INTRODUCTION

Oral drug delivery has been known for decades as the most widely utilized route of administration among all the routes that have been explored for the systemic delivery of drugs via various pharmaceutical products of different dosage forms. The major advantage of this category is that, in addition to the convenience of reduced frequency of administration, it provides blood levels that are devoid of the peak-and-valley effect which is characteristic of the conventional intermittent dosage regimen. Sustained release dosage forms are designed to complement the pharmaceutical activity of the medicament to achieve better selectivity and a longer duration of action. Colchicine is a major alkaloid from Colchicum autumnale L. and is found also in other Colchicum species. Its primary therapeutic use is in the treatment of gout, but it has been used also in the treatment of familial Mediterranean fever (periodic disease). Although the precise mode of action of colchicine in the treatment of gout is unknown, it is considered to act against the inflammatory response to urate crystals, by possibly inhibiting neutrophil chemotaxis toward urate crystals.

Keywords: Colchicine, Sustained release tablet, 2\textsuperscript{nd} full factorial design, Similarity factor.

Abstract

The study on the effect of polymer concentration on in vitro drug release profile revealed that there is a change in vitro drug release parameters \((t_{50}, t_{80} \text{ and MDT})\) with a change in polymer concentration. Fraction of HPMC K4M, HPMC K100 M, and Ethyl Cellulose were required to be 15, 10, and 7 \% respectively for designing optimized batch F7. The release rate of Colchicine decreased proportionally with an increase in the concentration of ethyl cellulose and HPMC K100 M. Also the high amount of HPMC K4M leads to the less initial release and sustain effect. A theoretical drug release profile was generated using pharmacokinetic parameters of Colchicine. The value of \(t_{50}\) and \(t_{80}\) of experimental drug release profile was found to be 242 min and 529 min respectively. The similarity factor \(f_{2}\) was applied between the in vitro drug release profile of optimizing batches and theoretical profile, which indicate a decent similarity between all in vitro drug release profiles \((t_{50} = 68.28 \text{ for } F7\)). All the batches except F1 and F3 show the value of \(t_{80}\) value within a range. Batch F7 showed the highest \(t_{50}\) \((t_{50} = 68.28)\) among all the batches and this similarity was also reflected in \(t_{80}\) \((≈ 256 \text{ min})\) and \(t_{80}\) \((≈ 554 \text{ min})\) values. A \(2^\text{nd}\) full factorial design was applied to systematically optimize in vitro drug release profile. The HPMC K4M (X), Concentration of HPMC K100 M (X), and concentration of Ethyl cellulose (X) were selected as independent variables. The time required for 50\% drug released \((t_{50})\), the time required for 80\% drug release \((t_{80})\), similarity factor \(f_{2}\), and mean dissolution time \(\text{MDT}\) were selected as dependent variables. The results of full factorial design indicate that the HPMC K4M (X), Concentration of HPMC K100 M (X), and concentration of Ethyl cellulose (X) have a significant effect on in vitro drug release profile. To find out the release mechanism the in vitro release data were fitted in the Korsmeyer-Peppas equation. All batches except F1 and F3 show anomalous diffusion-controlled release (combined mechanism of diffusion and case II transport).

Keywords: Colchicine, Sustained release tablet, 2\textsuperscript{nd} full factorial design, Similarity factor.
inhibiting the migration of granulocytes into the inflamed area.

MATERIALS AND METHOD

Colchicine was a gift sample, provided by Himedia Private Limited, Mumbai. Hydroxypropylmethylcellulose K4M, Hydroxypropylmethylcellulose K100M was a gift sample provided by Jaxani Pharmaceutical, Ahmedabad, India. Ethylcellulose, Dicalcium Phosphate, Lactose, Poly Vinyl Pyrrolidone K-30, Iso Propyl Alcohol, Talc, and Magnesium Stearate were used as filler purchased from S.D. Fine Chem. Ltd, Mumbai, India.

METHODOLOGY

Quantity of Colchicine, HPMC K4M, HPMC K100 M, Ethyl Cellulose, Dicalcium Phosphate, and Lactose as per formula was passed through 60 # and were mixed properly [Table 1]. For the preparation of the binder, PVP K-30 was dispersed in IPA. The drug and other excipients were granulated using the above-prepared binder solution. The mass was granulated using 20 #. The granules were dried at 40 °C. Dried granules were passed through 20 # sieve and the fines were separated using 40 # sieve to obtain 20-40 # granules. These granules were lubricated with a mixture of talc and magnesium Stearate (2:1). The lubricated granules were compressed into tablets using Minipress tablet compression machine.

Table 1: Composition of Colchicine Sustained release tablet

| Ingredients       | T1 | T2 | T3 | T4 | T5 | T6 | T7 | T8 |
|-------------------|----|----|----|----|----|----|----|----|
| Colchicine (mg)   | 6  | 6  | 6  | 6  | 6  | 6  | 6  | 6  |
| HPMC K4M (mg)     | 10 | 15 | 20 | 30 | 10 | 15 | 20 | 30 |
| HPMC K100 M (mg)  | 5  | 15 | 5  | 15 | 5  | 15 | 5  | 15 |
| Ethyl cellulose (mg) | 5  | 5  | 5  | 5  | 10 | 10 | 10 | 10 |
| DCP (mg)          | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 |
| Lactose (mg)      | 61 | 46 | 51 | 31 | 56 | 41 | 46 | 26 |
| PVP K-30 (%)      | 5  | 5  | 5  | 5  | 5  | 5  | 5  | 5  |
| Talc (%)          | 2  | 2  | 2  | 2  | 2  | 2  | 2  | 2  |
| Mag. Stearate (%) | 1  | 1  | 1  | 1  | 1  | 1  | 1  | 1  |

DSC Study

The physicochemical compatibilities of the drug and the used excipients were tested by differential scanning calorimetric analysis. The DSC analysis of the drug alone elicited a peak at 159 °C, very close to the reported value of Colchicine melting point, which is 155-157 °C as shown in Figures 1 and 2.
Figure 2: DSC Spectrum of Colchicine & excipients mixture

Evaluation parameters of Granules

Angle of repose \( \theta = \tan^{-1} (h/r) \)

Bulk density \( = \frac{\text{Weight of powder}}{\text{Bulk volume}} \)

Tapped density \( = \frac{\text{Weight of powder}}{\text{Tapped volume}} \)

**Compressibility Index:** The Granules was determined by Carr’s compressibility index 6.

\[ \text{Carr’s Index} \% = \left( \frac{\text{Tapped Density} - \text{Bulk Density}}{\text{Tapped Density}} \right) \times 100 \]

**Hausner’s Ratio:** It was determined by the following Equation:

\[ \text{Hausner’s Ratio} = \frac{\text{Tapped Density}}{\text{Bulk Density}} \]

**Evaluation of Tablets**

**Weight variation test:** To study weight variation, twenty tablets of the formulation were weighed using a Sartorius electronic balance 7.

**Drug content:** Five tablets were weighed individually, and powdered. The drug was extracted in 0.1 N HCl and Phosphate buffer pH 6.8, and the solution was filtered through the Whatman filter. The absorbance was measured at 350 nm 8.

**Hardness:** The five tablets was determined using the Monstan hardness tester 9.

**Thickness:** The tablets were determined by using vernier calipers 10.

**Friability:** Friability was checked using the Roche friabilator. Pre weighed 10 tablets were rotated for 4 min at 25 RPM 11.

**In-vitro drug release studies:** Drug release studies were carried out using a USP type II dissolution rate test apparatus for 2 hr in 0.1 M HCl (900 ml). At the end of the period, 10 ml of the samples were taken and analyzed for Colchicine content 12. The sample was analyzed using a UV spectrophotometer at 350 nm.

**Data Analysis:** To analyze the mechanism of drug release from the matrix tablets, the release data were fitted to the following equations:

**Zero-order kinetics:** \( Q_t = Q_0 + K_0 \cdot t \)

**First-order kinetics:** \( Q_t = \log Q_0 + K_1 \cdot t/2.303 \)

**Higuchi model:** \( Q_t = K_H \cdot t^{1/2} \)

**Korsmeyer-Peppas release model:** \( M_t / M_\infty = K \cdot t^n \)

Where \( M_t \) is the amount of drug released at time \( t \), \( M_\infty \) is the amount of drug released after infinite time, \( K \) is a kinetic constant incorporating structural and geometric characteristics of the tablet, and \( n \) is the diffusional exponent indicative of the drug release mechanism.

**Comparison of dissolution profiles:** The similarity factor \( (f_2) \) given by SUPAC guidelines for modified release dosage form was used as a basis to compare dissolution profile 14. The dissolution profiles are considered to be similar when \( f_2 \) is between 50 and 100. This similarity factor is calculated by the following formula,

\[ f_2 = 50 \log \left( 1 + \frac{1}{n} \sum_{t=1}^{n} \left( R_t - T_t \right)^2 \right)^{0.5} \times 100 \]

Where \( n \) is the number of dissolution times and \( R_t \) and \( T_t \) are the reference and test dissolution values at time \( t \). The mean dissolution time (MDT) of all batches was calculated using the following equation 15.

\[ \text{MDT} = \frac{\int_0^\infty t \cdot dM(t)}{\int_0^\infty dM(t)} \]

Where \( t \) is the midpoint between two sampling points and \( dM(t) \) is the additional mass in time.

**RESULT AND DISCUSSION**

The tablets of different formulations were subjected to various evaluation tests, such as thickness, uniformity of weight, hardness, friability, and drug content [Table 2]. All the formulations show values within acceptable limits. Drug Released from Trial Batches after 12 hr Dissolution Study had been shown in the following table 3. It has revealed that...
the polymer concentration has a significant effect on the 
drug release profile. From all these data, it can be seen that 
Batch T3 and T7 show the release profile matching with the 
thoretical Profile. Batch T3 shows the F2 Value of 55.58 and 
batch T7 shows 53.46. Batches T1, T3, T5, and T7 show More 
than 80 % Drug release after 12 hr. Batches T1 and T5 show 
initial high release of drug and it release around 80 % drug 
after 3 hours. So for matching with the theoretical profile, 
the optimum concentration of all these three polymers is 
necessary. The average concentration of HPMC K4 M 
(between 15-30 mg) with less concentration of HPMC K100 
M (between 5- 10 mg) and EC (between 5- 10 mg) shows a 
promising Approach for the development of sustained 
release dosage form of Colchicine.

Table 2: Evaluation of Preliminary Trial batches for various parameters

| Batch | T1 | T2 | T3 | T4 | T5 | T6 | T7 | T8 |
|-------|----|----|----|----|----|----|----|----|
| Angle of Repose (°) | 38.65 | 28.35 | 26.00 | 30.75 | 39.80 | 24.94 | 29.05 | 32.73 |
| Bulk Density (gm/cc) | 0.55 | 0.52 | 0.50 | 0.56 | 0.54 | 0.52 | 0.51 | 0.55 |
| Tapped density (gm/cc) | 0.71 | 0.66 | 0.58 | 0.72 | 0.68 | 0.62 | 0.62 | 0.72 |
| Carr’s Index (%) | 22.53 | 21.12 | 13.79 | 22.22 | 20.59 | 16.13 | 17.74 | 23.61 |
| Hauser’s Ratio | 1.29 | 1.26 | 1.16 | 1.29 | 1.26 | 1.19 | 1.21 | 1.30 |
| Avg. Weight (mg) | 121.04±0.64 | 120.74±0.65 | 120.18±0.79 | 120.19±0.62 | 120.94±0.77 | 120.83±0.24 | 120.87±1.59 | 120.65±0.49 |
| Drug Content (%) | 98.17±0.33 | 98.58±1.32 | 98.41±0.83 | 98.27±1.02 | 98.25±0.41 | 99.39±0.90 | 98.65±0.70 | 98.44±0.56 |
| Hardness (kg/cm²) | 5.66±0.28 | 5.73±0.11 | 5.73±0.30 | 5.66±0.11 | 5.66±0.41 | 5.80±0.40 | 5.86±0.50 | 5.60±0.20 |
| Friability (%) | 0.56 | 0.34 | 0.36 | 0.47 | 0.52 | 0.43 | 0.41 | 0.38 |

Table 3: Cumulative percentage drug release from Colchicine Sustained release tablets

| Time (Hr) | T1 | T2 | T3 | T4 | T5 | T6 | T7 | T8 |
|-----------|----|----|----|----|----|----|----|----|
| 0 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 |
| 1 | 35.03 | 18.41 | 15.55 | 13.58 | 29.13 | 19.22 | 15.85 | 13.04 |
| 2 | 61.09 | 26.08 | 26.97 | 27.33 | 58.69 | 26.07 | 27.29 | 24.10 |
| 3 | 89.24 | 36.10 | 36.93 | 38.54 | 79.24 | 30.03 | 36.07 | 31.81 |
| 4 | 89.84 | 40.62 | 44.89 | 43.02 | 81.84 | 34.99 | 43.75 | 37.03 |
| 6 | 90.05 | 52.60 | 56.32 | 52.72 | 83.05 | 47.30 | 60.22 | 45.86 |
| 8 | 89.58 | 62.51 | 70.53 | 61.53 | 86.06 | 58.29 | 70.62 | 55.17 |
| 10 | 89.14 | 70.79 | 78.51 | 68.58 | 86.58 | 67.62 | 77.97 | 62.59 |
| 12 | 89.07 | 76.09 | 87.45 | 73.12 | 87.07 | 74.37 | 81.95 | 71.72 |

Optimization of sustained-release tablet formulation 
using 2^3 full factorial Designs: It is therefore very essential 
to understand the complexity of pharmaceutical 
formulations by using established statistical tools such as 
factorial design. The response/s (Yi) is/are measured for 
each trial and then either simple linear, interactive, or 
Quadratic Model is fitted by carrying out multiple regression 
analysis and F-statistics to identify statistically significant 
terms. A statistical model incorporating interactive and 
polynomial terms was used to evaluate the response.

\[ Y = b_0 + b_1X_1 + b_2X_2 + b_3X_3 + b_{12}X_1X_2 + b_{23}X_2X_3 + b_{13}X_1X_2 + b_{123}X_1X_2X_3 \]

Where Y is the dependent variable, b0 is the arithmetic mean 
response of the eight runs, and bi is the estimated coefficient 
for the factor X. The main effects (X1, X2, and X3) represent 
the average result of changing one factor at a time from its 
low to high value [Table 4].

Formulation of Colchicine Sustained release tablet using 
2^3 full factorial designs: Different tablets formulations of 
Colchicine were prepared by wet granulation method. Drug, 
hydrophilic polymer, and a hydrophobic polymer, diluents 
were mixed. PVP K30 was used as the binder in wet 
granulation [Figure 4 &5]. PVP K30 dissolved in IPA and 
used as a binder. Bind the above dry mixture with PVP K30 
solution till granules are obtained. Pass granules through 20 
mesh sieve and dry in the oven at 40 °c for removal of 
moisture.
Table 4: Formulation and in vitro drug release characteristics of batches in 2³ Full Factorial Design

| Batches | HPMC K4M | HPMC K100M | EC | t₅₀ | t₈₀ | f₂ | MDT |
|---------|----------|------------|----|-----|-----|----|-----|
| F₁      | -1       | -1         | -1 | 117 | 450 | 43.91 | 153 |
| F₂      | 1        | -1         | -1 | 268 | 542 | 64.44 | 244 |
| F₃      | -1       | 1          | -1 | 129 | 496 | 52.4 | 178 |
| F₄      | 1        | 1          | -1 | 334 | 630 | 52.05 | 265 |
| F₅      | -1       | 1          | 1  | 220 | 556 | 54.79 | 186 |
| F₆      | 1        | -1         | 1  | 265 | 566 | 66.83 | 242 |
| F₇      | -1       | 1          | 1  | 256 | 554 | 68.28 | 239 |
| F₈      | 1        | 1          | 1  | 292 | 590 | 60.95 | 255 |

| Independent variable | Low (-1) | Medium (0) | High (1) |
|----------------------|----------|------------|----------|
| HPMC K4M (X1)        | 15       | 20         | 25       |
| HPMC K100M (X2)      | 3        | 6.5        | 10       |
| EC (X3)              | 3        | 5          | 7        |

Table 5: Composition of Factorial Design batches

| Ingredients          | F1 | F2 | F3 | F4 | F5 | F6 | F7 | F8 |
|----------------------|----|----|----|----|----|----|----|----|
| Colchicine           | 6  | 6  | 6  | 6  | 6  | 6  | 6  | 6  |
| HPMC K4 M            | 15 | 25 | 15 | 25 | 15 | 25 | 15 | 25 |
| HPMC K100 M          | 3  | 3  | 10 | 10 | 3  | 3  | 10 | 10 |
| Ethyl cellulose      | 3  | 3  | 3  | 3  | 7  | 7  | 7  | 7  |
| DCP                  | 30 | 30 | 30 | 30 | 30 | 30 | 30 | 30 |
| Lactose              | 60 | 50 | 53 | 43 | 56 | 46 | 49 | 39 |
| PVP K-30 in IPA      | 5 %| 5 %| 5 %| 5 %| 5 %| 5 %| 5 %| 5 %|
| Talc                 | 2 %| 2 %| 2 %| 2 %| 2 %| 2 %| 2 %| 2 %|
| Mag. Stearate        | 1 %| 1 %| 1 %| 1 %| 1 %| 1 %| 1 %| 1 %|

**In vitro drug release Study:** The in vitro release profile of formulations for 12 hours was tested according to the procedure described earlier. The in vitro drug release profiles of factorial batches are shown in Table 6. The statistical analysis of the factorial design batches was performed by multiple linear regression analysis. The t₅₀, t₈₀, f₂, and MDT values for the 8 batches (F₁ to F₈) showed a wide variation. The values of the correlation coefficient indicate a good fit.

Table 6: % Drug Release of Factorial Design batches after 12 Hr

| Time (Hr) | F1   | F2   | F3   | F4   | F5   | F6   | F7   | F8 |
|-----------|------|------|------|------|------|------|------|----|
| 0         | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00|
| 1         | 27.62| 18.73| 32.02| 16.53| 21.78| 25.20| 24.59| 18.73|
| 2         | 38.83| 31.59| 47.49| 27.93| 36.30| 34.29| 33.00| 32.35|
| 3         | 61.93| 43.11| 58.64| 35.51| 50.12| 42.81| 44.14| 42.18|
| 4         | 76.72| 50.10| 64.87| 41.85| 59.91| 49.74| 51.12| 47.51|
| 5         | 88.10| 67.54| 77.41| 56.21| 75.78| 64.56| 66.31| 60.20|
| 6         | 91.54| 79.52| 83.56| 70.50| 81.63| 77.54| 78.27| 73.39|
| 7         | 92.69| 87.65| 90.02| 77.23| 83.14| 84.39| 86.71| 82.13|
| 8         | 92.77| 90.35| 90.13| 82.12| 84.53| 86.85| 88.45| 85.22|
| 9         | 93.23| 92.10| 91.49| 83.87| 85.89| 89.97| 90.98| 88.34|
| 10        | 93.23| 92.10| 91.49| 83.87| 85.89| 89.97| 90.98| 88.34|
| 11        | 93.23| 92.10| 91.49| 83.87| 85.89| 89.97| 90.98| 88.34|
| 12        | 93.23| 92.10| 91.49| 83.87| 85.89| 89.97| 90.98| 88.34|

**THR:**
The F2 shows less initial release compared to F6 and F7 because it contains a higher amount of HPMC K4M which sustains the profile. From Batches F2, F6, and F7, batch F7 shows higher similarity than others with the theoretical profile. Also, it shows a higher f2 value than all other batches. (68.28) and it shows higher release in the initial period and sustains the release till 12 hrs matching with theoretical profile [Table 7].

Table 7: Summary of Regression analysis of Colchicine tablet

| Coefficients | t50    | t80    | f2     | MDT    |
|--------------|--------|--------|--------|--------|
| b0           | 235.125| 548    | 57.95625| 220.25 |
| b1           | 54.625 | 34     | 3.11125 | 31.25  |
| b2           | 17.625 | 19.5   | 0.46375 | 14     |
| b3           | 23.125 | 18.5   | 4.75625 | 10.25  |
| b12          | 5.625  | 8.5    | -5.03125| -5.5   |
| b23          | -1.875 | -14    | 1.43875 | 2.5    |
| b13          | -34.375| -22.5  | -1.93375| -13.25 |
| b123         | -7.875 | -2.0   | -1.93   | -4.5   |
| R²           | 0.9939 | 0.9992 | 0.9997 | 0.9932 |

Comparison of In-vitro Drug Release Profile: The similarity factor, f2, given by SUPAC guidelines for modified release dosage form was used as a basis to compare dissolution profiles. The f2 value for 68.28 of batch F7 indicates less difference in vitro drug release profile with theoretical release profile [Table 8 & 9]. The similarity between the theoretical release profile and the in vitro drug release profile of F7.

Table 8: Comparison of checkpoints between F7 batch and Theoretical profile

| Check Points | Theoretical value | Batch F7 |
|--------------|-------------------|----------|
| t50 (min)    | 242               | 256      |
| t80 (min)    | 529               | 554      |
| f2           | 50 - 100          | 68.28    |
| MDT (min)    | 278               | 239      |

Table 9: Comparison of % Drug Release of various batches after 12 Hr.

| Time (Hr) | F2       | F6       | F7       | THEORETICAL |
|-----------|----------|----------|----------|-------------|
| 0         | 0.00     | 0.00     | 0.00     | 0.00        |
| 1         | 18.73    | 22.98    | 24.59    | 31.00       |
| 2         | 31.59    | 34.29    | 33.00    | 37.27       |
| 3         | 43.11    | 42.81    | 44.14    | 43.54       |
| 4         | 50.10    | 49.74    | 51.12    | 49.81       |
| 6         | 67.54    | 64.56    | 66.31    | 62.36       |
| 8         | 79.52    | 77.54    | 78.27    | 74.90       |
| 10        | 87.65    | 84.39    | 86.71    | 87.45       |
| 11        | 90.35    | 86.85    | 88.45    | 93.72       |
| 12        | 92.10    | 89.97    | 90.98    | 100.00      |

Kinetic Modeling and Mechanism of Drug Release

All batches showed a higher correlation with the Higuchi plot than zero order and first order. Batch F1 and F3 showed Fickian diffusion-controlled release whereas other batches show the anomalous effect (combined mechanism of diffusion and case II transport). For Higuchi Model, all the batches except F1 show an r2 value of more than 0.925 [Table 10].

Table 10: Kinetic modeling of Factorial Design batches: R² Value, n value, and Release Mechanism

| Batch | Zero-order r² | First-order r² | Higuchi r² | Korsmeyer-Peppas r² | n | Release Mechanism |
|-------|---------------|---------------|------------|---------------------|---|-------------------|
| F1    | 0.768         | 0.434         | 0.925      | 0.905               | 0.496 | Fickian Diffusion |
| F2    | 0.941         | 0.542         | 0.989      | 0.991               | 0.643 | Anomalous Diffusion |
| F3    | 0.817         | 0.411         | 0.971      | 0.976               | 0.412 | Fickian Diffusion |
| F4    | 0.962         | 0.569         | 0.987      | 0.997               | 0.657 | Anomalous Diffusion |
| F5    | 0.841         | 0.472         | 0.965      | 0.951               | 0.543 | Anomalous Diffusion |
| F6    | 0.934         | 0.509         | 0.996      | 0.997               | 0.558 | Anomalous Diffusion |
| F7    | 0.931         | 0.505         | 0.995      | 0.994               | 0.554 | Anomalous Diffusion |
| F8    | 0.945         | 0.533         | 0.994      | 0.993               | 0.609 | Anomalous Diffusion |
Formulation and Evaluation of optimized Batch

Tables were prepared by the wet granulation method as discussed earlier and evaluated for various evaluation tests like Flow properties, Hardness, Friability, Average weight, In-vitro Drug Release. Results have been shown in the following table 11 & 12.

Table 11: Evaluation Parameters of Factorial Design Batches

| Parameters        | Value |
|-------------------|-------|
| Angle of Repose   | 26.75 |
| Bulk Density      | 0.53  |
| Tapped Density    | 0.62  |
| Carr’s index      | 14.51 |
| Hausner’s Ratio   | 1.16  |

Table 12: % Drug release of optimized batch after 12 Hr

| Time (Hr) | A1    | A2    | A3    | A4    | A5    | A6    | THR   |
|-----------|-------|-------|-------|-------|-------|-------|-------|
| 0         | 0.00  | 0.00  | 0.00  | 0.00  | 0.00  | 0.00  | 0.00  |
| 1         | 23.78 | 24.16 | 24.35 | 23.87 | 22.89 | 25.88 | 31.00 |
| 2         | 32.84 | 32.00 | 34.56 | 33.56 | 32.16 | 36.69 | 37.27 |
| 3         | 44.36 | 45.97 | 45.90 | 45.84 | 43.54 | 45.65 | 43.54 |
| 4         | 50.59 | 52.63 | 51.57 | 52.21 | 53.21 | 53.25 | 49.81 |
| 6         | 65.40 | 66.98 | 65.23 | 68.43 | 67.23 | 68.11 | 62.36 |
| 8         | 72.66 | 80.11 | 79.86 | 79.62 | 78.87 | 78.97 | 74.90 |
| 10        | 87.38 | 86.86 | 87.50 | 87.84 | 89.39 | 86.39 | 87.45 |
| 11        | 89.42 | 89.23 | 89.45 | 90.19 | 90.85 | 90.85 | 93.72 |
| 12        | 90.41 | 90.87 | 90.67 | 91.82 | 92.51 | 90.64 | 100.00 |

Optimized batch shows very good flow properties. It shows all the value within its range. The hardness varies in the range of 5-6 kg/cm². All six tablets show a good dissolution profile, matching well with the theoretical profile. It shows more than 90 % drug release after 12 Hrs.

CONCLUSION

After the trial work, it was concluded that batch T3 showing a promising future for factorial design to optimize the concentration of sustained-release polymer with hardness at 5-6 Kg/cm². The release rate of Colchicine decreased proportionally with an increase in polymer viscosity and polymer concentration. A 2³ full factorial design was applied to systemically optimize in vitro drug release profile. The HPMC K 4 M (X₁), HPMC K100M (X₂), and Ethyl Cellulose(X₃) were selected as independent variables. The time required for 50% drug released (t₅₀), the time required for 80% drug release (t₈₀), similarity factor f₂, and mean dissolution time (MDT) were selected as dependent variables. The similarity factor f₂ was applied between the in vitro drug release profile of factorial design batches and the theoretical drug release profile. Batch F7 showed the highest f₂ (f₂ = 68.28) among all the batches. All the batches show good linearity with Highchi’s equation. From in vitro drug release profile of all batches, batch F7 indicates similarity with desired release profile.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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