RESEARCH PAPER

Development and Evaluation of Zaltoprofen Solid Dispersion-Loaded Sustained Release Matrix Tablets

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ABSTRACT:

Objective: The objective of the present study was to develop and evaluate sustained release matrix tablets of Zaltoprofen to achieve controlled drug release and improve therapeutic efficacy. **Materials and Methods:** Sustained release matrix tablets were prepared by wet granulation method using polymers such as HPMC K15M and Ethylcellulose. FTIR was performed to evaluate drug–excipient compatibility. prepared formulations were evaluated for pre-compression, post-compression like drug content, swelling index, in-vitro drug release and stability studies. **Results and Discussion:** FTIR analysis confirmed the absence of any significant drug–excipient interaction, indicating good compatibility. All formulations showed acceptable flow properties and complied with pharmacopoeial requirements. The optimized formulation (ZST5) exhibited 98.78% cumulative drug release up to 24 hours with good swelling index (91.89%). Drug release followed controlled release mechanism. Stability study confirmed no significant changes in formulation parameters. Zaltoprofen, a non-steroidal anti-inflammatory drug (NSAID), exhibits poor aqueous solubility and short biological half-life, which necessitates formulation strategies to enhance its dissolution and prolong drug action. Sustained release matrix tablets offer an effective approach to maintain drug concentration in the body for an extended period and reduce dosing frequency, thereby improving patient compliance. **Conclusion:** From the study, it was concluded that sustained release matrix tablets of Zaltoprofen were successfully developed and provided controlled drug release for prolonged duration, improving therapeutic efficacy and patient compliance

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INTRODUCTION

Pain is a common clinical condition that significantly affects quality of life. Analgesics are drugs used to relieve pain and are broadly classified into non-opioid (NSAIDs, acetaminophen) and opioid analgesics. NSAIDs are effective for mild to moderate pain but are associated with gastrointestinal and renal side effects. Opioids, on the other hand, are used for severe pain and act by binding to opioid receptors, influencing both sensory and emotional components of pain. [1-2]

Pain management can be achieved through various mechanisms such as reducing nociceptor sensitivity, blocking pain transmission, and altering pain perception. Analgesics remain the primary approach for managing different types of pain, including acute and chronic conditions.[3]

Sustained release (SR) drug delivery systems are designed to release drugs at a controlled rate over an extended period, thereby maintaining therapeutic drug levels and improving patient compliance. Matrix tablets are widely used SR systems due to their simplicity, cost-effectiveness, and ability to accommodate high drug doses. These systems use hydrophilic and hydrophobic polymers such as HPMC, ethyl cellulose, xanthan gum, and chitosan to control drug release. SR systems offer advantages like reduced dosing frequency and improved therapeutic efficacy, but may have limitations such as dose dumping and reduced dose flexibility. Drug selection for SR formulation depends on factors like solubility, half-life, absorption, metabolism, and protein binding. Proper selection of polymers and formulation strategies is essential for achieving desired drug release profiles. [4-6]

Materials

Polymers such as HPMC K15M and Ethylcellulose were used as release-retarding agents. Other excipients including Microcrystalline Cellulose (MCC), Talc, and Magnesium Stearate and isopropyl alcohol were purchased from chemdyes ltd., Rajkot, Gujarat, India.

Preparation of Sustained Release Matrix Tablets

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Sustained release matrix tablets of Zaltoprofen were prepared by wet granulation method. All ingredients were accurately weighed and passed through sieve #30. The drug and excipients (except talc and magnesium stearate) were mixed thoroughly and granulated using a mixture of isopropyl alcohol and water (70:30). The wet mass was passed through sieve #16 and dried at 50–60°C. The dried granules were passed through sieve #24, lubricated with talc and magnesium stearate, and compressed into tablets using a rotary tablet compression machine. [7-9] (Table 1).

Factorial Design of Formulation:

A 3^2 factorial design was employed to optimize the formulation of sustained release matrix tablets of Zaltoprofen. In this design, two independent variables were selected:

X_1: Amount of HPMC K15M

X_2: Amount of Ethylcellulose

Each factor was studied at three levels (low, medium, high). A total of 9 formulations (ZST1–ZST9) were prepared as per the design. The dependent variables (responses) were:

Y_1: % cumulative drug release

Y_2: Swelling index

This design helps in evaluating the effect of independent variables and their interaction on drug release behavior and tablet characteristics. [10]

Calculation for Equivalent weight of drug

Amount of Drug added: 1000 mg

Obtained weight of Solid Dispersion: 2.07825 gm (2078.25 mg)

Actual dose of drug: 240 mg

Weight of drug		Weight of solid Dispersion (mg)
1000	-	2078.25
240	-	(?)

Equivalent Weight of solid Dispersion $= \frac{240 \text{ X } 2078.25}{1000} = 498.78$ mg

Table 1: Formulation sustained release matrix tablet using 3^2 Factorial design

Ingredients (mg)	ZST1	ZST2	ZST3	ZST4	ZST5	ZST6	ZST7	ZST8	ZST9
Weight of solid dispersion	498.78	498.78	498.78	498.78	498.78	498.78	498.78	498.78	498.78
Ethylcellulose (mg)	20	30	40	20	30	40	20	30	40
HPMC K15M (mg)	40	40	40	40	60	60	80	80	80
MCC (mg)	76.22	66.22	56.22	56.22	46.22	36.22	36.22	26.22	16.22
PVP K30 (mg)	5	5	5	5	5	5	5	5	5
Talc (mg)	4	4	4	4	4	4	4	4	4
Mg Stearate (mg)	6	6	6	6	6	6	6	6	6
Isopropyl Alcohol: Water (70: 30)	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.	q.s.
Total (mg)	**650**	**650**	**650**	**650**	**650**	**650**	**650**	**650**	**650**

Determination of Melting Point of Zaltoprofen

Melting point of Zaltoprofen was measured by melting point apparatus. Minimum amount of drug was placed in a thin-walled capillary tube closed at one end. This capillary was then mounted in a melting point apparatus with thermometer and then their temperature range over which Gemigliptin melts is measured. [11] The readings were taken in triplicate.

Identification by UV-Visible Spectrophotometry

UV-Visible spectrophotometry (Shimadzu UV spectrophotometer 1900) was employed for the quantitative estimation of drug concentration and determination of λmax due to its simplicity, accuracy and sensitivity. Standard stock solution of Zaltoprofen was prepared by dissolving 10 mg of drug in 100 ml of suitable solvent to obtain a concentration of 100 µg/ml. For determination of λmax, the stock solution was scanned between 200–400 nm using a UV-Visible spectrophotometer against solvent as a blank. Working solutions of concentrations 3, 6, 9, 12 and 15 ppm were prepared by pipetting 0.3, 0.6, 0.9, 1.2 and 1.5 ml, respectively, from the stock solution (100 µg/ml) and diluting up to 10 ml with solvent. The absorbance of these working solutions was measured in triplicate at λmax (338 nm) against solvent as a blank. [12]

Pre-Compression Parameters

Pre-compression parameters were evaluated to assess the flow properties and compressibility of the powder blend, ensuring uniform die filling and efficient tablet formation. Bulk density, tapped density, Hausner's ratio, Compressibility index, Angle of repose, were all measured. Good flow qualities were indicated by the powder mixture's minimum Carr's index, Hausner's ratio, and Angle of repose. [13-16]

Bulk density: The apparent bulk density was assessed by pouring the blend into a graduated cylinder and measuring both the bulk volume and weight of the powder.[13]

$$\textbf{Bulk density (gm/ml)} = \frac{\textbf{Mass of powder (gm)}}{\textbf{Bulk volume of powder (ml)}}$$

Tapped density: The measuring cylinder, initially filled with a known mass of blend, underwent 100 taps. Subsequently, the minimum volume occupied in the cylinder and the weight of the blend were measured. [13]

$$\textbf{Tapped density (gm/ml)} = \frac{\textbf{Mass of powder (gm)}}{\textbf{Tapped volume of powder (ml)}}$$

Compressibility Index: Compressibility is indirectly associated with the relative flow rate, cohesiveness, and particle size distribution of the powder. Tapped density and bulk density measurements are useful for estimating the compressibility of a material. [14]

$$\textbf{Compressibility Index (\%)} = \frac{\textbf{Tapped density} - \textbf{Bulk density}}{\textbf{Tapped density}} \textbf{ X 100}$$

Hausner's ratio: The Hausner's ratio serves as an indicator of the flow property of either particles or granules. It is calculated as the ratio of tapped density to bulk density. A value less than 1.25 indicates excellent flow, while a value greater than 1.25 suggests poor flow property. The Hausner's ratio of the granules can be determined using the equation, [15]

$$\textbf{Hausner's ratio} = \frac{\textbf{Tapped density}}{\textbf{Bulk density}}$$

Angle of repose (Ø): The angle of repose is defined as the maximum angle achievable between the surface of a pile of powder and the horizontal plane. It is measured using the fixed funnel standing method. [16]

In this method, the mass of granules is permitted to flow out of the funnel orifice onto a piece of paper placed on a horizontal surface. This results in the formation of a pile of granules on the paper. The angle of repose is calculated using the equation:

$$\textbf{Tan } \theta = \frac{h}{r} \qquad \theta = \tan^{-1}\frac{h}{r}$$

Where, θ = Angle of repose, h = Height of pile, r = Radius of pile

Post Compression Parameters

Thickness and diameter: Tablet thickness and diameter were measured by Digi-matic Vernier calipers (Aerospace Digimatic Vernier Calliper). Five tablets were randomly collected and their thickness and diameter were measured by placing between two arms of Vernier calipers. [13]

Weight variation: Twenty tablets were randomly collected and average weight was determined by using an electronic balance (Table 2). [14]

Table 2: Standard values for weight variation

Average weight of tablet	% deviation
≤ 80 mg	10
80 - 250 mg	7.5
≥ 250 mg	5

Hardness: Tablet hardness has been defined as the force required to break a tablet in a diametric compression test and was measured by using Monsanto type hardness tester (D. K Scientific, Ahmedabad). [15]

Friability test: The friability of tablets was measured by Roche type friabilator (Bhavana,India). Twenty tablets were initially weighed and then tablets were placed in friabilitor at 25 rpm for 4 min then tablets were deducted and weighed again. [13-15] Loss in weight should not be more than 1%. % friability determined by using following equation.

$$\textbf{\% Friability} = \frac{\textbf{(Initial weight} - \textbf{Final weight)}}{\textbf{Initial weight}} \textbf{ X 100}$$

Drug content: Ten tablets were powdered and an amount equivalent to 240 mg of Zaltoprofen was accurately weighed and dissolved in 25 ml of 0.1 N HCl. The solution was filtered, and 1 ml of filtrate was diluted up to 10 ml with 0.1 N HCl. The absorbance of the resulting solution was analyzed by UV spectrophotometer (Shimadzu UV spectrophotometer 1900) at 338 nm. [16]

Swelling Index: The extent of swelling was determined in terms of percentage weight gained by the tablets. One tablet from each formulation was kept in dissolution apparatus USP type I (basket) (DKB instruments) containing volume of 900 ml 0.1N HCl. At regular time interval, tablets were withdrawn, soaked on tissue paper and weighed, and then percentage weight gain by the tablet was calculated using the formula. [17-18]

$$\textbf{\% S. I.} = \frac{\textbf{(Final weight of tablet} - \textbf{Initial weight of tablet)}}{\textbf{Initial weight of tablet}} \textbf{x 100}$$

In Vitro Drug release study: Percentage drug release of Zaltoprofen sustained release matrix tablet was determined by USP type II (paddle type) (DKB instrument) dissolution apparatus. This test performed using 900 ml of 0.1 N HCl at 37° ± 0.5 °C at 50 rpm. 5 ml sample solution was withdrawn from dissolution apparatus at regular time interval and the same quantity of sample was replaced with fresh dissolution media. The sample was filtered through 0.45 µm membrane filter. Absorbance of these samples was analyzed by using UV spectrophotometer at 338 nm.[19]

Stability Study: Stability studies (Stability chamber Patel scientific instruments PVT. LTD) were conducted on the optimized formulation for one month at 40°C ± 2°C and 75% ± 5% RH. Tablets were

evaluated, thickness, hardness, %swelling index drug content and drug release profile. [20]

RESULT

Determination of Melting Point of Zaltoprofen

Melting point determination was carried out to confirm the purity and identity of Zaltoprofen using a melting point apparatus. The observed melting point values were found to be 137. 69°C.which is nearer to reported melting point range 135 – 141 °C of Zaltoprofen, confirming the identity of the drug (Table 3).

Table 3: Melting Point of Zaltoprofen

Sr. No.	Reported Melting Point	Observed Melting point
1.	137.69°C	135 – 138 °C
2.		139 – 141 °C
3.		139 – 141 °C

Estimation of Drug by UV Spectrophotometric Method

UV spectrophotometric analysis of Zaltoprofen was carried out in suitable solvent. The drug showed maximum absorbance (λmax) at 338 nm. Calibration curve was constructed by plotting concentration versus absorbance, which showed good linearity over the concentration range of 3–15 ppm (Table 4, Figure 1).

Table 4: Absorbance of different concentration of Zaltoprofen in Water

Sr. No.	Concentration (ppm)	Absorbance			Mean Absorbance ± S. D.
		I	II	III	
1.	3	0.179	0.185	0.172	0.179 ± 0.0065
2.	6	0.338	0.332	0.345	0.338 ± 0.0065
3.	9	0.489	0.493	0.484	0.489 ± 0.0045
4.	12	0.664	0.658	0.662	0.661 ± 0.0031
5.	15	0.819	0.825	0.816	0.820 ± 0.0046

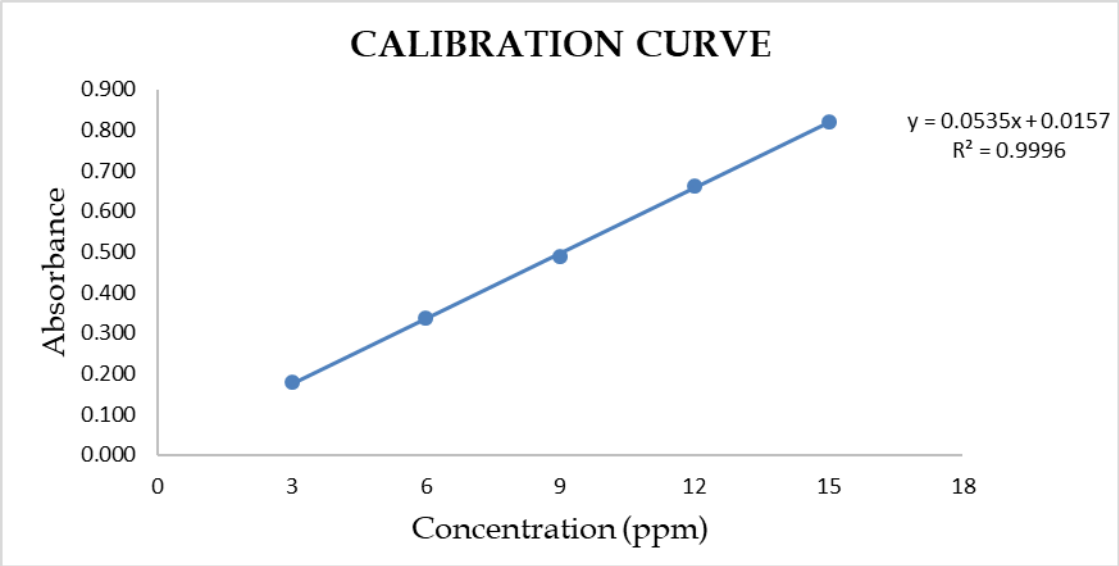

Figure 1: Calibration curve of Zaltoprofen

PRE-COMPRESSION PARAMETERS

All formulation blends were evaluated for bulk density and tapped density. Bulk density was found to be in the range of 0.80 ± 0.01 gm/cm³ to 0.90 ± 0.02 gm/cm³ and tapped density was found to be in the range of 0.93 ± 0.03 gm/cm³ to 1.17 ± 0.03 gm/cm³.Carr's index of all formulation blends lies within the range of 12.90 ± 0.42 to 24.79 ± 0.50 %. From Carr's Index, flow of powder was found to be fair to passable. Hausner's ratio of all formulations was found in the range of 1.15 ± 0.01 to 1.33 ± 0.01. From Hausner's ratio, flow of powder was found to be good.Angle of repose of all formulations was in the range of 28.61 ± 0.38 to 33.70 ± 0.88. From observed angle of repose, flow of powder was found to be good to fair (Table 5).

Table 5: Bulk density, Tapped density, Carr's index, Hausner's ratio and Angle of Repose data

Batch	Bulk density (gm/cm³)	Tapped density (gm/cm³)	Carr's index	Hausner's ratio	Angle of repose (Ø)
ZST1	0.83 ± 0.04	1.09 ± 0.05	23.85 ± 0.83	1.31 ± 0.01	29.76 ± 0.71

ZST2	0.86 ± 0.03	1.14 ± 0.05	24.56 ± 0.83	1.33 ± 0.01	33.70 ± 0.88
ZST3	0.81 ± 0.03	0.93 ± 0.03	12.90 ± 0.42	1.15 ± 0.01	28.61 ± 0.38
ZST4	0.85 ± 0.02	1.12 ± 0.03	24.11 ± 0.46	1.32 ± 0.01	30.48 ± 0.74
ZST5	0.88 ± 0.02	1.17 ± 0.03	24.79 ± 0.50	1.33 ± 0.01	31.48 ± 0.45
ZST6	0.90 ± 0.02	1.15 ± 0.03	21.74 ± 0.46	1.28 ± 0.01	32.57 ± 0.97
ZST7	0.86 ± 0.03	1.09 ± 0.05	20.10 ± 0.71	1.27 ± 0.01	28.61 ± 0.38
ZST8	0.80 ± 0.01	1.03 ± 0.02	22.33 ± 0.41	1.29 ± 0.01	32.02 ± 0.81
ZST9	0.81 ± 0.03	0.93 ± 0.03	12.90 ± 0.42	1.15 ± 0.01	28.61 0.38

POST COMPRESSION PARAMETERS

All formulations were evaluated for post-compression parameters including weight variation, thickness, hardness, friability, and drug content. The weight variation of all formulations was found to be in the range of 649.00 ± 1.41 mg to 650.20 ± 1.01 mg, indicating uniformity of tablet weight. Thickness of all tablets was found to be in the range of 2.83 ± 0.06 mm to 3.50 ± 0.10 mm. Hardness of tablets was found to be in the range of 6.33 ± 0.58 kg/cm² to 8.33 ± 0.29 kg/cm², indicating good mechanical strength. Friability of all formulations was found to be in the range of 0.11% to 0.45%, which is within acceptable limits (<1%). Drug content of all formulations was found to be in the range of 98.47 ± 0.43% to 99.32 ± 0.65%, indicating uniform distribution of drug in all batches (Table 6).

Table 6: Weight variation, Thickness, Diameter, Hardness, Friability and Drug Content Data

Batch	Weight variation (mg)	Thickness (mm)	Hardness (kg/cm^2)	Friability (%)	Drug Content (%)
ZST1	649.70 ± 1.53	2.83 ± 0.06	6.33 ± 0.58	0.45	99.09 ± 0.69
ZST2	649.20 ± 1.11	2.87 ± 0.06	6.83 ± 0.58	0.34	99.17 ± 0.74
ZST3	649.00 ± 1.41	3.33 ± 0.46	7.17 ± 0.29	0.31	99.30 ± 0.05
ZST4	650.10 ± 1.29	3.30 ± 0.35	8.00 ± 0.87	0.22	98.57 ± 0.60
ZST5	649.30 ± 1.49	3.37 ± 0.42	8.33 ± 0.29	0.11	98.47 ± 0.43
ZST6	649.45 ± 1.39	3.30 ± 0.46	8.17 ± 0.29	0.15	99.20 ± 0.51
ZST7	649.50 ± 1.10	3.35 ± 0.21	7.67 ± 0.29	0.27	99.32 ± 0.65
ZST8	650.20 ± 1.01	3.20 ± 0.44	8.00 ± 0.50	0.18	98.80 ± 0.91
ZST9	649.35 ± 1.23	3.50 ± 0.10	7.83 ± 0.58	0.25	99.05 ± 0.56

Swelling Index (%)

The swelling index study was carried out to evaluate the hydration and swelling behavior of the polymeric matrix tablets of Zaltoprofen. It was observed that the swelling index increased progressively with time for all formulations due to hydration and water uptake. At 1 hour, swelling index values ranged from 15.82% to 26.87%, which further increased to 33.88%–51.85% at 6 hours and 51.39%–75.79% at 12 hours. At 18 hours, the swelling index reached a maximum in the range of 63.13% to 91.89%, with the optimized formulation (ZST5) showing the highest swelling index (91.89%). The increase in swelling index with increasing polymer concentration indicates the formation of a strong gel layer, which plays a crucial role in controlling drug release. However, after prolonged time, slight reduction in swelling was observed due to erosion and dissolution of the outer gel layer into the dissolution medium. These results confirm that the swelling behavior of the matrix tablets significantly contributes to sustained drug release. (Figure 2).

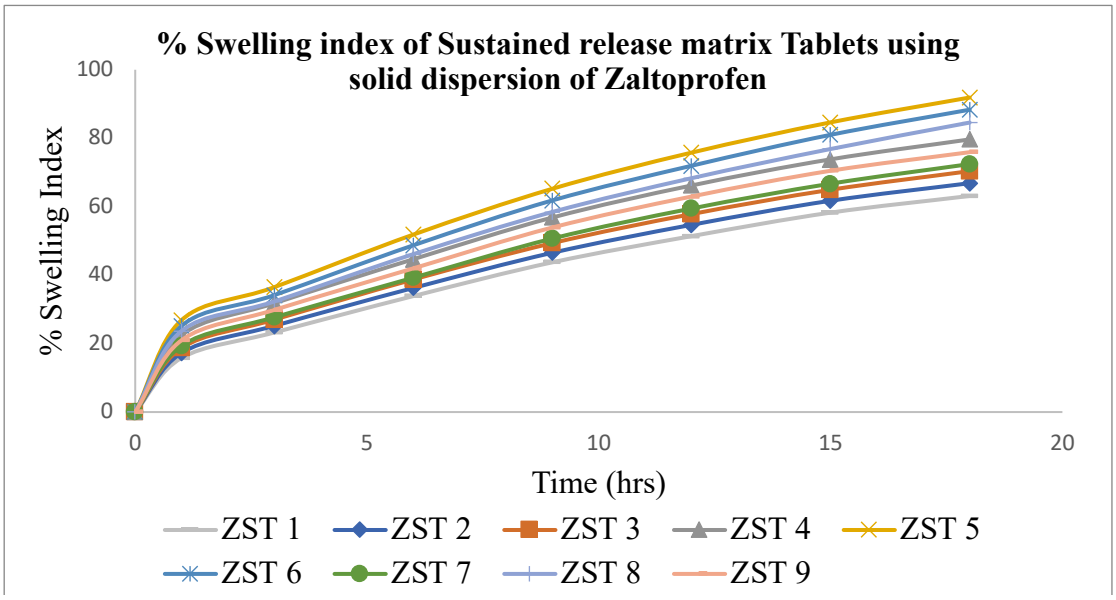

Figure 2: % swelling index vs Time of batches ZST1-ZST3

% Cumulative Drug Release study

In-vitro drug release study of Zaltoprofen sustained release matrix tablets was carried out using USP type II (paddle) apparatus in 0.1 N HCl (pH 1.2) at 37 ± 0.5°C and 50 rpm. The results indicated that an increase in polymer concentration resulted in a decrease in the drug release rate.

Formulations ZST1–ZST3 released 81.71%, 85.16% and 86.63% of drug within 24 hours, respectively. Formulations ZST4–ZST6 showed 90.63%, 98.78% and 96.48% drug release within 24 hours. While formulations ZST7–ZST9 released 88.10%, 91.81% and 89.78% of drug within 24 hours, respectively. Among all formulations, batch ZST5 exhibited the highest drug release (98.78%), indicating optimized sustained release behavior. Overall, increase in polymer concentration retarded the drug release, confirming controlled release characteristics of the matrix system (figure 3).

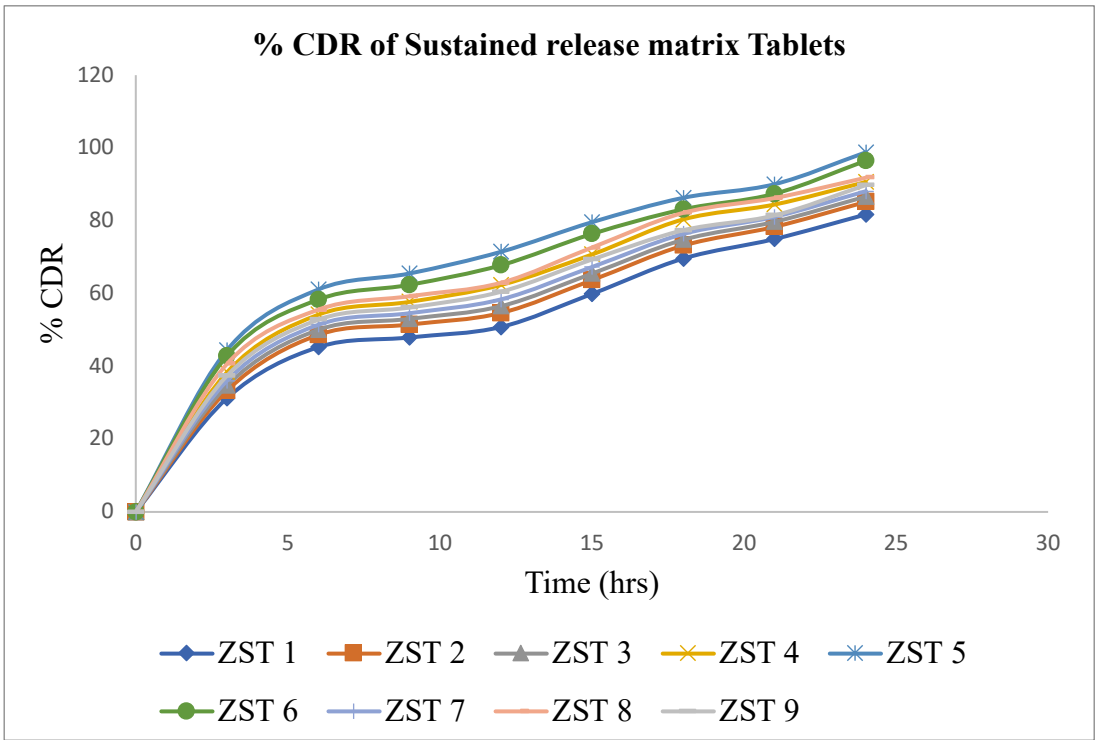

Figure 3: % CDR vs Time of batches ZST1-ZST9

STATISTICAL ANALYSIS

A statistical model that includes polynomial and interactive terms is employed to analyze the response and table 6.14 shows the results for dependent variables.

$$Y = B_0 + B_1 X_1 + B_2 X_2 + B_{12} X_1 X_2 + B_{11} X_1^2 + B_{22} X_2^2 + E$$

Table 7: Observed Dependent Variables for 3^2 Factorial Design

Batch	% swelling index	% CDR
ZST1	63.13	81.71
ZST2	66.86	85.16
ZST3	70.38	86.63
ZST4	79.65	90.63
ZST5	91.89	98.78
ZST6	88.33	96.48
ZST7	72.44	88.10
ZST8	84.57	91.81
ZST9	75.92	89.78

Table 8: Summary of ANOVA Analysis

Source	Sum of Square	Degree of Freedom	Mean Square	F Value	P Value
% Swelling index (Y_1)					
Regression	733.34	5	146.67	10.46	0.0408
Residual	42.05	3	14.02	-	-
Total	775.39	8	-	-	-
% CDR (Y_2)					
Regression	221.65	5	44.33	16.28	0.0220
Residual	8.17	3	2.72	-	-
Total	229.82	8	-	-	-

Equations for 3^2 factorial design, summary of ANOVA analysis and summary of polynomial equation as shown in Table 8 for all dependent variables. From the result of ANOVA table, it was found that F_{cal} values were much greater than F_{tab} for all formulations indicating that all factors had statistically significant effect on all dependent variables (Table 7 and 8).

Statistical analysis for % Swelling index

The ANOVA results indicated that the model for % swelling index (Y_1) was statistically significant, with an F-value of 10.46 and a p-value of 0.0408. The low residual value confirmed that the model adequately fits the experimental data.

Polynomial equation for % Swelling index:

$$Y_1 = 90.71 + 3.24\ B_1 + 5.43\ B_2 - 0.9425\ B_{12} - 6.13\ B_1^2 - 14.41\ B_2^2$$

The quadratic equation indicates that both formulation variables positively influence the swelling index, with factor B_2 having a stronger effect than B_1. The negative interaction term suggests an antagonistic combined effect of the variables. Significant negative quadratic terms confirm a nonlinear relationship, indicating the existence of an optimum concentration range beyond which further increases in polymer levels reduce swelling. Overall, the model demonstrates that controlled swelling is achieved by balancing the concentrations of both factors, with B_2 playing the dominant role.

The contour and 3D response surface plots demonstrated that Ethylcellulose and HPMC K15M have a significant combined effect on the swelling index. Maximum swelling (~91.8%) was observed at intermediate levels of both polymers, indicating the presence of an optimum region and a pronounced quadratic relationship. At higher polymer concentrations, the swelling index decreased due to increased matrix densification, which restricted polymer relaxation and reduced water uptake. The predicted versus actual plot showed close agreement, confirming the accuracy and reliability of the developed model. Overall, the study indicated that balanced concentrations of both polymers are essential to achieve optimum swelling behavior and effective matrix hydration (Figure 4,5,6).

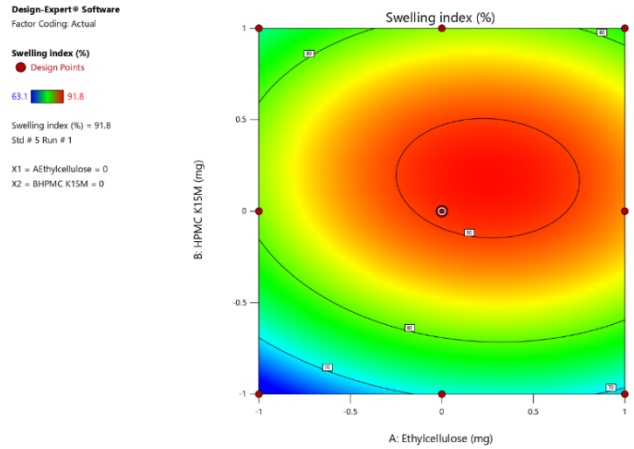

Figure 4: Contour plot showing the effect of Ethylcellulose (X_1) and HPMC K15M (X_2) on % Swelling index

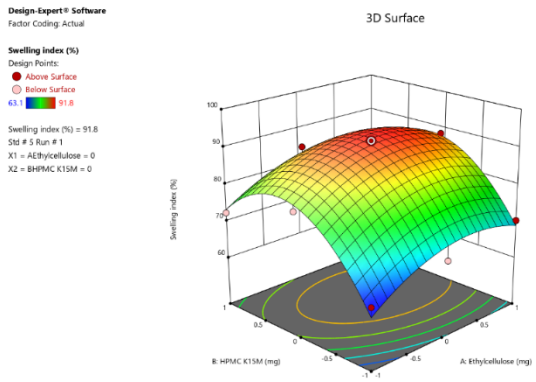

Figure 5: 3D surface plot showing the effect of Ethylcellulose (X_1) and HPMC K15M (X_2) on Swelling index

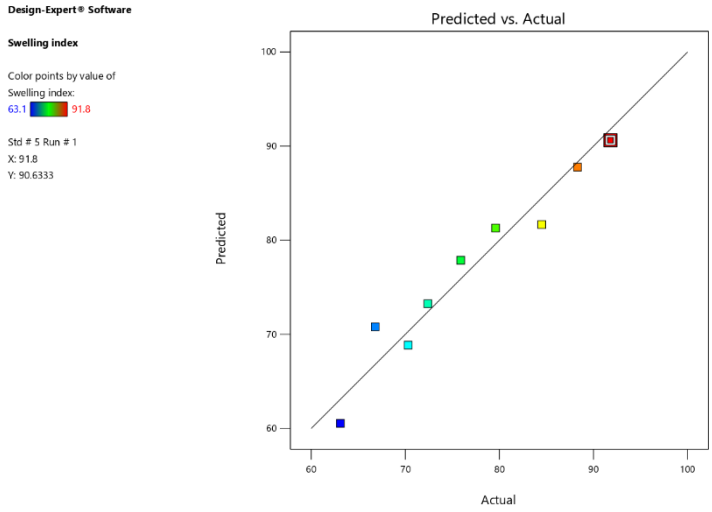

Figure 6: Actual value vs predicted value of % Swelling index

Statistical analysis for % CDR

The ANOVA results for % cumulative drug release (Y_2) showed that the model was statistically significant, with an F-value of 16.28 and a p-value of 0.0220. The low residual value indicated a good fit of the model.

Polynomial equation for % CDR

$$Y_2 = 97.32 + 2.08\ B_1 + 2.70\ B_2 - 0.8100\ B_{12} - 3.03\ B_1^2 - 8.10\ B_2^2$$

The quadratic equation indicates that both formulation variables positively influence % cumulative drug release at 24 hours, with factor B_2 showing a stronger effect than B_1. The negative interaction term suggests an antagonistic combined effect, while the negative quadratic terms confirm a nonlinear relationship and the existence of an optimum concentration range. Overall, the model demonstrates that controlled and near-complete drug release at 24 hours is achieved by optimizing the levels of both factors, with B_2 playing the dominant role.

The contour plot and 3D response surface analysis indicated that Ethylcellulose and HPMC K15M had a significant combined effect on % cumulative drug release at 24 hours. Maximum drug release (~98.78%) was observed at intermediate levels of both polymers, suggesting that balanced concentrations are essential for optimal performance. At higher polymer concentrations, drug release decreased due to increased matrix density and formation of a thicker gel barrier, which restricted drug diffusion. The predicted versus actual plot showed good agreement, confirming the reliability and accuracy of the developed model. Overall, the study concluded that maintaining polymers at optimum levels ensures controlled and near-complete sustained drug release (Figure 7,8,9).

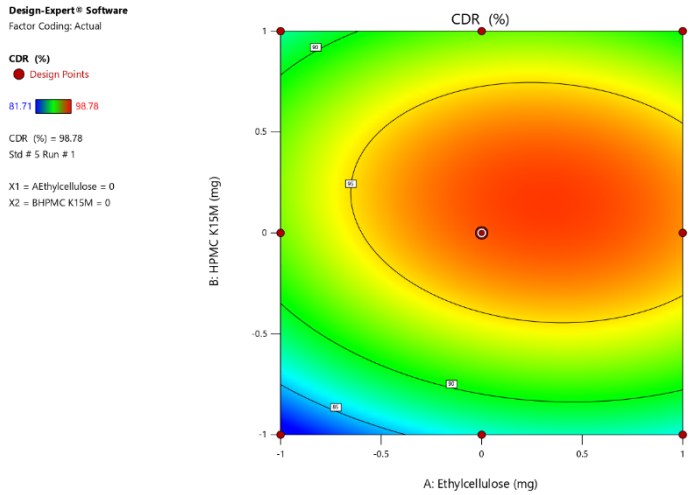

Figure 7: Contour plot showing the effect of Ethylcellulose (X_1) and HPMC K15M (X_2) on % CDR

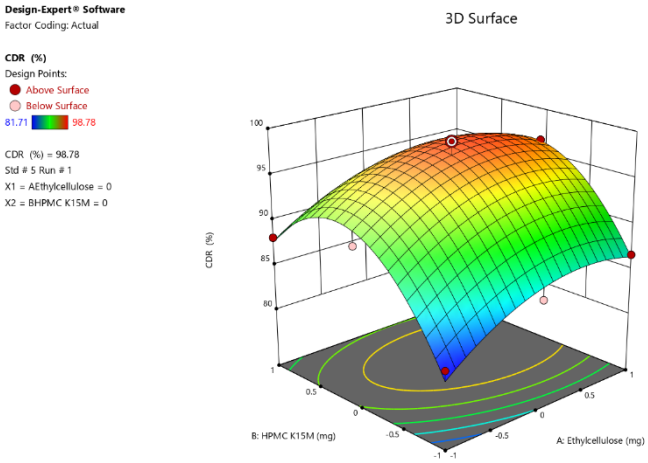

Figure 8: 3D surface plot showing the effect of Ethylcellulose (X_1) and HPMC K15M (X_2) on % CDR

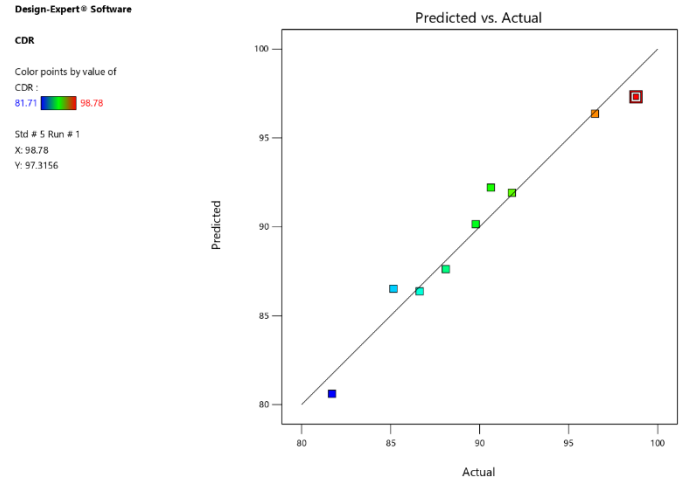

Figure 9: Actual value vs predicted value of % CDR

STABILITY STUDY

Stability studies were conducted to evaluate the influence of storage conditions on the physicochemical properties and performance of the optimized formulation. The optimized batch (ZST5) was subjected to accelerated stability conditions to assess any changes in tablet thickness, hardness, swelling index, drug content and drug release profile. The study was carried out to ensure the integrity and therapeutic effectiveness of the formulation during storage. From the data of % cumulative drug release after stability, it was found that there was no significant change in the amount of drug released from the optimized formulation. Stability data showed that all the

parameters were within acceptable limits, indicating no significant variation in the results. The prepared batch ZST5 was found to be stable over a period of one month. Comparison of % CDR values before and after stability testing indicated that there was no significant change in the drug release profile. Stability data revealed that all parameters remained within acceptable limits with only minor changes observed. Thus, the optimized batch ZST5 was found to be stable over a period of one month (Table 9,10 and Figure 10).

Table 9: Result of the Stability study

Parameters	Optimized batch (ZST5)	Optimized batch after 1 month
Thickness (mm)	3.37 ± 0.42	3.03 ± 0.47
Hardness (kg/cm^2)	8.33 ± 0.29	8.47 ± 0.06
Drug Content (%)	98.47 ± 0.43	98.24 ± 0.35

Table 10: % Cumulative Drug Release of Stability batch

Time (hrs)	% CDR of ZST5 Initial	% CDR of ZST5 after 1 Month
0	0	0
3	44.45	42.26
6	61.11	60.97
9	65.51	64.18
12	71.45	70.23
15	79.6	78.34
18	86.3	85.48
21	90.03	87.29
24	98.78	96.90

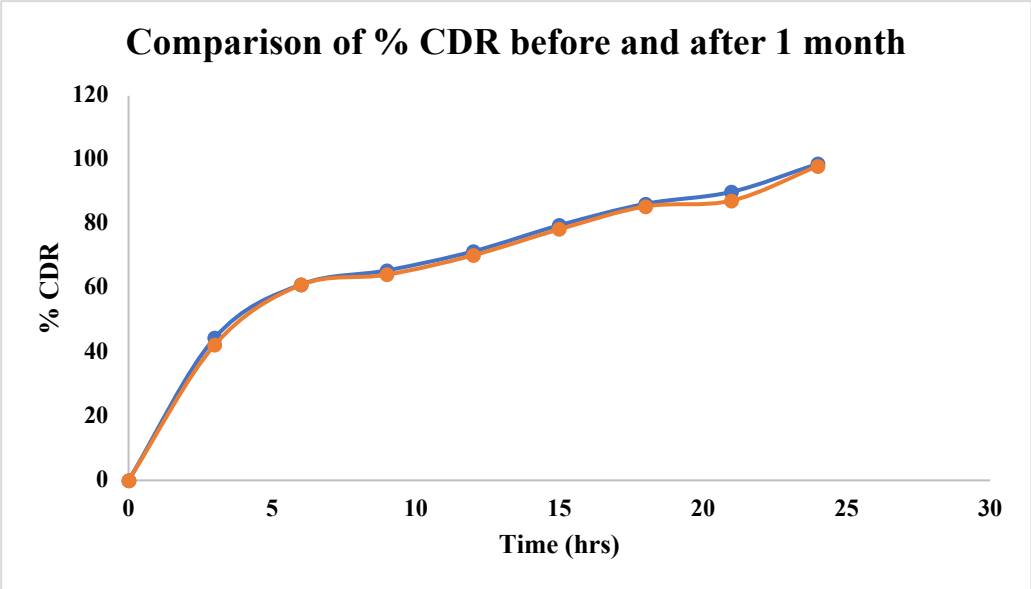

Figure 10: Comparison of % CDR of ZST5 batch Before and After 1 month

CONCLUSION

The present study was aimed at the formulation and evaluation of sustained release matrix tablets of Zaltoprofen using solid dispersion technique to enhance solubility and improve therapeutic efficacy. Sustained release tablets were prepared by wet granulation method using polymers such as HPMC K15M and Ethylcellulose. The prepared granules were evaluated for pre-compression parameters such as bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose. The results indicated good flow properties and compressibility of granules, confirming their suitability for tablet compression. Post-compression evaluation of the prepared tablets including weight variation, hardness, friability, thickness and drug content showed that all parameters were within acceptable limits as per pharmacopeial specifications, indicating good mechanical strength and uniform drug distribution. Swelling index studies demonstrated proper hydration and gel layer formation, which played an important role in controlling drug release. The optimized formulation (ZST5) exhibited satisfactory tablet properties and sustained drug release up to 24 hours. Drug release kinetics revealed that the optimized batch followed zero order kinetics, indicating controlled and prolonged drug release. Stability studies confirmed that there was no significant change in the drug release profile after storage, indicating good stability of the formulation. Thus, it can be concluded that sustained release matrix tablets of Zaltoprofen can be successfully formulated using solid dispersion technique, which enhances

solubility and provides controlled drug delivery, thereby improving therapeutic efficacy and patient compliance.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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