An Anti-Inflammatory and Analgesic Drug Etoricoxib Investigated by Design of Experimentation (DOE) and in Vitro Characterization

Ramarao CHT* and Reshma K

Department of Pharmaceutics, Sri Venkateswara College of Pharmacy, India

*Corresponding author: Ch Taraka Ramarao, Department of Pharmaceutics, Sri Venkateswara College of Pharmacy, India, Tel: 91-9949900905; Email: tarak.pharm60@gmail.com

Abstract

The objective studies enhance drug release of etoricoxib by Binders, disintegrant& β- Cyclodextrin. The 2 level factorial designs employing (DOE) Design expert software; 3 independent with 3 central points. The prepared granules and tablets were subjected to flow, physical characteristics and dissolution. The optimized formulation exhibited 4 independent variables Y1 (DR 30), Y2 (DR 60), Y3 (DR 90) Y4 (T50 30), Y5 (DE10). DoE used to find response surface plots, optimization and Desirability and analysis of variance (ANOVA), $p < 0.005$ indicates that the ANOVA of responses (dependent variables) Y1, Y2, Y3, Y4& Y5 is significant. The formulation Fa, formulated employing PVP as binder (factor A) and potato starch as disintegrant (factor B) had the highest drug release rate of 95 % in 1 h. The desirability function was 0.90170 and the predicted and experimental values had strong correlations.

Keywords: Anova; Doe; Pvp; Dissolution Efficiency; Potatostartch

Introduction

Etoricoxib, a widely prescribed anti-inflammatory and analgesic drug belongs to class-II under BCS, Poor watery dissolvability of the medication likewise brings about troubles in the detailing of strong dose structures and prompts poor and variable disintegration rate and oral bioavailability. The biopharmaceutical consideration dosage forms are reported Ramarao CT, et al. [1] tablets structure contains various excipients to fill different needs. Fastener is a basic fixing in tablet that impacts tablet characters. The binder, disintegrant and β-cyclodextrin are widely employed for enhance drug release employed are reported Reshma K, et al. [2], Chowdary KPR, et al. [3], Ramarao CHT, et al. [4-8].

Experimental

Etoricoxib and croscarmellose were gift samples from M/s Natco Pharma. Ltd., Hyderabad, Di Calcium Phosphate IP (SD fine-chem. limited, Mumbai), β Cyclodextrin (Balaji drugs private limited), Gelatin (MERCK Specialties private limited), Potato starch (SD Fine chem), CCS (Dr.Reddy's laboratories, Hyderabad), Poly vinyl Pyrrollidone (LOBA chemie PVT.LTD, Mumbai), Talc (LOBA chemie PVT.LTD, Mumbai), Magnesium Stearate (Oxford laboratory, Mumbai) I.P were procure from commercial source . All the materials use were of pharmacopeia grades.

Experimental Design

DoE used to develop response surface plots, best fitting model, parameters with coefficient of variation (CV), coefficient of determination(R^2), adjusted R^2, Predicted R^2, Adeq Precision, optimization , Desirability, analysis of variance (ANOVA), 'F' test and 'P' values. The Binders (acacia/ PVP(X1), Disintegrants Potato starch/ Cros carmellose (X2) and β Cyclodextrin (X3) concentrations with Statistical

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models. To find interaction terms were used to evaluate the effect of the three factors on the The optimized formulation exhibited 4 independent variables Y1 (DR 30), Y2 (DR 60), Y3 (DR 90) Y4 (T50 30), Y5 (DE10) on the prepared tablets as per factorial design model. The polynomial terms was used to evaluate the responses basing on $Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_{12}(X_1 X_2) + \beta_3(X_3) + \beta_{13}(X_1 X_3) + \beta_{2,3}(X_2 X_3) - \beta_{123}(X_1 X_2 X_3)$. Where Y is the dependent variables here β_0 is mean response of the 8 runs; and β1, β2 and β_3 are the estimated coefficients for the factors X1, X2 and X3 respectively. The interaction terms (X1X2, X1X3 and X2X3) shows the responses.

Preparation of Tablets

The wet granulation process was used to prepare the formula are reported Ramarao CHT, et al. [9].

Content Active Ingredients

Five tablets were accurately weighed and pulverised. The equivalent of 60 mg tablet powder was placed in boiling test tubes and extracted with 4 into 10ml methanol, collected into a 50ml volumetric flask, and the volume was increased to 50ml in methanol the solution, diluted with phosphate buffer pH 7.4 at 284nm using the UV-spectrophotometric method.

Hardness

By using MONSANTO hardness tester.

Friability

By using ROCHY friabilator.

Disintegration Time (DT)

Using LABINDIA tablet disintegration test apparatus using distilled water as fluid.

Dissolution Rate Studies

By using DS 8000 (LABINDIA) 8 station, 900 ml of phosphate buffer of pH 7.4 with the paddle stirrer at 50 rpm, a temperature of 37 ± 0.5^0C , The sample of the dissolution media 5ml was withdrawn through a filter (0.45 microns) at different intervals of time and analyzed by UV at 284nm [10-17].

Statistical Analysis

The dissolution characteristics were analyzed as per zero and first order kinetic model, statistically by ANOVA using design expert software [18-24].

Results and Discussion

All the tablets prepared evaluated for assay, hardness, friability, disintegration time, physical parameters shown hardness 4.5-5.7kg/cm^2, friability was less than 0.90%, drug content of tablets 100±2.5%, DT was found 2.30 to 7.40 min. In all situations, the correlation coefficient value (r) in the first order model was higher than that in the zero order models, first order dissolution profile. This study used a 2^3 Factorial Design to investigate the individual main and combined effects of three factors: X1, X2and X3. The dissolution parameters Y1, Y2, Y3, and Y4& Y5 were subjected to ANOVA to find out the significance of individual main and combined effects of the factors involved shown in Table 1. The results of ANOVA are given significant (p < 0.05) & counter plots, 3D surface plots shown in Figure 1.

Source	Sum of Squares	df	Mean Square	F-value	p-value	Remark
Model	622.75	7	88.96	13.24	0.0288	significant
A-Beta CD	117.2	1	117.2	17.44	0.025	
B-Acacia/PVP	14.74	1	14.74	2.19	0.2352	
C-Starch/CCS	156.82	1	156.82	23.33	0.0169	
AB	70.81	1	70.81	10.53	0.0476	
AC	0.1922	1	0.1922	0.0286	0.8765	
BC	127.36	1	127.36	18.95	0.0224	
ABC	135.63	1	135.63	20.18	0.0206	
Residual	20.16	3	6.72			
Lack of Fit	20.16	1	20.16			
Pure Error	0	2	0			
Cor Total	642.91	10				

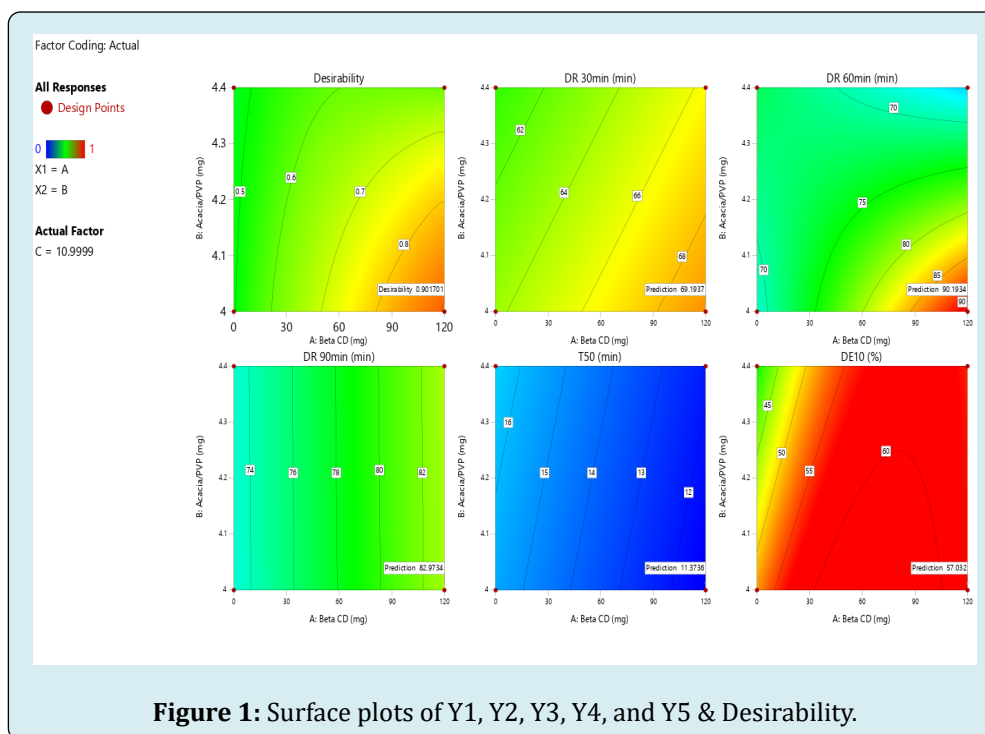**Table 1:** ANOVA of DR 60 Employing Factorial Design.

Figure 1: Surface plots of Y1, Y2, Y3, Y4, and Y5 & Desirability.

Conclusion

The etoricoxib tablets developed succefully by doe and achieved quality by design (QBD) [25] desirability and other surface and counterplots. It is an excellent contribution for enhancing oral bioavailability.

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