RESEARCH ARTICLE ON IMMEDIATE RELEASE TABLET

Design, Formulation, and *In-vitro* Evaluation of Immediate Release Tablet of Etoricoxib using Quality by Design Approach

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Abstract

The current research aimed to formulate and evaluate the immediate-release tablet of etoricoxib. Etoricoxib belongs to BCS class II drugs; hence the solubility was enhanced using different techniques, thus achieving the dissolution of the drug. The formulation with maximum solubility enhancement was selected as the final formulation for the preparation of immediate-release tablets. These tablets were prepared using the wet granulation technique. Sodium starch glycolate was used as a super disintegrant, microcrystalline cellulose was used as a binder, and sodium bicarbonate was used as effervescent material for the preparation of an immediate-release tablet. Different trial batches were prepared and the formulations were optimized using design expert software. The optimized formulation was prepared and evaluated for different post-compression parameters. The disintegration time was found to be 2 minutes 16 seconds and the percent cumulative drug release was found to be 90.30%. The pharmacokinetic behavior of the drug was studied and first-order kinetics was found to be the best-fit model for immediate-release tablets. The accelerated stability study for the immediate-release tablet was carried out at 40°C ± 75% RH and different parameters were evaluated and were found within specified limits. Thus immediate release tablets of etoricoxib were found to be a promising candidate for the treatment of acute pain or arthritis.

Keywords: Solubility, Optimization, Pharmacokinetic study, Super disintegrants, Stability study.

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INTRODUCTION

Gout or arthritis refers to a systematic autoimmune disease that causes chronic joint inflammation and bone destruction. [1,2] It is one of the most common arthritides which is commonly caused by hyperuricemia. Hyperuricemia is a consequence of renal under-excretion of uric acid which refers to too much accumulation of uric acid in the blood and thus in joints, which leads to the formation of sharp crystals. It is associated with circadian events of the body. Attack of gout mostly occurs in the night hours.[3] These changes are associated with circadian events of the body and sleep.[4] Etoricoxib 5-Chloro-6-methyl-3-[4-(methylsulfonyl)phenyl]-2,3-bispyridine is the drug mainly used for the treatment of gout or arthritis. Etoricoxib effectively inhibits isoform 2 of enzyme cyclooxygenase i.e. COX 2.[5] It has approximately 106-fold selectivity for COX 2 inhibition over COX 1. It diminishes prostaglandin and arachidonic acid generation. [5,6] Gout is arthritis with a very high level of uric acid in the blood; thus, in joints, it leads to the formation of very sharp crystals. It commonly occurs in the big toe and its symptoms generally appear in the middle of the night or early morning as at this time there is very sudden and severe pain in joints. [6] There is a risk among patients with low purine intake 24 hours before the attack. When breaking down purine body produces uric acid. The present invention relates to the formulation and development of a bilayer tablet with an immediate-release etoricoxib tablet. The tablet of the present invention features a balance between a conventional tablet and an immediate-release tablet of etoricoxib which provides a significantly more uniform, efficient delivery of both the antigout drugs as compared to other marketed formulations currently available. This dosage form may be used in the same indication as an individual tablet of Etoricoxib now in clinical use. However, it is especially useful where it is desirable to provide immediate relief in pain and arthritis with the

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administration of a single dose with immediate effect.

MATERIAL AND METHODS

Etoricoxib was received as a gift sample from Medipol Pharmaceutical Pvt. Ltd. Baddi. Poloxomer 188, β-cyclodextrin, and aerosil have been purchased from Yarrow Chem Products. Magnesium stearate was purchased from Loba Chemie private limited. Sodium starch glycolate was purchased from signet Pharmaceuticals Pvt. Ltd.

Phase Solubility Study of Etoricoxib

Aqueous solutions were prepared in different ratios using solid dispersion physical mixture technique using polymer poloxomer 188 and polyvinylpyrrolidone K30 (PVP K30), a solid dispersion kneading technique using polymer poloxomer 188 and polyvinylpyrrolidone K30 (PVP K30), complexation physical mixture technique and complexation kneading technique using polymer beta-cyclodextrin, and co-crystallization technique using succinic acid as conformer and were spectrophotometrically assayed at different wavelengths. The equilibrium constant was determined according to the phase solubility diagram according to Higuchi and Connors in 1965. The maximum solubility was found to be that of solid dispersion physical mixture drug and poloxomer 188 (1:3) and was thus selected for the preparation of immediate release tablet. [7-9]

Drug and polymer compatibility study

Infrared Spectroscopy (IR) Study

The Fourier Transform Infrared Spectroscopy (FTIR) of the drug etoricoxib and physical mixture solid dispersion of drug and poloxomer 188 (1:3) was performed using an FTIR spectrophotometer. The sample pellet was the compound in an IR spectrophotometer and was scanned at the wavelength of 4000 to 400 cm-1 and the resolution was 4 cm-1.

Differential scanning calorimetry Study

DSC of drug and solid dispersion physical mixture was carried out using a differential scanning calorimeter and the scanning rate was found to be 10°C/minute at a 30 to 300°C temperature under the nitrogen flow of 40 mL per minute.

X-Ray diffraction Study

XRD study of pure drug etoricoxib and solid dispersion physical mixture drug and poloxomer 188 (1:3) was performed to study the crystalline or amorphous behavior of the drug under the CuKa targeted monochromatized radiation, the voltage of 30 kV and current mA at ambient temperature. The condition scanned mode was used for data collection as the step size of 0.01°C. The scanned range was found to be 30 to 300°C.

Preparation and optimization of an immediate-release tablet

A wet granulation technique prepared the immediate-release tablet for 60 mg of the drug etoricoxib. The medication and super disintegrant sodium starch glycolate were weighed and passed through sieve no. 120. The concentration of sodium starch glycolate were 5, 12.5, and 20 mg, respectively. Table 1 represents the formula composition.

Preliminary trial batches of immediate-release etoricoxib

Preliminary trial batches prepared by super disintegrant sodium starch glycolate in different concentration, effervescence agent (sodium bicarbonate), lactose

Table 1: Preliminary trial batches of immediate-release etoricoxib:

Ingredients	F1	F2	F3	F4	F5	F6	F7	F8	F9	F10	F11	F12	F13
Solid Dispersion (Etoricoxib and Poloxomer 188) Physical Mixture (1:3)	360	480	480	240	360	240	240	360	480	240	480	360	360
Microcrystalline Cellulose	14	14	14	14	14	14	14	14	14	14	14	14	14
Lactose Monohydrate	142	27	145	224.5	139.5	267	252	152	24.5	294.5	17	137	127
Sodium Starch Glycolate	5	5	12.5	12.5	12.5	5	20	5	12.5	12.5	20	20	20
Sodium Bicarbonate	20	15	20	20	15	15	15	10	10	10	15	10	20
Starch	4	4	4	4	4	4	4	4	4	4	4	4	4
Magnesium Stearate	3	3	3	3	3	3	3	3	3	3	3	3	3
Aerosil	2	2	2	2	2	2	2	2	2	2	2	2	2
Total Weight	550	550	550	550	550	550	550	550	550	550	550	550	550

monohydrate, and aerosil remains fixed and is shown in Table 1.

Table 2: Optimization of immediate release tablet using 3 factors 3 level box Behnken design:

Run	Concentration of Etoricoxib (mg)	concentration of Sodium starch glycolate (mg)	Concentration of sodium bicarbonate (mg)
1	90	5	20
2	120	5	15
3	120	12.5	20
4	60	12.5	20
5	90	12.5	15
6	60	5	15
7	60	20	15
8	90	5	10
9	120	12.5	10
10	60	12.5	10
11	120	20	15
12	90	20	10
13	90	20	20

Optimization of immediate release (IR) etoricoxib tablets using 3 factors 3 level Box Behnken Design

By means of three factors at three-level full factorial design entails 13 preparations that remain intended, as shown in Table 2.

Formulation of immediate-release tablet

A tablet containing 60 mg of etoricoxib was prepared using the wet granulation technique as represented in the formula in Table 1. Solid dispersion containing etoricoxib and poloxomer 188 (1:3) ratio, sodium starch glycolate, and lactose were passed through sieve no. 40#. Starch was added as a binder to the shifted powder. Granules were prepared by adding 1 to 2 drops of distilled water in shifted powder in a mortar pestle. Granules were dried in an oven at 20°Ctill a loss of drying of 1.5 to 2% is achieved. Dried granules were passed through a 20# sieve. Lubricants and glidants were added to the granules, passed through a 60# sieve, and punched using a single punch machine.

Post-compression Characterization of Parameters

Tablet Appearance was acknowledged through visual parameters that color, odor, and texture. Monsanto hardness tester was used to measure the hardness of the tablet. Five randomly selected inserts were tested for each formulation from the individual weight of their interest.[10] The thickness of the tablet was determined using Mitutoyo Digital Vernier Caliper. Friability was determined using the Roche friability tester. For 20 tablets were randomly selected, the average weight was determined, and then the tablets were individually weighed to collect the standard deviation.6 tablets were randomly chosen for the disintegration test. The disintegration test was carried out in simulated gastric fluid at 37 ± 0.5°Ctemperature, depriving the disc and thus expanding the disintegration apparatus. *In-vitro* dissolution,

Table 3 Solubility of Etoricoxib in methanol and distilled water taking methanol as cosolvent:

S.No	Solvent	Wavelength (λmax)	Solubility (10µg/mL)
1	Methanol	235	7.531

studies were performed using Lab India Type II dissolution apparatus using 1000 mL of 0.1N HCl as dissolution medium at 37 ± 0.5°C at 50 rpm rotation speediness for 30 minutes and analyzed on UV spectrophotometer on 234 nm wavelength, respectively.

Statistical Analysis of Responses

Design expert software version 11.0.6.1 (STATEASE) was used to draw the surface response plots and counter-plots.

Release kinetics

The results of the in vitro drug release evaluation were fitted by various kinetic estimations, including zero order, first order, Higuchi Matrix, and Pappas Model, to enable an understanding of the mechanism and kinetics of drug release. Drug release statistics are taken into consideration by the Pappas equation to define an example that will exemplify a good fit for the formulation. k is the kinetic constant, n is the diffusion exponent, and Mt/M is the percentage of the drug released at time t.[11]

Stability study

A stability study for immediate release (IR) tablets was conceded as per ICH guidelines at 40 ± 2°C/75 ± 5% RH by adopting a thrombolab TH 90S stability chamber for 3 months. The different parameters analyzed were hardness, friability, weight variation, and cumulative drug release. All the parameters were analyzed for 3 months after 15 days interval and were found within the limit.

RESULTS AND DISCUSSION

Phase Solubility Study

The solubility of the pure drug was determined in methanol and distilled water using methanol as cosolvent and is represented in Table 3.

Solubility Enhancement

Solubility enhancement of pure drug etoricoxib was carried out using different techniques such as solid dispersion, complexation, and co-crystallization technique, and the maximum solubility was found that of solid dispersion (drug and poloxomer 188) physical mixture in 1:3 drug-polymer ratio represented in Table 4 and thus selected as a final formulation for the preparation of immediate release tablet of etoricoxib.

Determination of absorption maxima (λ_{max})

The absorption maxima of the drug using UV was determined

Table 4: Results of solubility by solid dispersion physical mixture drug and poloxomer 188 (1:3)

S.No	Solubility Enhancement Technique	Brief Description	Drug Polymer Ratio	Wavelength (λ max)	R2 Value	Solubility (10 µg/mL)	Solubility (20 µg/mL)
1.	Solid Dispersion	Physical Mixture (Drug and Poloxomer (188)	1:3	234	0.980	37.8	44.33

Table 5: Micromeritic study of a blend of etoricoxib tablets:

Formulation Code	Bulk density (g/mL)	Tapped density (g/mL)	Carr's Index (%)	Hausner's Ratio	Angle of Repose
F1	0.53	0.56	5.33	1.05	23.6
F2	0.43	0.49	12.2	1.13	28.9
F3	0.63	0.68	7.35	1.007	24.22
F4	0.47	0.54	12.96	1.14	32.02
F5	0.59	0.62	5.58	1.05	18.02
F6	0.48	0.51	4.95	1.04	17.06
F7	0.551	0.558	6.29	1.15	18.2
F8	0.242	0.247	2.04	1.02	14.6
F9	0.39	0.43	1.72	1.10	19.3
F10	0.39	0.43	1.72	1.10	21.35
F11	0.63	0.68	7.35	1.07	28.4
F12	0.43	0.49	9.30	1.13	22.65
F13	0.36	0.42	14.2	1.16	23.8

by dissolving 20 µg/ mL of the drug in phosphate buffer pH 6.8 and further dilution was prepared using phosphate buffer

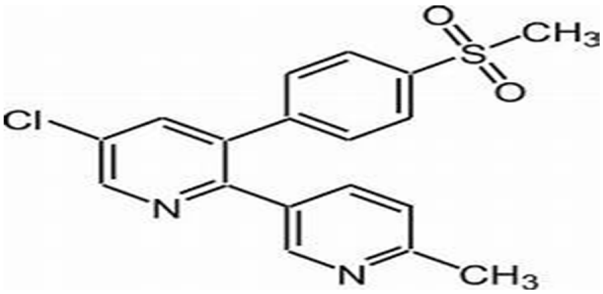

Figure 1: Chemical Structure of Etoricoxib

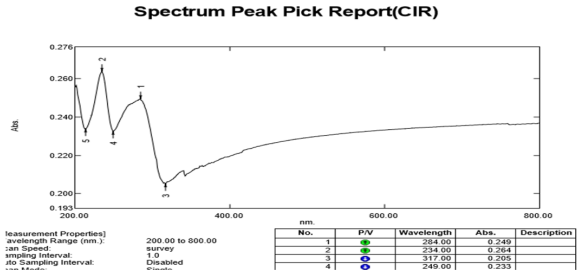

Figure 2: Determination of absorption maxima of solid dispersion physical mixture drug and poloxomer 188 (1:3)

as a solvent and is shown in Figures 2 and 3.

Drug and polymer compatibility study

FTIR study of the drug etoricoxib and solid dispersion physical mixture is shown in Figures 4a and 4b. In the FTIR of pure etoricoxib and poloxomer 188, no additional peaks were

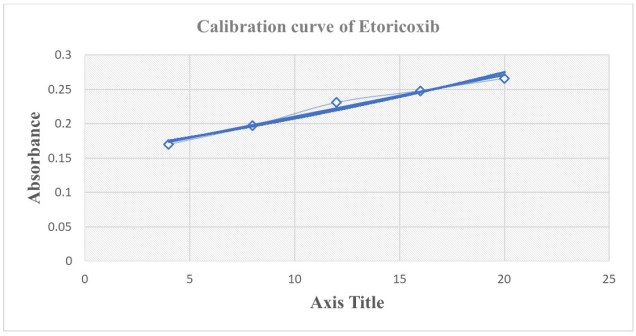

Figure 3: Calibration curve of solid dispersion physical mixture drug and poloxomer 188 (1:3)

observed compared to pure etoricoxib, indicating that they are compatible.

DSC of the drug etoricoxib and solid dispersion physical mixture drug and poloxomer 188 is represented in Figures 5a and 5b. DSC curve of the pure drug etoricoxib exhibits an endothermic peak at 139°Cwhich corresponds to the intrinsic melting point and represents the purity of the drug. The differential scanning calorimetry (DSC) of etoricoxib and poloxomer 188 is represented in Figure 5b. The DSC study of etoricoxib and poloxomer 188 reveals comparatively less melting point than a pure drug, indicating that the crystalline form has been converted into an amorphous form, indicating the solubility of pure drug etoricoxib has been enhanced.

XRD Study of pure drug etoricoxib and solid dispersion physical mixture drug and poloxomer 188

The XRD of the pure drug etoricoxib was performed to study

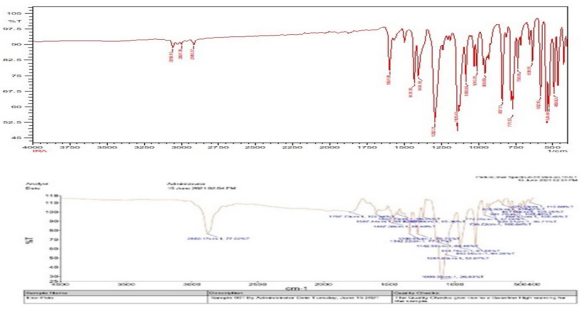

Figure 4: (A) FTIR spectra of pure drug etoricoxib (B) FTIR spectra of drug Etossricoxib and Poloxomer 188.

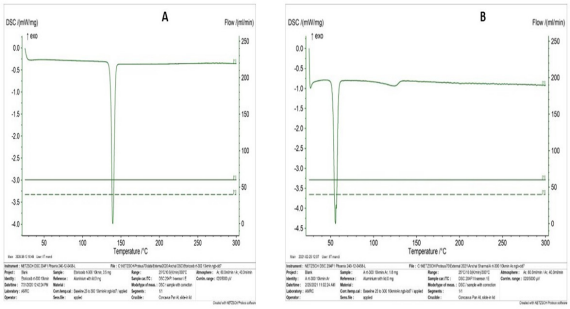

Figure 5: A) DSC of pure drug etoricoxib B) DSC of drug etoricoxib and poloxomer 188.

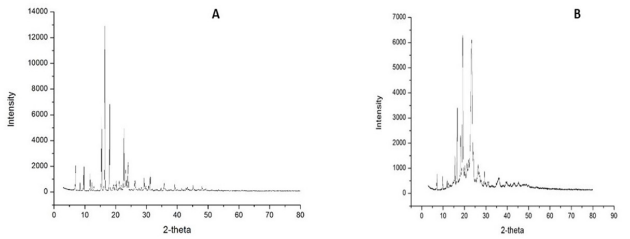

Figure 6 :(A) X-ray diffraction (XRD) study of pure drug etoricoxib (B) X-ray diffraction (XRD) study of solid dispersion physical mixture drug and poloxomer 188.

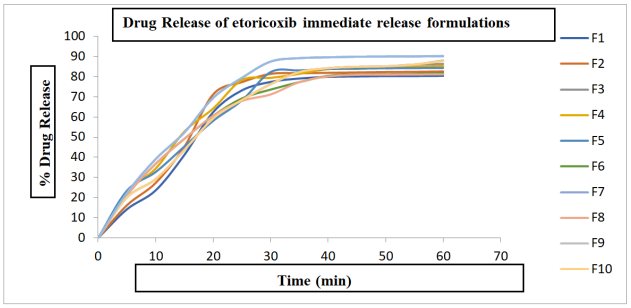

Figure 7: Percent (%) drug release of etoricoxib immediate release formulation

Table 7: Experimental result and predicted values of the response variable q+5% (Y1) and disintegration time (Y2)

Run	Y1			Y2		
	Actual value	Predicted value	% Error*	Actual value	Predicted value	% Error
1	80.40	81.22	-1.0096	2.32	1.98	17.17172
2	82.60	81.89	0.867017	2.40	2.33	3.004292
3	86.32	86.12	0.232234	1.49	1.63	-8.58896
4	85.30	85.52	-0.25725	1.48	1.57	-5.73248
5	84.35	86.19	-2.13482	1.56	1.93	-19.171
6	81.77	81.28	0.602854	2.19	2.28	-3.94737
7	90.13	90.48	-0.38683	1.45	1.52	-4.60526
8	81.14	81.95	-0.98841	2.54	2.64	-3.78788
9	88.11	86.85	1.450777	2.31	2.29	0.873362
10	87.71	86.25	1.692754	2.34	2.23	4.932735
11	90.30	91.09	-0.86727	1.48	1.58	-6.32911
12	90.14	91.15	-1.10806	2.12	1.88	12.76596
13	92.15	90.42	1.913294	1.38	1.22	13.11475

% Error = (Actual Value – Predicted Value) * 100/Predicted Value

Table 7: Post-compression characteristics of immediate release etoricoxib.

Formulation	Hardness (kg/cm2)	% Friability	Weight Variation (mg)	Disintegration Time (min)	Q+5%
F1	4.12	0.76	559	2.32	80.4
F2	4.02	0.84	556	2.4	82.6
F3	4.03	0.81	543	1.49	86.32
F4	4.07	0.78	552	1.48	85.3
F5	4.01	0.89	547	1.56	84.35
F6	4.12	0.82	563	2.19	81.77

F7	4.13	0.83	556	1.45	90.13
F8	4.15	0.85	553	2.54	81.14
F9	4.06	0.76	551	2.31	88.11
F10	4.07	0.77	542	2.34	87.71
F11	4.11	0.83	559	1.48	90.3
F12	4.09	0.81	539	2.12	90.14
F13	4.02	0.72	547	1.38	92.15

the crystalline nature of the drug etoricoxib. In the XRD, etoricoxib shows sharp peaks of diffractogram (2θ) were 12.13, 15.12, 16.18, 18.6, and 22.15° indicating the presence of highly crystalline. XRD study of solid dispersion of pure drug etoricoxib and poloxamer 188 reveals comparatively less number of peaks concerning pure drug which indicates that the crystalline form has been changed into amorphous form, thus the solubility of pure drug etoricoxib has been enhanced as represented in Figure 6 (A) and 6 (B).

Micromeritic study

The powder blend of each batch was studied for micrometric properties. The various properties were identified which are represented as bulk density, tapped density, compressibility index, Hausner's ratio, and angle of repose. Table 5 summarizes the observed value of precompression parameters of each batch as:

It was observed that F1, F3, F5, F6, F7, F8, F9, F10, F12 and F3 had excellent flow properties and F2 and F11 had very good flow properties. However, F4 had the highest value for the angle of repose and hence demonstrated fair flow properties. (Table 5)

Preparation and Evaluation of immediate-release etoricoxib tablets based on the runs obtained using design expert software

The various post-compression parameters of the immediate-release tablet as hardness, friability, weight variation, disintegration time, and cumulative drug release are summarized in Table 6 and a graphical representation of cumulative drug release is represented in Figure 7.

Response surface analysis of formulation characteristics

Response surface analysis of Q+5%

The factors affecting Q+5% were the concentration of etoricoxib (A), sodium starch glycolate (B), and sodium bicarbonate (C) (p=0.0008) as represented from the given equation 1:

Q+5% = 73.07 + 0.3025*A + 4.366*B + 0.366*C (r2 = 0.9255)1

The observed in Q+5% in the etoricoxib layer varied from 80.4 % to 92.15 % (maximum for 13 runs). The predicted value of Q+5% (Y1) acquired by the model using representing

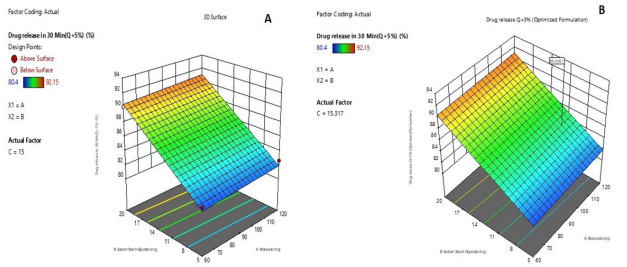

Figure 8: (A) Response surface graph showing the varying concentration of sodium starch glycolate and etoricoxib on drug release, (B) Response surface graph showing the varying concentration of sodium bicarbonate and etoricoxib on drug release.

equation was compared with values observed and low percent error concluded the designated model with good predictability. r2 ascertained good data fitting. Based on the value and sign of coefficient, it can be concluded that a positive effect was shown in all three factors on Q+5% as shown in figure 8 (a and b) that represented the response surface graph. The statistical analysis concerned in Table 7 represents the experimental results and predicted value of Q+5% and disintegration time

Response surface analysis of disintegration time

The factors affecting disintegration time were the concentration of Etoricoxib (A), sodium starch glycolate (B), and sodium bicarbonate (C) P = 0.00082 which is represented in equation 2.

ln(Disintegration Time) = 4.58 + 0.027*A – 0.377*B-0.33*C (R2 = 0.9255) 2

The disintegration time observed in the immediate release etoricoxib layer varied from 1.38 to 2.54 minutes. (minimum disintegration time of 1.38 min.) The observed and predicted disintegration time values obtained in the above equation were compared. A low %error of <5% represents that this model has good predictability. Based on the value and sign of coefficient, it may wind up that etoricoxib concentration had a negligibly small positive effect of ln (disintegration time), while the concentration of sodium starch glycolate and sodium bicarbonate had negative effects. However, the concentration of API (A) did not affect ln (disintegration time). The influence of variation in concentration of sodium starch

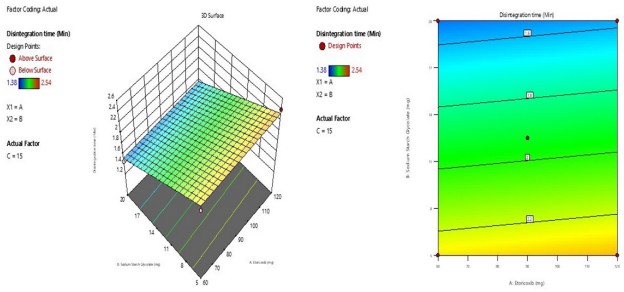

Figure 9: (A) Response surface graph showing the consequence of the concentration of etoricoxib and varying concentrations of sodium starch glycolate and sodium bicarbonate on disintegration time. (B) correlating response factor of formulation development of immediate release Etoricoxib on disintegration time.

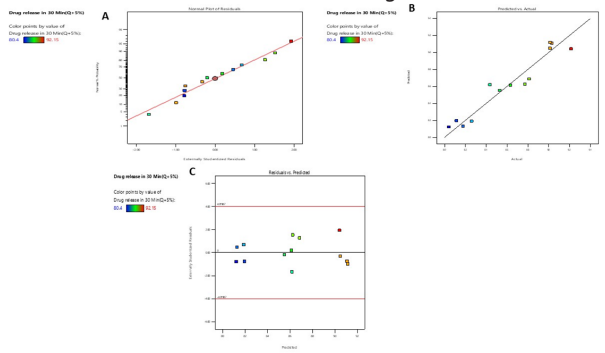

Figure 10: (A) Represent normal probability plot of extremely studentized residual (B) Predicted vs actual number plot (C) Represent externally studentized residual vs predicted values of drug release Q+5%

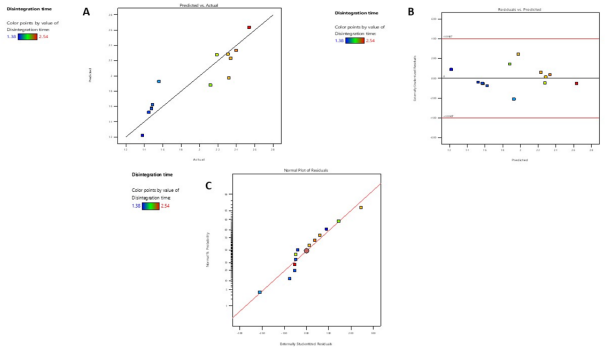

Figure 11: Diagnostic plot of disintegration time (A) predicted vs actual plot (B) studentized residual vs predicted values (C) normal probability plot of externally studentized residual of disintegration time

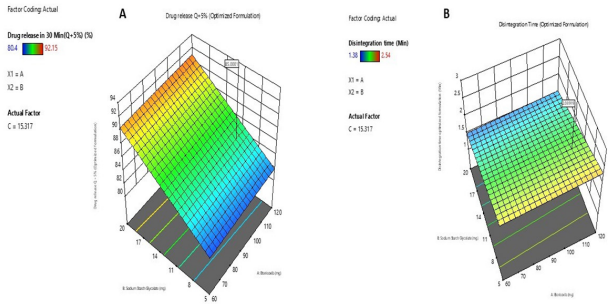

Figure 12: (a) Response surface graph showing (A) predicted value for Q+5% (B) predicted value for disintegration time

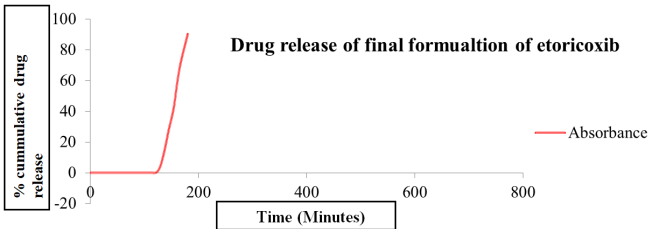

Figure 13: Percent cumulative drug release of optimized immediate-release etoricoxib tablet

glycolate (B) and sodium bicarbonate (C) on Y2 was examined while keeping the etoricoxib constant concentration, as represented in Figure 9.

Diagnostic analysis of formulation data of immediate-release etoricoxib

The diagnostic plots were used for the investigation of the proposed model of Goodness of fit. Figure 10 (a) represents a normal probability plot of extremely studentized residual, which represents that most of the colored paints representing values of Q+5% were placed around the normal probability line, thus assuring normality of residuals and relevant analysis for response data and thus suggested. Figure 10(b) predicted vs actual number plot to look for variables that might be influenced Q+5% where in close contact with the predicted values. Figure 10 (c) represents externally studentized residual vs predicted values, which revealed that the colored points of Q+5% lay within the set limits. The predicted vs actual plot which confirmed that the experimentally observed value of disintegration time was in close contact with predicted values. Figure 11 (b) represents externally studentized residual vs predicted values, which revealed that disintegration time values within the set limits were represented by colored points. 11 (c) Represents a normal probability plot of externally studentized residual, which indicates that relevant analysis of response data was suggested and proved using colored points of disintegration time which were present around the normal probability line.

The predicted vs actual plot which confirmed that the experimentally observed value of disintegration time was in close contact with predicted values. Figure 11 (b) represents externally studentized residual vs predicted values, which revealed that disintegration time values within the set limits were represented by colored points. 11 (c) Represents a normal probability plot of externally studentized residual, which indicates that relevant analysis of response data was suggested and proved using colored points

Table 8: Composition of optimized formulation

Factor	Name	Level	Low Level	High Level	Standard Deviation
A	Etoricoxib	111.2311	60	120	0
B	Sodium Starch Glycolate	10.25571	5	20	0
C	Sodium Bicarbonate	15.31702	10	20	0

Table 9: Point prediction of optimized formulation

Response	Predicted Mean	Predicted Median	Std Dev	SE Mean	95% PI low	Data Mean	95% PI high
Q+5%	85.5174	85.5174	1.247439	0.71325	83.90392	87.13089	78.9236
Disintegtration Time	1.570192	1.570192	0.214043	0.122384	1.293341	1.847044	0.438787

Table 10: Confirmation of observed value of optimized batch

Response	Mean	Median [*]	Std Dev	N	SE Pred	95% PI low	Data Mean	95% PI high
Drug release in 30 Min(Q+5%)	85.00014	85.00014	1.247439	2	1.006664	82.72291	85.685	87.27737
Disintegration time	2.039193	2.039193	0.214043	2	0.17273	1.648452	1.58	2.429935

Table 11: Accelerated stability study for immediate release tablet

S.No	Parameters	Results before stability study	Results after the stability study
1	Hardness	3.32	3.33
2	Friability	0.72	0.71
3	Weight Variation	3.2	3.1

ofdisintegration time which were present around the normal probability line.

Optimization and validation

Optimization and validation of formulated etoricoxib immediate release layer

To obtain the optimized formulation the desirability function was explored using design expert software, which was achieved using a set paradigm of maximum Q+5% and minimum disintegration time. Therefore, an additional Etoricoxib immediate release layer was prepared for validation composition and point prediction for optimized formulation (Tables 8 and 9) with desirability function and confirmation that experimental value lies within the limit has been represented.

After the optimization study, the predicted value for Q+5% was found to be 85.00014 and the predicted value for disintegration time was found to be 2.039193. The mean value obtained for Q+5% and disintegration time of the optimized immediate release Etoricoxib was found in desired limits. The layer was thus confirmed to be optimized. Further confirmation study was performed to confirm the results predicted by the software Table 10.

Preparation of immediate-release tablet of etoricoxib

The final formulation of the immediate-release tablet was prepared after confirming the results predicted by the software after the optimization study. The tablets were subjected to various quality control tests to ensure their integrity.

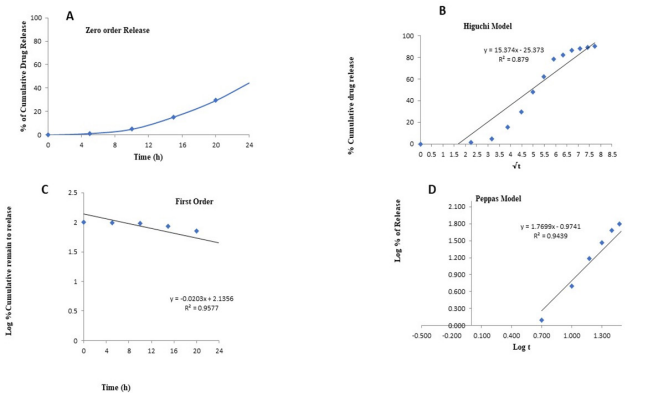

Figure 14: Dissolution model release kinetics for immediate release etoricoxib A. Zero order release B. Higuchi Model C. First order release D. Peppas model

Post-compression analysis

The tablet had a smooth surface. They were biconvex, elegant, and white. The two layers could be distinguished. In the formulated tablet no tablet defect was observed. The average thickness and diameter were found to be 3.89 ± 0.0098 and the average diameter was found to be 12.36 ± 0.0098 cm. The prepared tablet had the mean hardness of 4.02 ± 0.1022 kg/cm^2 while the % friability was observed to be 0.88, and thus was found within the limit as specified. The average weight of the tablet was 552 mg which was within the specified limit. Disintegration time for immediate-release tablets was found to be 2 min 16 seconds which complies with the pharmacopoeial limit for immediate-release tablets. HCl buffer with pH 1.2 was used to study the in-vitro release

of immediate-release tablets for 2 hours. According to the scope of the study, drug release had to be observed during this time duration. Figure 13 depicts in vitro drug release of optimized immediate-release etoricoxib tablets.

The in vitro dissolution data represents 90.30% of drug release in one hour. Thus the formulation proves the requirement for an immediate-release tablet in one hour. The dissolution study was followed by analyzing the mathematical model of dissolution. A comparative *in-vi*tro drug release kinetic is given in Figure 14 which exhibits the *in-vi*tro release pattern of the formulation.

Stability study

In the present work, immediate-release tablets of Etoricoxib were prepared and evaluated for different parameters. All the parameters were found to be within acceptable limits. A stability study was carried out to ensure the quality and safety of the formulation. Optimized formulation was selected for the stability study. Formulations were kept under different storage conditions for two months. The storage conditions provided to study the stability of the tablet were 40°C ± 75% Relative Humidity (RH). The conditions are compiled with the ICH guidelines.

The tablets were packed in a suitable container in an oven and humidity chamber under the above-mentioned storage conditions, respectively. It was kept into consideration that the temperature and humidity condition provided should be constant. The tablets were checked at two-month intervals and evaluated for certain parameters like hardness, disintegration, and drug content. The results obtained were compared with those obtained by evaluating tablets before they were kept for stability studies and the results are represented in Table 11, respectively.

CONCLUSION

Immediate-release tablets are a very versatile modification to the conventional tablet dosage form. The design of the present immediate-release tablet of etoricoxib provides a high degree of patient compliance as the chronic joint pain of gout or arthritis will be reduced immediately. Numerous factors affecting drug release were bought to light after successful completion. The effect of sodium starch glycolate on disintegration and drug release was studied. It was observed that disintegration time was decreased because of increased sodium starch glycolate concentration and thus increased drug release. It was because of the swelling property of sodium starch glycolate, which leads to faster release of components of the tablet. Sodium bicarbonate is an effervescence agent that also contributes to faster drug release. The outcomes were promising and future research may contribute a potential candidate in the treatment of gout or arthritis. The method is cost-effective and efficient and does not require sophisticated instrumentation.

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Nil

Conflict of Interest

All authors declare that they have no conflict of interest.

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