significant increase in the drug release. In the formulations F1, F2 and F3 showing 90.9%, 86.2% and 89.55 drug release, F4, F5 and F6 showing 88.13%, 95.84% and 84.6% drug release of F7, F8 and F9 showing 86.76%, 92.34% and 93.72% drug release respectively. Formulation F5 shows the highest drug release 95.84% within 30 minutes.

As the concentration of super disintegrant hibiscus rosa sinesis mucilage powder that significant effect on disintegration characteristics as well as drug release. But the higher concentration of mucilage had negative impact on drug release & disintegration time.

Addition of Drug: β-cyclodextrin inclusion complex leads to improve the dissolution characteristics and solubility of drug at optimum concentration (1:5). So, considering the above results it was found that the formulation F5 was found to be optimized formulation from the data obtained. It is observed from the formulation F5 which shown disintegration time 30±1.25 sec. and percentage cumulative drug release shown 95.84±2.08 within 30 minute.

The best formulations F5 was analyzed for stability testing. The formulations were found to be stable.

Acknowledgements

The author is thankful to the management of Shri Bherulal pharmacy institute, Indore. For providing necessary facilities to carry out the research work and heartily thankful to my guide Dr. Jayanti Mukherjee and my Co-Guide Ms. Komal Tikariya for providing all the support and encouragement to carry out this studies.

References

[1] SunidhiMahant, ShivaliSingla, Sachin Goyal, Bhimi Kumari. (2017). Abhishek Soni Formulation and Evaluation of Mouth Dissolving Tablets of Ondansetron Hydrochloride Using Plantago ovata (Isapghula) Mucilage as Natural Super Disintegrating Agent. International Journal of Pharmaceutical Sciences and Drug Research, 2017, 9(5): 240-246.

[2] RajniBala, ReechaMadaan, Vibhu, Aneesh, and Dr. Sandeep Arora. Isolation and Evaluation of Hibiscus Rosa- Sinensis Leaf Mucilage as Superdisintegrant. European Journal of Pharmaceutical And Medical Research ejpmr, 2016, 3(8), 434-440.

[3] https://en.m.wikipedia.org/wiki/Etoricoxib.

[4] https://pubchem.ncbi.nlm.nih.gov/compound/Etoricoxib#sectionComputed Properties.

[5] https://www.medicineindia.org/pharmacology-for-generic/208/etoricoxib.

[6] K. Srinivasarav. (2017). An Overview on Preformulation for Pharmaceutical Product Development and Drug Excipient Incompatibility Studies. International Journal of Pharma and Chemical Research. I Volume 3 I Issue 2 I Apr-Jun I 2017(5.1.A).

[7] Shivani Kala and Divya Juyal. (2016). Preformulation and characterization studies of aceclofenac active ingredient. The Pharma Innovation Journal, 2016; 5(9): 110-119 (5.1.B).

[8] B. P. Patel, J. K. Patel, G. C. Rajput, and R. S. Thakor. Formulation and Evaluation of Mouth Dissolving Tablets of Cinnarizine Indian Journal of Pharmaceutical Sciences July-August.

[9] Chowdaryk, P. R., K. Surya Prakasa Rao, and·Amar Ayireddy. Formulation and evaluation of etoricoxib solid dispersions employing starch phosphate, pvp and peg 4000 – a factorial study Asian journal of pharmaceutical and clinical research, vol. 4, suppl, 2, 2011 (5.1.D).

[10] Shivani Kala and Divya Juyal. Preformulation and characterization studies of aceclofenac active ingredient. The Pharma Innovation Journal, 2016, 5(9): 110-119.

[11] Gupta Ashish, Bhadoria Juhi, Darwhekar, G. N. (2019). Formulation and Evaluation of Orodispersible Tablet of Atorvastatin Calcium by Using Hibiscus rosasinesis Mucilage as Natural Superdisintegrant. Journal of Drug Delivery & Therapeutics, 2019,

9(6): 90-94.

[12] Shivani Kala and Divya Juyal. (2016). Preformulation and characterization studies of aceclofenac active ingredient. The Pharma Innovation Journal, 2016, 5(9): 110-119.

[13] K. Srinivasarav. (2017). An Overview on Preformulation for Pharmaceutical Product Development and Drug Excipient Incompatibility Studies. International Journal of Pharma And Chemical Research, I Volume 3 I Issue 2 I Apr-Jun I 2017(5.1.A).

[14] Shivani Kala and Divya Juyal. (2016). Preformulation and characterization studies of aceclofenac active ingredient. The Pharma Innovation Journal, 2016, 5(9): 110-119 (5.1.B).

[15] Liberman, H. A., Lachmann, L., and Shwartz, J. B. Pharmaceutical Dosage Forms: Tablets. Vol. 1, 2nd ed, Marcel Dekker Inc., USA; 285-327.

[16] Gupta Ashish, Bhadoria Juhi, Darwhekar, G. N. (2019). Formulation and Evaluation of Orodispersible Tablet of Atorvastatin Calcium by Using Hibiscus rosasinesis Mucilage as Natural Superdisintegrant. Journal of Drug Delivery & Therapeutics, 2019; 9(6): 90-94.