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# Design of Extended Release Matrix Tablet of Tramadol hydrochloride Using Combination of Hydrophobic and Hydrophilic Polymer

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## ABSTRACT

The aim of design of oral extended drug delivery system is to achieve a prolonged therapeutic effect by continuously releasing medicament over an extended period of time after administration of a single dose. An attempt was made to formulate Tramadol Extended Release (ER) matrix tablet using combination of hydrophobic and hydrophilic polymer consisting of ethyl cellulose, HPMC K15M, carbopol, and xanthan gum. The polymeric concentration of hydrophobic and hydrophilic polymer was optimized and was found that drug to polymeric ratio (hydrophobic and hydrophilic) of 1:0.75:0.75 was appropriate for the formulation of Tramadol ER tablet. The concentration of hydrophobic polymer was kept constant were as the combination of hydrophilic polymer was attempted and combined to hydrophobic polymer to retard the drug release for 24-hour from the matrix tablet. A total of nine formulations (F1-F9) of Tramadol matrix tablet, with different concentration of hydrophobic and hydrophilic polymer were used with other excipients. The tablets were compressed by direct compression method after subjecting the blend to blend physical parameters studies like studies like angle of repose, bulk density, tapped density, Carr's index. The results obtained were satisfactory. Post compression parameters like hardness, weight variation, friability, drug content analysis and *in-vitro* release profiles of drug from all the formulations could be best expressed by Higuchi's equation, as the plots showed high linearity ($R^2$: 0.942-0.995). To confirm the diffusion mechanism, the data were fit into Korsmeyer equation. The formulations F-1 to F-6 showed good linearity ($R^2$: 0.961 to 0.993), which indicate the mechanism is diffusion coupled with erosion.

**Keywords:** Sustained drug delivery system, matrix tablet, hydrophobic and hydrophilic polymer, pharmacokinetic and pharmacodynamics, release kinetics.

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## INTRODUCTION

Design of extended drug delivery system is to achieve a prolonged therapeutic effect by continuously releasing medicament over an extended period of time after administration of a single dose. Sustained release constitutes any dosage form that provides medication over an extended time period. In general, the sustained release dosage form is to maintain therapeutic blood or tissue level of drug for a prolonged period usually accomplished by attempting slow first order fashion. In recent years sustained release dosage forms continuous to draw attention in the field of research for improved patient compliance and decreased incidence of adverse drug reaction. Systems that are designed as prolonged release can also be considered as attempts at achieving sustained-release delivery. [1-2] Repeat action tablets are an alternative method of sustained release in which multiple doses of drug are contained within a dosage form, and each dosage is related to a periodic interval. Delayed release systems, function by maintaining the drug within the dosage form for some time before release. [3] Commonly the release rate of drug is not altered and does not result in sustained delivery once drug release has begun. Successful fabrication of extended release products is usually difficult & and involves consideration of physicochemical properties of drug, pharmacokinetic behavior of drug, route of administration, disease state to be treated and, most importantly, placement of the drug in dosage form total will provide the desired temporal and spatial delivery pattern for the drug. [4] The slow first order release obtained by an extended release preparation is generally achieved by the release of the drug from a dosage form. In some cases, this can be achieved by retarding the release of drug from a dosage form and in some cases; this is accomplished by a continuous release process.

The basic rationale for extended drug delivery is to alter the pharmacokinetic and pharmacodynamics of pharmacologically active moieties by using novel drug delivery systems or by modifying the molecular structure and/or physiological parameters inherent in a selected route of administration. It is desirable that the duration of drug action become more to design properly. Rate controlled dosage form, and less, or not at all, a property of the drug molecules inherent kinetic properties. [5] As mentioned earlier, primary objectives of extended drug delivery are to ensure safety and to improve efficiency of drugs as well as patient compliance. This can be achieved by better control of plasma drug levels and frequent dosing. For conventional dosage forms, only the dose (D) and dosing interval (C) can vary and, for each drug, there exists a therapeutic window of plasma concentration, below which therapeutic effect is insufficient, and above which toxic side effects are elicited. This is often defined as the ratio of median lethal dose ($LD_{50}$) to median effective dose ($ED_{50}$).

**Table 1: Formulation of Tramadol hydrochloride matrix tablets using different ratios of polymers (F1-F9)**

| S. No | Ingredient (in mg) | Formulation | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| 1 | Tramadol hydrochloride | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 | 100 |
| 2 | Ethyl cellulose | 75 | 75 | 75 | 75 | 75 | 75 | 75 | 75 | 75 |
| 3 | HPMC K15M | 75 | - | - | 50 | 25 | 50 | 25 | - | - |
| 4 | Carbopol | - | 75 | - | 25 | 50 | - | - | 50 | 25 |
| 5 | Xanthan gum | - | - | 75 | - | - | 25 | 50 | 25 | 50 |
| 6 | MCC | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 | 150 |
| 7 | Aerosil | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 | 3 |
| 8 | Magnesium steareate | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |
| | Total weight | 410 | 410 | 410 | 410 | 410 | 410 | 410 | 410 | 410 |

## MATERIALS AND METHODS

Tramadol hydrochloride were obtained from Cipla Ltd, Dewas, Madhya Pradesh. Ethyl Cellulose, HPMC K15M, Carbopol, Xanthan gum, MCC, Aerosil and Magnesium stearate were from Loba Chemie Mumbai, India.

Tramadol hydrochloride ER tablets were prepared by direct compression method with different polymers like ethyl cellulose, HPMC K15M, carbopol and xanthan gum in various drug**:** polymer ratio as shown in Table 1.

### Direct compression technique [6-7]

### Sieving

Tramadol hydrochloride was passed through sieve #40. Ethyl cellulose, HPMC K15M, carbopol, xanthan gum, MCC was passed through sieve # 40.

### Dry mixing

The above sieved materials were mixed thoroughly by tumbling method in a polythene bag.

### Lubrication

The dry blend was lubricated with Aerosil & Magnesium Stearate.

### Compression

Then the lubricated dry blends were subjected to compression using a tablet punching machine-10, B tooling 12 mm round punches. Parameters like average weight, hardness and friability were checked during compression as in process quality measures.

### Evaluation of Formulation [8-10]

### Bulk density

Bulk density of a compound varies substantially with the method of crystallization, milling or formulation. Bulk density is determined by pouring presieved blend

into a graduated cylinder via a large funnel and measure the volume and weight as is given by.

**Bulk density = weight of the blend /bulk volume of the blend**

### Tapped density

Tapped density is determined by placing a graduated cylinder containing known mass of blends on a mechanical tapper apparatus, which is operated for a fixed number of taps until the powder bed volume has reached a minimum volume. Using the weight of the drug in the cylinder and this minimum volume, the tapped density may be computed.

**Tapped density =weight of blends/ tapped volume of blends**

### Carr's index

Carr's index is measured using the values of the bulk density and tapped density.

The following equation is used to find the Carr's index

$$CI = \frac{(TD - BD)}{TD} x100$$

Where, TD – Tapped density, BD – Bulk density

### Angle of repose

The manner in which stresses are transmitted through a bed and the beds response to applied stress are reflected in the various angles of friction and repose. The most commonly used of these is angle of repose, which may be determined experimentally by a number of methods. The method used to find the angle of repose is to pour the powder in a conical heap on a level, flat surface and measure the inclined angle with the horizontal pile.

$$\tan \theta = h/r$$

$$\theta = \tan^{-1} h/r$$

Where, h- Height of the heap and r- Radius of the heap.

### Fourier transforms infra-red spectroscopy (FTIR)

The FTIR analysis was conducted for the structure characterization. FTIR spectra of the pure drug, pure polymers and mixture of both were recorded. Formulations were taken in a KBr pellet using BOMEN MB SERIES FTIR instrument. [11-12] Approximately 5 mg of samples were mixed with 50mg of spectroscopic grade KBr; samples were scanned in the IR range from 500 to 3500 $cm^{-1}$, with a resolution of 4 $cm^{-1}$.

### Thickness and diameter

The thickness and diameter of the tablets were found out using Vernier Caliper and the results were expressed in millimeter. A ± 5% may be allowed depending on the size of the tablet.

### Hardness test

Tablets require a certain amount of strength or hardness and resistance to friability to withstand mechanical shocks of handling in manufacture, packing and shipping. The hardness of tablet was measured by Monsanto hardness tester. Ten tablets from the batch were used for hardness studies and results are expressed in $Kg/cm^2$.

### Weight variation test

Ten tablets were selected at random, individually weighed in a single pan electronic balance and the average weight was calculated. The uniformity of weight was determined according to I.P specification. As per I.P values were not more than two of individual weight would deviate from average weight by not more than 5% and none deviate by more than twice that percentage.

### Friability test

It was performed in Roche Friabilator apparatus where the tablets were subjected to the combined effect of abrasion and shock by utilizing a plastic chamber that revolves at 25 rpm dropping the tablets at a distance of six inches with each revolution. Preweighed samples of 20 tablets were placed in the Friabilator, which is then operated for 100 revolutions. The tablets are then dusted and reweighed. Conventional compressed tablets that loose less than 0.5 to 1% of their weight are generally considered acceptable.

$$\%\,Friability = \frac{\text{Weight loss}}{\text{Weight of tablets before operation}} \times 100$$

### Drug content analysis

Tramadol hydrochloride tablet was tested for their drug content. The tablet was finely powdered in a mortar and pestle. Tablet equivalent to 100 mg of Tramadol hydrochloride was accurately weighed and transferred to a 100 ml standard flask. [13-14] To the drug powder, methanol was added and made up to the volume with distilled water. It was shaken thoroughly for 30 minutes to ensure complete solubility of the drug. 10 ml of the resultant liquid was pipetted out in another standard flask and volume was made up to 100 ml with distilled water. The absorbance of the final solution was measured at 274 nm in a UV-Visible spectrophotometer (Shimadzu). The amount of drug and the percentage purity of each formulation were evaluated.

### *In-vitro* dissolution studies

Tablet dissolution was assessed using standard USP dissolution apparatus type II. The dissolution media used was 900 ml of 0.1N HCl (pH 1.2) solution at 37 ± 0.5°C for first 2 h, and pH 7.4 phosphate buffer solution (900 ml) for the rest of the period at speed of rotation was 50 ± 1 rev/min. The temperature was maintained at 37 ± 0.5°C. At predetermined time intervals, an aliquot of 5 ml sample was withdrawn, and made up to 10 ml with Phosphate Buffer. [15]

The absorbance was measured spectrophotometrically in a UV-Visible spectrophotometer (Shimadzu) at 274 nm. After each withdrawal 5 ml of Phosphate Buffer was replaced to maintain the total volume constant. The dissolution studies were performed for an hour and the cumulative percentage of drug released from the tablets was calculated and plotted against time. The amount of Tramadol hydrochloride was calculated from the calibration curve.

### Release Kinetic Study [16-18]

Different kinetic equations (zero order, first order, Higuchi's equation, Korsmeyer equation) were applied to intercept the release from matrix system.

Zero order equation:

$$M = M_0 - K_0 t$$

In this equation M is the amount of drug remaining undissolved at time t, M0 is the amount of drug undissolved at t = 0 and K0 is the corresponding release rate constant

Higuchi Square Root Law equation:

$$Q = K_s \text{ root } t$$

Where Q (Q = 100 - M) is the amount of drug dissolved at time t and Ks is the corresponding rate constant.

First order release equation:

$$\ln M = \ln M_0 - K_1 t$$

Where M is the amount of drug undissolved at time t, M0 is the amount of drug undissolved at t = 0 and $K_1$ is the corresponding release rate constant.

The Korsmeyer equation:

$$M_t/M_\alpha = K_k t$$

Where $K_k$ is the Korsmeyer release rate constant.

**Table 2: FTIR Spectrum of Drug**

| Drug | OH-s (3200-3400) | Aromatic (3000-3100) | CH-s (2800-3000) | C=0 (1600-1900) | CN (1400-1500) | OH-s (1200-1400) | CH-b (1300-1400) |
|---|---|---|---|---|---|---|---|
| FTIR of Tramadol hydrochloride | 3344.3 | 3015 | 2928 | 1593 | 1470.2 | 1245.3 | 1369.4 |

**Table 3: Characterization of Tramadol hydrochloride blends (Pre compression parameters)**

| Batch | Angle of repose (θ) | Bulk density (g/ml) | Tapped Density (g/ml) | Carr's index |
|---|---|---|---|---|
| F1 | 26.07 ± 0.8 | 0.54 | 0.67 | 19.2 |
| F2 | 25.25 ± 0.6 | 0.54 | 0.69 | 18.5 |
| F3 | 28.45 ± 0.47 | 0.51 | 0.61 | 17.2 |
| F4 | 25.12 ± 0.6 | 0.57 | 0.64 | 18.5 |
| F5 | 26.10 ± 0.5 | 0.57 | 0.61 | 17.7 |
| F6 | 23.91 ± 0.4 | 0.55 | 0.68 | 19.2 |
| F7 | 27.46 ± 0.5 | 0.53 | 0.66 | 18.4 |
| F8 | 27.01 ± 0.7 | 0.52 | 0.67 | 18.2 |
| F9 | 25.92 ± 0.8 | 0.54 | 0.65 | 19.7 |

Mean ± S.D (standard deviation), n = 3

## RESULTS AND DISCUSSION

The blends of matrix tablet were prepared and Pre compression parameters like the angle of repose, bulk density, tapped density and Carr's index was characterized. [19-20]

### Angle of repose

The angle of repose for the blend of Tramadol hydrochloride and excipients was done. The angles of repose of different formulations were found between 23.91 ± 0.4 to 28.45 ± 0.47. The angle of repose of different formulations was ≤ 28.45 which indicates that material had excellent flow property. So it was confirmed that the flow property of blends were free flowing. All the values were mentioned in the Table 3.

### Bulk density and True density

The bulk density of blend of Tramadol hydrochloride and excipients were found between 0.57 g/ml to 0.66 g/ml .True density were found between 0.54 g/ml to 0.65 g/ml.

### Carr's index

The measurement of free flowing powder can also be done by Carr's index. The Carr's index for all the formulations was found to be 17.2-19.7 which reveals that the blends have fair flow character. The results are shown in Table 3.

### Drug Excipient Compatibility Studies

FTIR analysis was conducted for the structure characterization and drug excipient Compatibility to which Tramadol hydrochloride showed the following character. [21-22]

### Characterization of Tramadol hydrochloride Matrix Tablets (Post Compression Parameters) [23-25]

The tablets of different formulations of Tramadol hydrochloride were subjected to various evaluation tests, such as hardness, thickness weight variation, friability and drug content. All the results are shown in Table 4.

### Thickness

The thickness of the tablets was found out using Vernier Caliper and the thickness found to be in the range of 4.02-4.62 mm.

### Hardness test

The hardness of tablet was measured by Monsanto hardness tester. Ten tablets from the batch were used for hardness studies and results showed they were in between 6.1-6.6 Kg/cm$^2$. This is appropriate for matrix tablet.

### Weight variation test

The uniformity of weight was determined according to I.P specification and results showed that all the formulation passes the test.

### Friability test

The Friability of all the formulation was below 1% as per IP specification.

### Drug content analysis

Tramadol hydrochloride matrix tablet was tested for their drug content and all the formulation showed drug content more than 95%.

### *In vitro* dissolution studies

The formulation F1, F2, F3 which contains combination of ethyl cellulose, HPMC K15M, carbopol, xanthan gum respectively. The concentration of ethyl cellulose was kept constant, while other polymers were taken in same amount. Formulation F2 which contain combination of ethyl cellulose and carbopol showed the least release compared to other two formulation of 45.32% at the end of 12$^{th}$ hour and release of 74.31% at the end of 24$^{th}$ hour but the release was below therapeutic index of Tramadol though it shows an extended release, it fails to be the best batch. The results are shown in Table 5.

The formulation F4, F5 which contains combination of ethyl cellulose, HPMC K15M, carbopol, respectively. The concentration of Ethyl Cellulose was kept constant, while the concentrations of other two polymers were varied. Formulation F5 contained combination of ethyl cellulose, HPMC K15M and carbopol, but carbopol in a

higher concentration showed the least release in comparison to the other two formulations. It showed a release 63.8% at the end of 12th hour and release of 95.24% at the end of 24th hour and was better than F4.

The formulation F6, F7 contained a combination of ethyl cellulose, HPMC K15M and xanthan gum respectively. The concentration of ethyl cellulose was kept constant, while the concentrations of other two polymers were varied in the ratio of 1:2 and 2:1. Both the formulation were able retard the drug release up to 12th hour, but not able to sustain it till the 24th hour.

The formulation F8, F9 contained a combination of ethyl cellulose, carbopol and xanthan gum respectively. The concentration of ethyl cellulose was kept constant, while the concentration of other two polymers was varied. Formulated batch of F8 also showed a good retarded release of 76.21% at the end of 12th hour and 99.64% at the end of 12th hour which is better than F9.

From the above data, F5 was chosen as the best formulation the in comparison to the other formulations as it showed the least drug release of 63.80% at 12th hour and 95.24% at 24th hour, but within the therapeutic index of the drug.

### Release kinetic study

Among the all six formulation, it was observed that F5 showed sustained release *In-vitro* release of Tramadol hydrochloride of the matrix tablet. This release rate was sustained may due to inhibition of wetting and penetration of dissolution fluid in the hydrophilic matrix by hydrophobic part of the polymer which results hardening of the matrix which further delay the drug dissolution process. [23-25]

**Table 4: Characterization of Tramadol hydrochloride matrix tablets (Post compression parameters)**

| Batch | Thickness (mm) | Hardness (Kg/cm2) | Friability (%) | Average Weight (mg) | Content Uniformity (%) |
|---|---|---|---|---|---|
| F1 | 4.62 ± 0.12 | 6.2 ± 0.05 | 0.45± 0.005 | 412 ± 2.05 | 100.2 ±2.04 |
| F 2 | 4.02 ± 0.09 | 6.2 ± 0.03 | 0.32 ± 0.004 | 416 ± 2.04 | 98.2 ± 1.06 |
| F 3 | 4.25 ± 0.16 | 6.4 ± 0.05 | 0.19 ± 0.003 | 422 ± 4.12 | 98.7 ±2.02 |
| F 4 | 4.19 ± 0.07 | 6.6 ± 0.02 | 0.21 ± 0.002 | 394 ± 2.02 | 101.2 ±2.04 |
| F 5 | 4.11 ± 0.05 | 6.1 ± 0.03 | 0.54 ± 0.004 | 400 ± 4.02 | 102.3 ±1.03 |
| F 6 | 4.32 ± 0.19 | 6.2 ± 0.02 | 0.49 ± 0.011 | 398 ± 2.05 | 101.5 ±1.06 |
| F 7 | 4.26 ± 0.22 | 6.2 ± 0.02 | 0.74 ± 0.006 | 418 ± 3.04 | 98.2 ±1.02 |
| F8 | 4.22 ± 0.11 | 6.5 ± 0.04 | 0.46 ± 0.004 | 416 ± 3.05 | 99.2 ±1.08 |
| F9 | 4.42 ± 0.002 | 6.5 ± 0.02 | 0.42 ± 0.003 | 398 ± 3.02 | 98.23±1.04 |

Mean ± S.D (standard deviation), n = 3

**Table 5: *In vitro* dissolution profile**

| Time (in hours) | Cumulative (%) release | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 | F9 |
| 1 | 13.51 ± 0.69 | 5.41 ± 3.82 | 16.12 ± 0.87 | 11.21 ± 0.95 | 5.41 ± 0.56 | 11.75 ± 0.69 | 7.5 6 ± 0.94 | 16.5 ± 1.56 | 11.58 ± 1.23 |
| 2 | 16.27 ± 1.03 | 14.23 ± 1.81 | 27.08 ± 0.99 | 20.46 ± 1.54 | 11.53 ± 0.94 | 15.26 ± 0.95 | 12.64 ± 1.21 | 19.59 ± 2.36 | 20.49 ± 0.95 |
| 3 | 25.36 ± 0.69 | 21.70 ± 2.16 | 33.43 ± 1.32 | 31.87 ± 1.32 | 24.99 ± 0.84 | 20.85 ± 0.92 | 21.41 ± 1.09 | 21.88 ± 1.54 | 25.64 ± 0.56 |
| 4 | 30.00 ± 1.04 | 28.32 ± 1.46 | 43.02 ± 0.89 | 37.95 ± 0.84 | 30.13 ± 0.69 | 25.69 ± 0.83 | 29.45 ± 0.94 | 26.72 ± 0.91 | 31.23 ± 1.45 |
| 5 | 47.27 ± 1.05 | 33.78 ± 1.55 | 48.66 ± 0.98 | 47.76 ± 0.91 | 34.99 ± 1.51 | 29.32 ± 0.82 | 35.64 ± 0.76 | 39.16 ± 1.69 | 40.70 ± 1.98 |
| 6 | 59.53 ± 0.71 | 35.24 ± 1.77 | 55.12 ± 1.47 | 54.32 ± 1.11 | 40.99 ± 1.64 | 40.23 ± 1.24 | 45.43 ± 0.73 | 46.88 ± 1.54 | 49.92 ± 2.12 |
| 8 | 69.75 ± 1.51 | 39.28 ± 1.21 | 65.14 ± 1.25 | 60.72 ± 1.45 | 49.71 ± 1.22 | 55.21 ± 1.64 | 64.23 ± 0.81 | 56.43 ± 1.97 | 60.69 ± 2.04 |
| 10 | 81.76 ± 0.92 | 42.35 ± 0.99 | 79.56 ± 1.89 | 65.78 ± 0.77 | 57.75 ± 0.64 | 69.54 ± 0.95 | 76.21 ± 0.88 | 66.85 ± 2.36 | 71.43 ± 1.54 |
| 12 | 86.23 ± 1.89 | 45.32 ± 0.86 | 92.35 ± 1.21 | 73.33 ± 0.92 | 63.80 ± 0.76 | 80.65 ± 0.53 | 88.65 ± 0.91 | 76.21 ± 1.54 | 81.26 ± 1.24 |
| 24 | 95.68 ± 0.65 | 74.31 ± 1.04 | 96.07 ± 0.82 | 96.45 ± 0.64 | 95.24 ± 0.95 | 96.23 ± 0.97 | 99.56 ± 1.32 | 99.64 ± 0.86 | 97.47 ± 0.81 |

Mean ± S.D (standard deviation), n = 3

**Table 6: Release kinetic study**

| Formulation | Zero order | First order | Higuchi's equation | Korsmeyer |
|---|---|---|---|---|
| F1 | 0.813 | 0.625 | 0.942 | 0.961 |
| F2 | 0.917 | 0.591 | 0.977 | 0.965 |
| F3 | 0.820 | 0.660 | 0.939 | 0.972 |
| F4 | 0.888 | 0.613 | 0.982 | 0.963 |
| F5 | 0.936 | 0.634 | 0.995 | 0.950 |
| F6 | 0.895 | 0.751 | 0.954 | 0.960 |
| F7 | 0.819 | 0.631 | 0.929 | 0.959 |
| F8 | 0.908 | 0.761 | 0.967 | 0.955 |
| F9 | 0.881 | 0.690 | 0.971 | 0.969 |

To know the mechanism of drug release from these formulations, the data were treated according to zero order (cumulative amount of drug released vs time), first-order (log cumulative percentage of drug remaining vs time), Higuchi's (cumulative percentage of drug released vs square root of time), and Korsmeyer (log cumulative percentage of drug released vs log time) equations along with pattern. The results of release rate kinetic data for all the other equations can be seen in Table 6. When the data were plotted according to the first-order equation, the formulations showed a fair linearity, with regression values between 0.625 and 0.761. Release of the drug from a matrix tablet containing hydrophilic polymers generally involves factors of diffusion. Diffusion is related to transport of drug from the dosage matrix into the in vitro study fluid depending on the concentration. As gradient varies, the drug is released, and the distance for diffusion increases. [26] This could explain why the drug diffuses at a comparatively slower rate as the distance for diffusion increases, which is referred as square-root kinetics or Higuchi's kinetics. In our experiments, the *in vitro* release profiles of drug from all the formulations could be best expressed by Higuchi's equation, as the plots showed high linearity ($R^2$: 0.942-0.995). To confirm the diffusion mechanism, the data were fit into Korsmeyer equation. The formulations F-1 to F-6 showed good linearity ($R^2$: 0.961

to 0.993), which indicate the mechanism is diffusion coupled with erosion.

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A total of nine formulations (F1-F9) of Tramadol matrix tablet, with different concentration of hydrophobic and hydrophilic polymer were used with other excipients. The tablets were punched by direct compression method after subjecting the blend to preformulation studies like angle of repose, bulk density, tapped density, carr's index. The results obtained were satisfactory. Post compression parameters like hardness, weight variation, friability, drug content analysis and *in-vitro* release profiles of drug from all the formulations could be best expressed by Higuchi's equation, as the plots showed high linearity ($R^2$: 0.942-0.995). To confirm the diffusion mechanism, the data were fit into Korsmeyer equation. The formulations F-1 to F-6 showed good linearity ($R^2$: 0.961 to 0.993), which indicate the mechanism is diffusion coupled with erosion.

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