



# FORMULATION AND EVALUATION OF SUSTAIN RELEASE MATRIX TABLETS OF DICLOFENAC SODIUM AND CHLORZOXAZONE

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**Abstract:** The main aim of the present work was to formulate sustain release matrix tablets of Diclofenac sodium and chlorzoxazone using various concentration of crosslinking agents like HPMC (K15, K35) polymers. Sustain release formulation are those which delivers the drug locally or systemically at a predetermined rate for a fixed period of time. The matrix tablet was prepared by direct compression method using by various concentration of chitosan and sodium alginate with combination of various release retardant polymer. The powder mixtures were subjected to various pre-compression parameters such as angle of repose, bulk density, tapped density and Carr's index shows satisfactory result and the compressed tablets are evaluated for post-compression parameters such as weight variation, thickness, hardness, friability, drug content, in-vitro dissolution and stability studies. In-vitro dissolution studies were carried out for 24 hours using 0.1 N HCL for first 2 hours and pH 6.8 phosphate buffer for 24 hours and the result showed that formulations F4 and F7 showed good dissolution profile to control the drug release respectively. Formulation containing higher concentration of chitosan and sodium alginate along with polymers sustained the drug release for the period of 24 hours. The compatibility of the drug, polymers and other excipients were determined by FT-IR Spectroscopy. Results showed that the drug was compatible with polymers and other excipients. The release data was fitted to various mathematical models such as Zero-order, First-order, Higuchi equation and Korsmeyer- Peppas model to evaluate the kinetics and the drug release. The drug release followed first order and the mechanism was found to be non-Fickian. The stability studies were carried out for 3 months and result indicates that the selected formulations (F4 and F7) were stable.

**Key words:** Diclofenac sodium, Chlorzoxazone, Carbopol 934P, Chitosan, sodium alginate, sustain release matrix tablet.

### **Introduction:**

Sustained drug delivery systems are aimed to control the rate of drug release and to maintain desire drug level in the blood which is therapeutically effective for an extended period of time. Thus the reduction of both total dose of drug administered and the incidence of adverse side effects better patient compliance can be achieved [1, 2]. The most commonly used method for modulating the drug release is to include it in a matrix system [2]. Sustained release matrix tablet is relatively easy to fabricate by incorporating drug molecules in slowly disintegrating or inert porous materials.

Chlorzoxazone (5-chloro-2,3-dihydro-1,3-benzoxazol-2-one) is a centrally acting muscle relaxant used to treat muscle spasm and the resulting pain and discomfort [3]. Chlorzoxazone may act by inhibiting calcium and potassium influx which would lead to neuronal inhibition and muscle relaxation. It is having a shorter half life (1.1hour) with the dose administration of 3-4 times a day leads to decreased patient compliance [3, 4]. In order to decrease the frequency of drug administration and for improving better patient compliance a sustained-release formulation of Chlorzoxazone is desirable[5,6].

Diclofenac sodium was used as a model drug for patients who have osteoarthritis. The main side effects of this drug are nausea, gastritis, skin erythema and headache. In addition, this drug has a short half- life (1-2 h) and oral drug bioavailability approximately 50% due to the first-pass metabolism by the liver [7,8]. It was the basic aim to be made into sustained release dosage form that can be sustained levels of drug therapy, minimize the frequency of drug administration and overcome its side effect.[9]

Hydroxy Propyl Methyl Cellulose (HPMC) is the extensively used synthetic polymer derived from the cellulose. It is most widely used as the gel forming agent in the formulation of sustained release dosage form [10]. Its various grades have been used as release retarding agents and for different drugs [11]. When it contacts with aqueous fluids were gets hydrated and to forms the viscous gel layer through which drug will be released by diffusion and/or by erosion of the matrix [12]. Hydroxy Propyl Methyl Cellulose are non-toxic nature, undergoes easy compression, having enough swelling properties and it can accommodate high levels of drug. The rate and extent of hydration of HPMC can influence the drug release from the dosage form through polymer swelling, drug dissolution, diffusion and matrix erosion. Based on different grades of HPMC and their optimum concentration in the formulation drug release rate can be modified [10, 12]. In the present work, the individual and combination effect of different grades of HPMC were studied in Chlorzoxazone [13].

**MATERIALS AND METHODS:****MATERIALS:****Table 1: List of materials used**

| Sr. No | MATERIALS                   | COMPANY NAME                  |
|--------|-----------------------------|-------------------------------|
| 1.     | Chlorzoxazone               | Ajanta Pharma, Mumbai         |
| 2.     | Diclofenac Sodium           | Ajanta Pharma, Mumbai         |
| 3.     | HPMC-K35                    | Colorcorn, Mumbai             |
| 4.     | HPMC K15                    | Colorcorn, Mumbai             |
| 5.     | Micro crystalline cellulose | S.D fine chem limited, Mumbai |
| 6.     | Magnesium stearate          | S.D fine chem limited, Mumbai |
| 7.     | Talc                        | S.D fine chem limited, Mumbai |

**Method:**

**Preparation of sustain release matrix tablets by direct compression method** Chlorzoxazone and Diclofenac Sodium matrix tablets were prepared by direct compression method. The corresponding amount of drug and excipients were accurately weighed and mixed properly and the matrix tablets were prepared by direct compression using punching machine. Each tablet contains 80 mg of Chlorzoxazone and Diclofenac Sodium. The content was mixed thoroughly in a mixer for 10 minutes. The lubricant and glidants were added to the above mixture and again mixed for 5 minutes. Then the mixture was directly compressed on a Rotary Tablet Machine (single punch, Inco) equipped with a 8 mm standard flat faced punch and die set. The effect of HPMC K15M and HPMC K100M were studied individually and their combination at 1:1 and 1:2 ratios were also observed. The compositions of different tablet formulations are shown in Table 1.

**Table no 2: Formulation development of Chlorzoxazone and Diclofenac Sodium by direct compression technique**

| FORMULA CODE                             | F1  | F2  | F3  | F4  | F5  | F6  | F7  | F8  |
|--|-----|-----|-----|-----|-----|-----|-----|-----|
| <b>Chlorzoxazone</b>                     | 250 | 250 | 250 | 250 | 250 | 250 | 250 | 250 |
| <b>Diclofenac Sodium</b>                 | 50  | 50  | 50  | 50  | 50  | 50  | 50  | 50  |
| <b>HPMC-K35</b>                          | 10  | 20  | 30  | 50  |     |     |     |     |
| <b>HPMC K15</b>                          | -   |     |     |     | 10  | 20  | 30  | 50  |
| <b>Magnesium Stearate</b>                | 3   | 3   | 3   | 3   | 3   | 3   | 3   | 3   |
| <b>Talc</b>                              | 2   | 2   | 2   | 2   | 2   | 2   | 2   | 2   |
| <b>Micro crystalline cellulose QS to</b> | 400 | 400 | 400 | 400 | 400 | 400 | 400 | 400 |

\*All quantities are in milligrams (mg) only.

### Pre-compression Study of Powder Blend:

**Table 3: Evaluation Results of Powder Blend Diclofenac Sodium + Chlorzoxazone**

| Formulations Number | Bulk Density (gm/cc) | Tapped Density (gm/cc) | Carr's Index (%) | Hausner's Ratio | Angle of Repose ( $\theta$ ) |
|---------------------|----------------------|------------------------|------------------|-----------------|------------------------------|
| <b>F1</b>           | 0.3716±0.0011        | 0.4101±0.0025          | 7.27±0.659       | 1.177±0.0076    | 29.73 ±0.41                  |
| <b>F2</b>           | 0.3803±0.0005        | 0.4120±0.0026          | 7.58±0.514       | 1.053±0.0060    | 25.33 ±0.63                  |
| <b>F3</b>           | 0.3843±0.0015        | 0.4120±0.005           | 7.43±0.760       | 1.059±0.0088    | 28.44 ± 0.35                 |
| <b>F4</b>           | 0.376±0.0020         | 0.4270±0.0037          | 13.78±0.386      | 1.073±0.0053    | 0.52±27.48                   |
| <b>F5</b>           | 0.355±0.0017         | 0.4600±0.0024          | 17.31±0.794      | 1.224±0.011     | 0.13 ± 31.34                 |
| <b>F6</b>           | 0.3810±0.0045        | 0.4880±0.0065          | 18.42±0.120      | 1.24±0.0020     | 0.30 ± 28.26                 |
| <b>F7</b>           | 0.3850±0.0081        | 0.4384±0.133           | 10.88±0.030      | 1.123±0.0021    | 27.20 ± 0.42                 |
| <b>F8</b>           | 0.3803±0.0005        | 0.4120±0.0026          | 7.58±0.514       | 1.053±0.0060    | 24.33 ±0.63                  |

### Compatibility studies using FT-IR

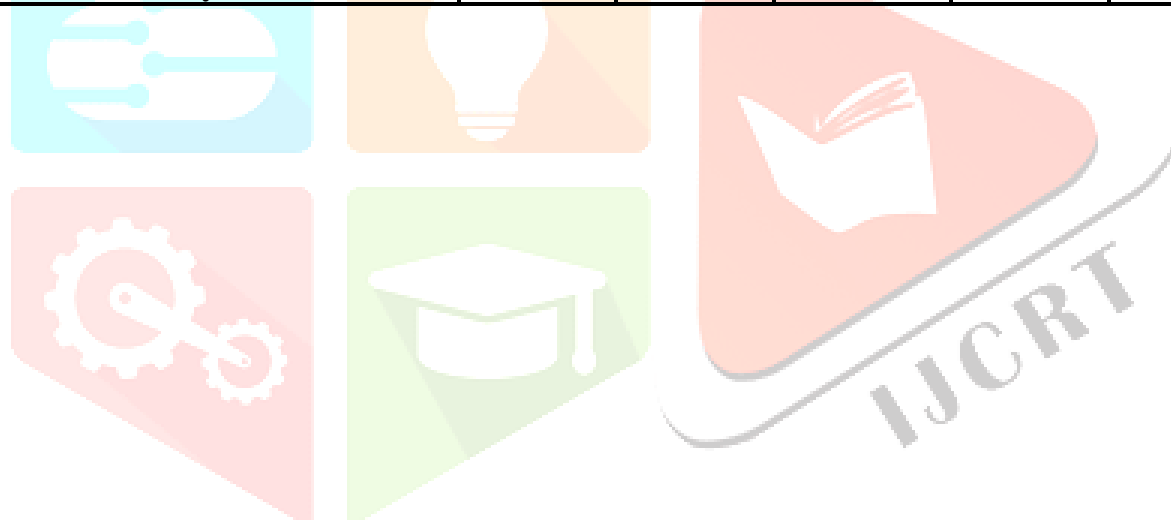
Infra-red spectrum of drug, polymers and mixture of both were determined by KBr disks method. Samples were prepared in KBr disks by means of a hydrostatic press at 5 tons pressure for 5 min and obtained spectra were shown in the **figure no: 1-4**.

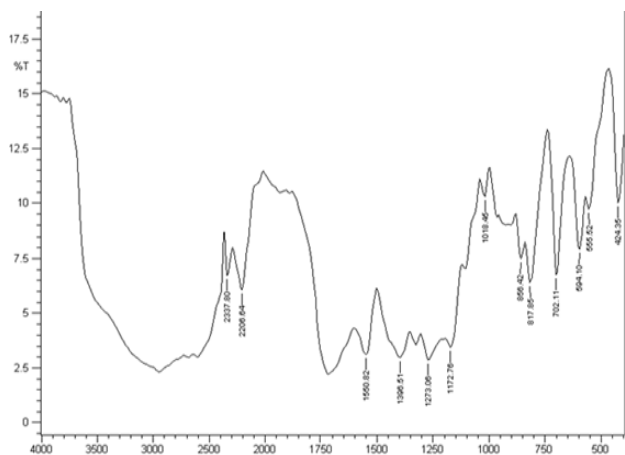
All the characteristic peaks of Chlorzoxazone and Diclofenac Sodium were present in the spectrum of drug and polymer mixture, indicating compatibility between drug and polymer. From the results, it was concluded that there was no interference of the functional group as the principle peaks of the Chlorzoxazone

and Diclofenac Sodium were found to be unaltered in the drug- polymer physical mixtures, indicating that they were compatible chemically. The spectrum confirmed that there is no significant change in the chemical integrity of the drug.

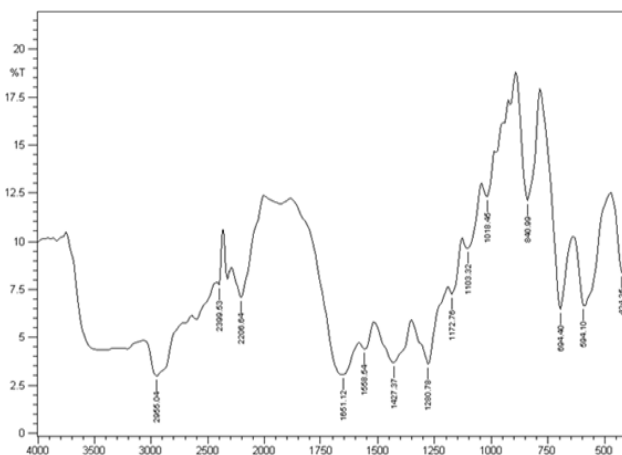
**Table 13: Interpretations of IR-spectrum**

| Ingredients  | Functional groups with wave number (cm <sup>-1</sup> ) |         |         |         |         |
|--|--|---------|---------|---------|---------|
|  | N-H (s)  | N-O (b) | C-H(b)  | C-O(s)  | O-H (b) |
| <b>Chlorzoxazone + Diclofenac Sodium</b>                               | 1651.12  | 1558.54 | 1427.37 | 1280.78 | 840.99  |
| <b>Chlorzoxazone + Diclofenac Sodium + HPMC-K35</b>                    | 1653   | 1550.82 | 1388.79 | 1273.06 | 895.00  |
| <b>Chlorzoxazone + Diclofenac Sodium + HPMC K15</b>                    | 1643.41  | 1550.82 | 1396.56 | 1273.06 | 856.42  |
| <b>Chlorzoxazone + Diclofenac Sodium + Micro Crystalline Cellulose</b> | 1650   | 1550.82 | 1396.51 | 1273.06 | 856.42  |
| <b>Chlorzoxazone + Diclofenac Sodium + Magnesium stearate</b>          | 1645   | 1550.82 | 139879  | 1273.06 | 864.14  |
| <b>Chlorzoxazone + Diclofenac Sodium + Physical Mixture</b>            | 1705   | 1550.82 | 1388.79 | 1273.06 | 864.14  |

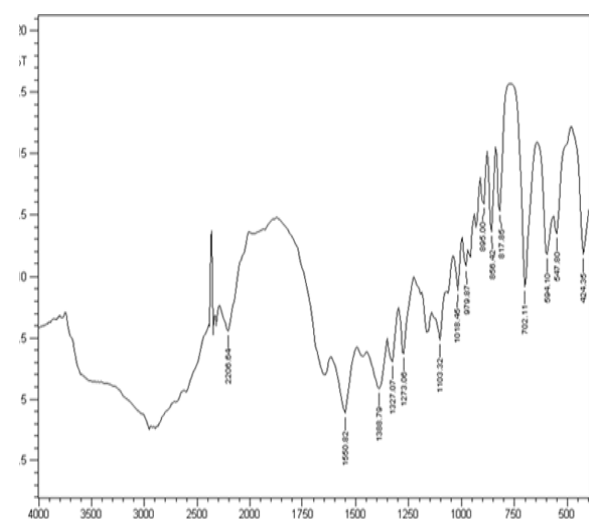




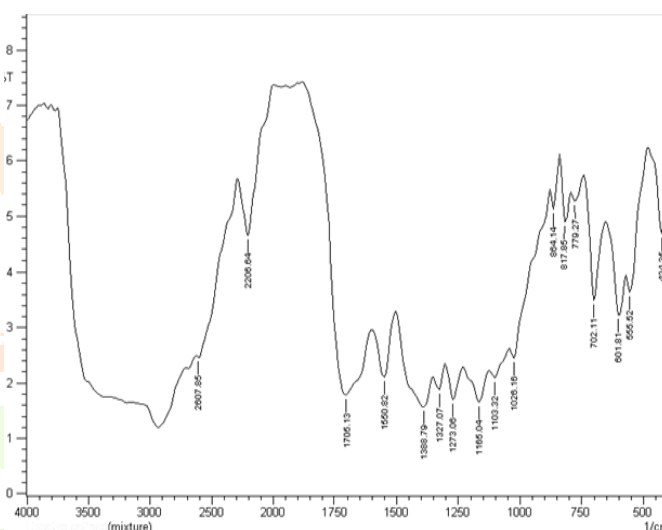
**Fig 1: IR Spectrum of Pure Drug**



**Fig 2: IR Spectrum of HPMC**



**Fig 3: IR Spectrum of MCC**



**Fig 4: Physical mixtures**

### Evaluation of Prepared tablets for post-compression study:

The oral disintegrating tablets prepared subjected for weight variation, thickness, hardness, friability, drug content, in vitro disintegrating time, wetting time, water absorption ratio, in vitro dissolution studies were carried out and the result was shown .

#### Weight Variation

With a tablet designed to contain a specific amount of drug in a specific amount of tablet formula, the weight of the tablet being made is routinely measured to help ensure that a tablet contains the proper amount of drug. In practice, 10 tablets were taken and weighed individually on a digital weighing balance. Average weight was calculated and the individual tablet weight was compared to the average. The tablet passes the test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

#### Thickness

Thickness of tablet is important for uniformity of tablet size. Thickness was measured using Vernier calliper. It was determined by checking three tablets from each formulation.

**Hardness**

Hardness is defined as the “force required to break a tablet in diametric compression test.” Hardness is hence, also termed as the tablet crushing strength. The resistance before usage depends on its hardness. Tablet hardness was measured with Pfizer hardness tester. A tablet was placed in the hardness tester and load required to crush the tablet was measured.

**Friability Test**

This test is performed to evaluate the ability of tablets to withstand abrasion in packing, handling and transporting. Friability generally reflects poor cohesion of tablet ingredients. Initial weight of 10 tablets is taken and these are placed in the friabilator, which consist of a circular plastic chamber, divided into 2-3 compartments. The chamber rotating at 25 rpm for 4 min and drops the tablets by a distance of 15 cm and gives 100 revolutions. After that the tablets are weighted once again. The difference in the weight is noted and expressed as percentage. It should be preferably below 1.0 %.

$$\% \text{ Friability} = (W1 - W2) / W1 \times 100$$

Where,

W1 = weight of tablets before test, W2 = weight of tablets after test.

**Content Uniformity**

Ten tablets were weighed and average weight is calculated. All tablets were crushed and powder equivalent to 10 mg drug was extracted with water and the solution was filtered through 0.45  $\mu$  membrane. The absorbance was measured spectrophotometrically at 284 nm against pH 6.8 phosphate buffer as a blank. Amount of drug present in one tablet was calculated.

**In- Vitro Dissolution studies**

The in vitro dissolution studies for all formulations were studied using USP type –II (paddle) dissolution test apparatus. 900 ml of phosphate buffer pH 6.8 was used as dissolution medium. The speed of the paddle was set at 50 rpm and the temperature of the medium was maintained at  $37 \pm 0.5$  °C. 5 ml samples were withdrawn at predetermined intervals up to 30 min and replacements were done with fresh dissolution medium. The samples were suitably diluted and analyzed for drug content by UV spectroscopy at 284 nm.



**Results and Discussion:****Physical evaluation of matrix tablets:**

After compression various quality control tests were carried out, which demonstrated following organoleptic properties *viz.* colour, odour and shape. All formulations (**F1 to F7**) were found to be white in colour, odourless and concave round flat with break-line on one side.

**Table no.4: Organoleptic properties of prepared tablets**

| Formulation code | Color       | Odour     | Shape   |
|------------------|-------------|-----------|---|
| F1               | White color | odourless | Concave, round and flat with break-line on one side |
| F2               | White color | odourless | Concave, round and flat with break-line on one side |
| F3               | White color | odourless | Concave, round and flat with break-line on one side |
| F4               | White color | odourless | Concave, round and flat with break-line on one side |
| F5               | White color | odourless | Concave, round and flat with break-line on one side |
| F6               | White color | odourless | Concave, round and flat with break-line on one side |
| F7               | White color | odourless | Concave, round and flat with break-line on one side |
| F8               | White color | odourless | Concave, round and flat with break-line on one side |

**Post-compression Parameters of Tablet:****Table no.5: Post-compression parameters results**

| Formulation | Diameter (mm)± SD | Thickness (mm)± SD | Weight variation (mg) | Hardness (kg/cm <sup>2</sup> ) | Friability (%) | Drug content (%) |
|-------------|-------------------|--------------------|-----------------------|--------------------------------|----------------|------------------|
| F1          | 7.82±0.012        | 3.9±0.09           | 399.89±0.12           | 7.3±0.04                       | 0.61±0.007     | 98.25±0.044      |
| F2          | 7.80±0.002        | 4.0±0.02           | 399.88±0.60           | 7.8±0.03                       | 0.52±0.005     | 100.31±0.037     |
| F3          | 7.85±0.007        | 4.2±0.01           | 401.12±0.52           | 8.0±0.07                       | 0.58±0.031     | 98.54±0.07       |
| F4          | 7.84±0.022        | 3.9±0.07           | 402.81±0.13           | 6.5±0.04                       | 0.72±0.016     | 99.67±0.087      |
| F5          | 8.0±0.015         | 4.0±0.04           | 401.80±0.32           | 6.8±0.08                       | 0.665±0.09     | 99.37±0.058      |
| F6          | 7.94±0.010        | 3.8±0.09           | 401.92±0.44           | 7.1±0.03                       | 0.714±0.01     | 98.97±0.073      |
| F7          | 7.97±0.016        | 4.1±0.01           | 402.61±0.60           | 6.0±0.05                       | 0.447±0.00     | 101.61±0.08      |
| F8          | 7.80±0.002        | 4.0±0.02           | 399.88±0.60           | 7.8±0.03                       | 0.52±0.005     | 100.31±0.037     |

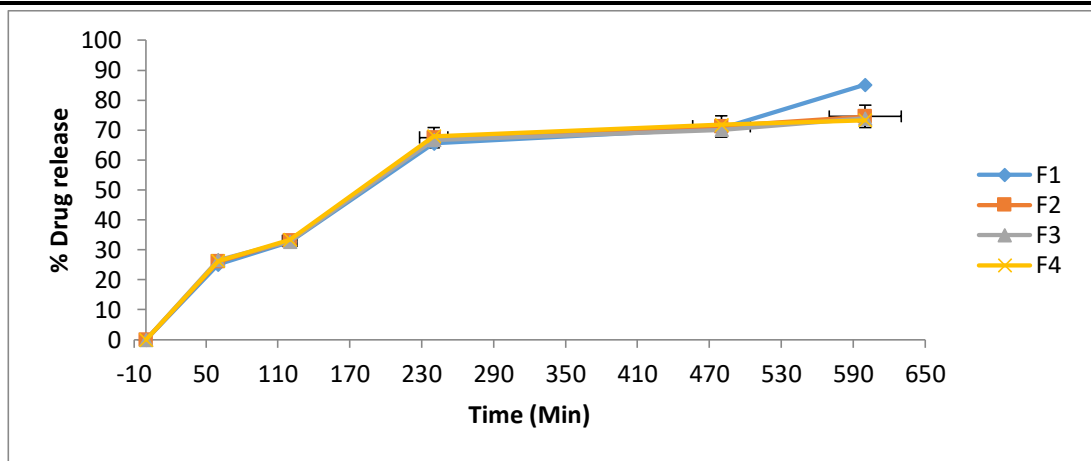


***In-vitro* drug release study:**

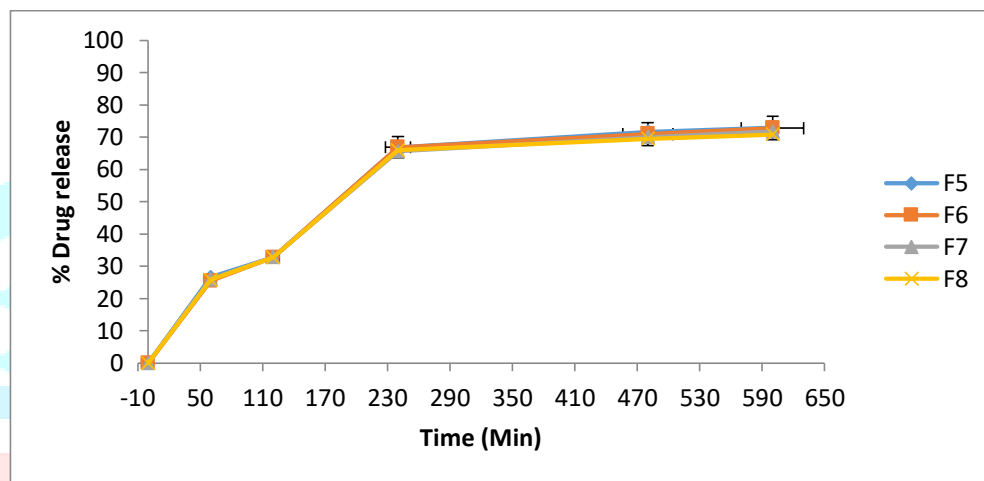
In this study HPMC (K15, K35) was chosen as polymer to explore their sustain release capability. The *in-vitro* release data for HPMC (K15, K35) based Chlorzoxazone and Diclofenac Sodium sustain released matrix tablet are represented in **table 17** and illustrated in **figure 10**. The *in-vitro* release of Chlorzoxazone and Diclofenac Sodium, from prepared matrix tablets formulations was mainly affected by dissolution medium, concentration of polymers HPMC (K15, K35). The *in-vitro* release of Chlorzoxazone and Diclofenac Sodium form prepared matrix tablets also depends on swelling behavior of the tablets, higher the tablet swells comparative the lesser amount of drug release. The *in-vitro* release study was performed in 0.1 N HCl for initial first 2 hrs, and then the medium was replaced by phosphate buffer pH 6.8) and study was continued for 12 hour. The *in-vitro* release of Chlorzoxazone and Diclofenac Sodium was higher in first 6-7 hours in all formulations. After 1 hour, approximately 19.50 % - 23.80% of Chlorzoxazone and Diclofenac Sodium from HPMC (K15, K35) tablets polymer has been released. Initially amount of drug release was higher but after 6-7 hrs drug release was retarded. Formulation F<sub>1</sub> do not contains any crosslinking agent, so almost all drugs was released at the end of 12 hrs. Formulation F<sub>2</sub>, F<sub>3</sub>, F<sub>5</sub>, and F<sub>6</sub> containing lower concentration of HPMC (K15, K35) showed almost all drug release within 10 hrs, 11 hrs, 12 hrs. respectively. Thus these formulations were not considered as good formulation as the maximum amount of drug was released before desire period of time i.e. 12 hrs. The ionic interaction between crosslinking agents and negatively charged polymers was greatly reduced at this pH 6.8 and forms a loose network with increase porous surface which allows great part of dissolution media. Formulation F<sub>3</sub> and F<sub>8</sub> containing highest concentration of HPMC (K15, K35) prolong the release of Chlorzoxazone and Diclofenac Sodium to 12 hrs. which might be due to the fact that the self-assembled poly electrolyte complexes film was formed on the surface of cross linking agent-polymer based system. Swelling study also showed that formulation which contains higher concentration of cross linking agent showed higher swelling capacity and prolonged the drug release to 12 hrs.

**Table 6: In-vitro drug release profile of Chlorzoxazone and Diclofenac Sodium sustain release matrix tablets.**

| Time (Hrs) | Cumulative Percentage Drug Release |                |                |                   |                |                |                   |                   |
|------------|------------------------------------|----------------|----------------|-------------------|----------------|----------------|-------------------|-------------------|
|            | F <sub>1</sub>                     | F <sub>2</sub> | F <sub>3</sub> | F <sub>4</sub>    | F <sub>5</sub> | F <sub>6</sub> | F <sub>7</sub>    | F <sub>8</sub>    |
| 0          | 0                                  | 0              | 0              | 0                 | 0              | 0              | 0                 | <b>18.34±0.43</b> |
| 1          | 25.12±0.09                         | 18.34±0.43     | 15.386±0.33    | 10.29±0.55        | 21.91±0.54     | 18.25±0.32     | 16.90±0.85        | <b>29.24±0.21</b> |
| 2          | 40.02±0.12                         | 29.24±0.21     | 26.905±0.45    | 25.64±0.62        | 30.92±0.43     | 29.25±0.22     | 25.99±0.42        | <b>35.45±0.33</b> |
| 4          | 58.82±0.14                         | 35.45±0.33     | 31.465±0.21    | 30.94±0.53        | 39.33±0.54     | 35.20±0.64     | 33.71±0.79        | <b>48.71±0.2</b>  |
| 6          | 72.41±0.14                         | 48.71±0.2      | 46.137±0.13    | 41.54±0.45        | 51.64±0.51     | 48.82±0.73     | 41.55±0.54        | <b>59.99±0.54</b> |
| 8          | 80.03±0.28                         | 59.99±0.54     | 52.186±0.43    | 48.96±0.38        | 63.93±0.65     | 61.73±0.85     | 54.08±0.64        | <b>68.41±0.55</b> |
| 10         | 91.61±0.34                         | 68.41±0.55     | 63.97±0.4      | 59.68±0.42        | 72.96±0.72     | 69.40±0.88     | 61.27±0.53        | <b>77.09±0.22</b> |
| 12         | 99.07±0.12                         | 77.09±0.22     | 71.33±0.5      | 63.38±0.38        | 81.23±0.42     | 77.73±0.95     | 75.14±0.43        | <b>85.86±0.26</b> |
| 14         | --                                 | 85.86±0.26     | 76.50±0.6      | 74.11±0.43        | 89.37±0.45     | 86.24±0.76     | 82.67±0.48        | <b>92.15±0.33</b> |
| 16         | --                                 | 92.15±0.33     | 85.96±0.6      | 83.39±0.14        | 95.39±0.62     | 92.28±0.87     | 88.75±0.48        | <b>99.31±0.42</b> |
| 18         | --                                 | 99.71±0.42     | 90.88±0.5      | 85.21±0.11        | 99.77±0.11     | 95.62±0.73     | 92.23±0.48        |                   |
| 20         | --                                 | --             | 98.54±0.4      | 93.39±0.14        | --             | 99.99±0.61     | 94.54±0.48        |                   |
| 24         | --                                 | --             | --             | <b>99.54±0.11</b> | --             | --             | <b>98.78±0.48</b> |                   |



**Fig 1: Fig 2: *In-vitro* drug release profile of Chlorzoxazone and Diclofenac Sodium sustain release matrix tablets F1 to F4.**



**Fig 2: *In-vitro* drug release profile of Chlorzoxazone and Diclofenac Sodium sustain release matrix tablets F5 to F8.**

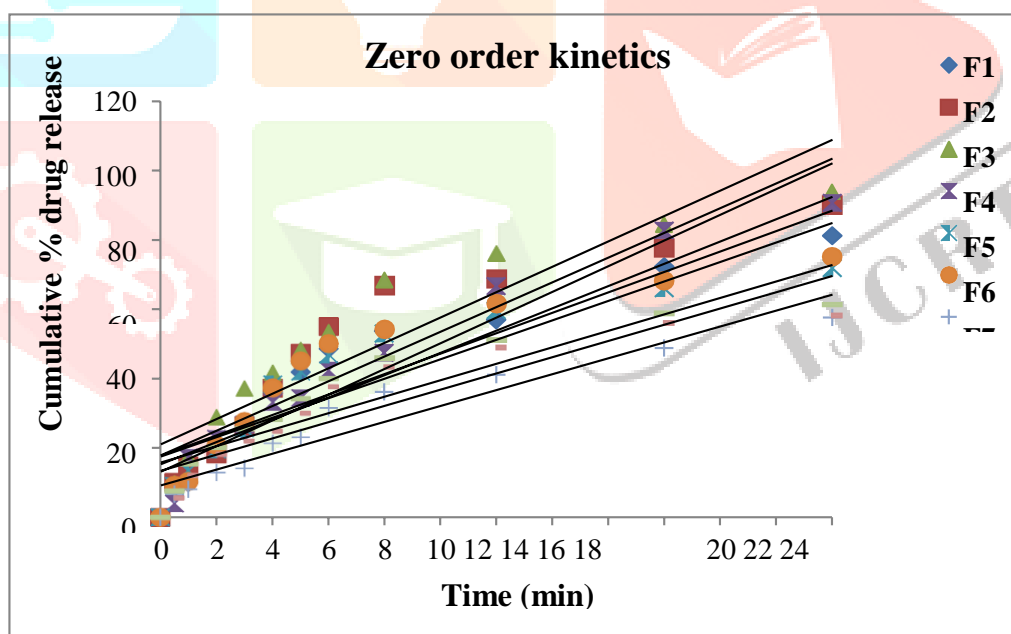
#### Release kinetic studies:

The *in-vitro* drug release data of all formulations were analyzed for determining kinetics of drug release. The obtained data were fitted to zero order kinetics, first order kinetics and Higuchi model. The highest correlation coefficient ( $r^2$ ) obtained from these method gives an idea about model best fitted to the release data. From the results of kinetic studies, the examination of correlation coefficient „ $r$ “ indicated that the drug release followed **first order release kinetics**. It was found that the value of „ $r$ “ for first order ranged from **0.981-0.992**, which is near to 1 when compared to Higuchi square root ranged from **0.892-0.958** and zero order ranged from **0.895-0.969**. So, it was understood to be following first order release pattern followed by all formulations. Further, to understand the drug release mechanism, the data were fitted into Korsmeyer Peppas exponential model  $M_t / M_a = Kt^n$ . Where  $M_t / M_a$  is the fraction of drug released after time ‘ $t$ ’ and ‘ $k$ ’ is kinetic constant and ‘ $n$ ’ release exponent which characterizes the drug transport mechanism. The release exponent ( $n$ ) ranges in between **0.483-0.7911**. For all the formulations  $F_1$  to  $F_9$  the values for ‘ $n$ ’

ranged above **0.89** which indicates that all the formulations followed **non-fickian** release mechanism. The relative complexity of the prepared formulations may indicate that the drug release mechanism was possibly controlled by the combination of diffusion and erosion.

**Table no. 7: Release exponent values and release rate constant values for different formulations**

| Batch          | Zero order     | First order    | guchi's plots  | Korsmeyer-Peppas plots |        | Best fit Model | Drug release mechanism |
|----------------|----------------|----------------|----------------|------------------------|--------|----------------|------------------------|
|                | R <sup>2</sup> | R <sup>2</sup> | R <sup>2</sup> | R <sup>2</sup>         | N      |                |                        |
| F <sub>1</sub> | 0.9293         | 0.982          | 0.9116         | 0.912                  | 0.597  | First order    | Non-Fickian            |
| F <sub>2</sub> | 0.969          | 0.974          | 0.8944         | 0.915                  | 0.594  | First order    | Non-Fickian            |
| F <sub>3</sub> | 0.916          | 0.984          | 0.9217         | 0.899                  | 0.6077 | First order    | Non-Fickian            |
| F <sub>4</sub> | 0.946          | 0.978          | 0.8926         | 0.892                  | 0.577  | First order    | Non-Fickian            |
| F <sub>5</sub> | 0.944          | 0.992          | 0.9581         | 0.902                  | 0.488  | First order    | Non-Fickian            |
| F <sub>6</sub> | 0.895          | 0.958          | 0.9022         | 0.929                  | 0.7911 | First order    | Non-Fickian            |
| F <sub>7</sub> | 0.896          | 0.981          | 0.9258         | 0.938                  | 0.4838 | First order    | Non-Fickian            |
| F <sub>8</sub> | 0.916          | 0.984          | 0.9217         | 0.899                  | 0.6077 | First order    | Non-Fickian            |



**Figure 3: Comparative Zero Order release profile of formulations F<sub>1</sub> to F<sub>8</sub>.**

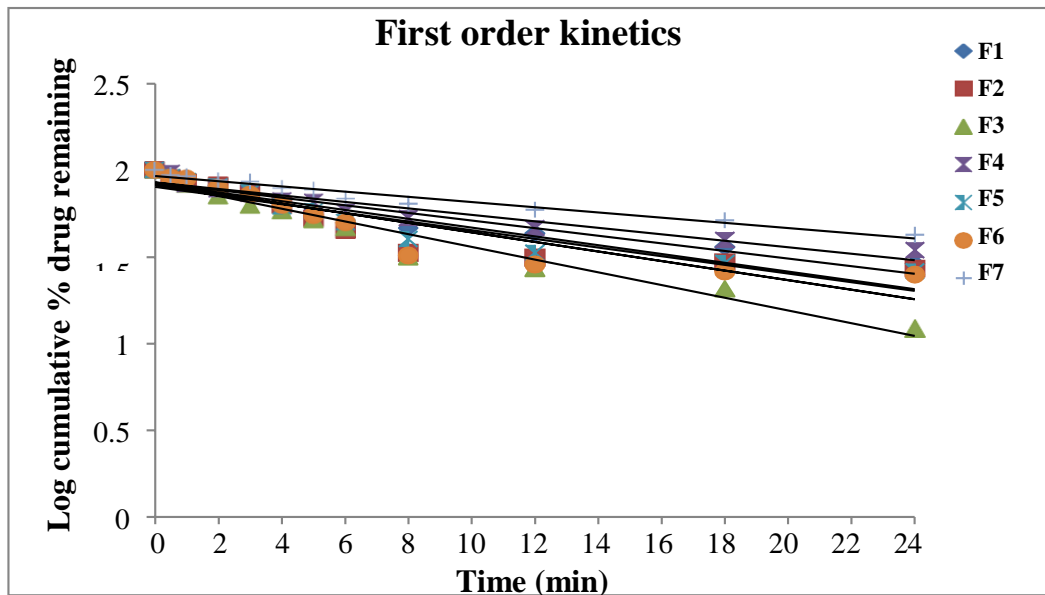


Figure 4: Comparative First Order release profile of formulations F<sub>1</sub> to F<sub>8</sub>

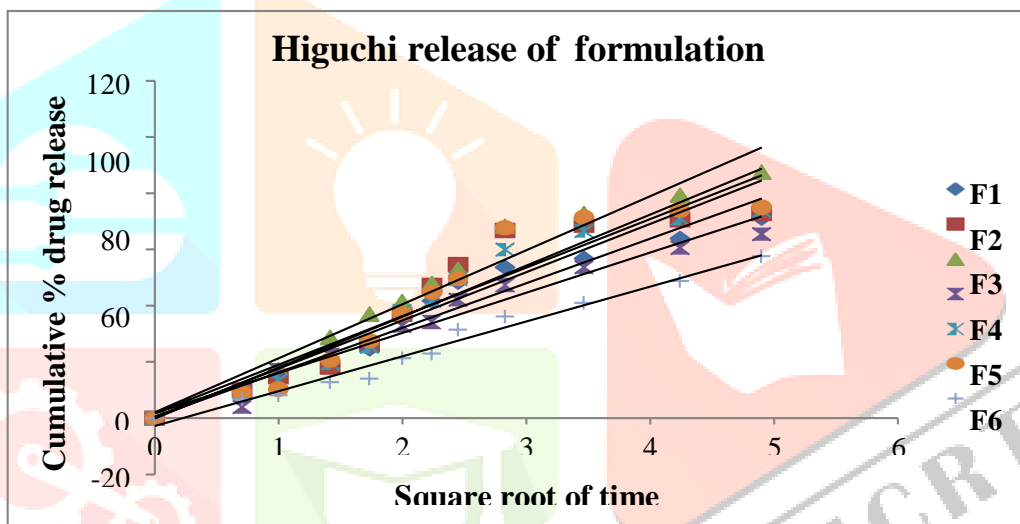


Figure 5: Comparative Higuchi release profile of formulations F<sub>1</sub> to F<sub>8</sub>

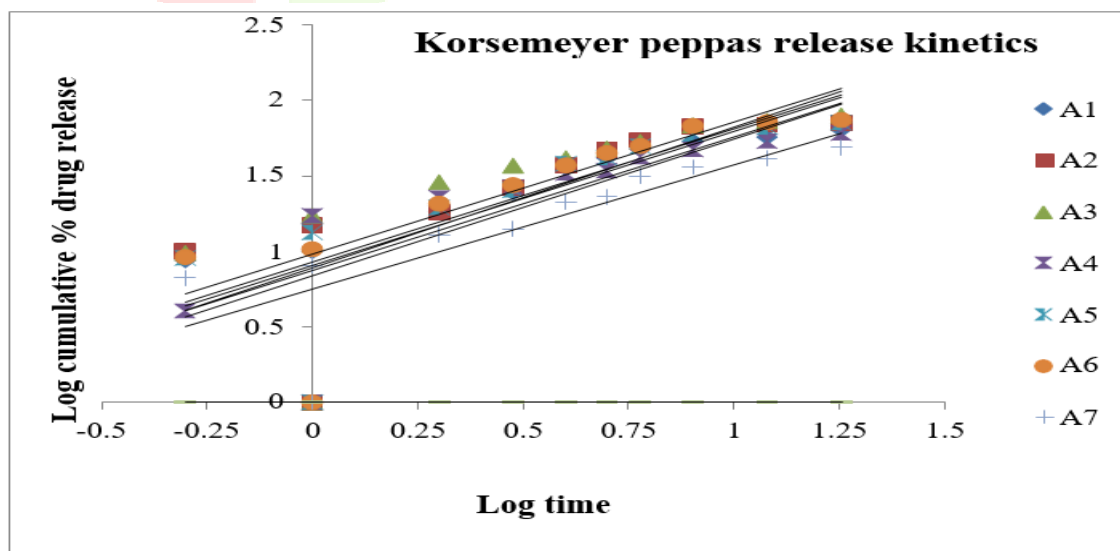


Fig 14: Comparative Korsmeyer peppas release profile of formulations F<sub>1</sub> to F<sub>8</sub>.

**DISCUSSION:**

The conc. Of the polymer increases than the drug release decreases.

1. The conc. Of the polymers K35 conc is 10 (F1) Batch , The drug release is 85.11% .
2. The conc. Of the polymers K35 conc is 20 (F2) Batch , The drug release is 74.56% .
3. The conc. Of the polymers K35 conc is 30 (F3) Batch , The drug release is 73.95% .
4. The conc. Of the polymers K35 conc is 50 (F4) Batch , The drug release is 73.32% .
5. The conc. Of the polymers K15 conc is 10 (F5) Batch , The drug release is 72.92% .
6. The conc. Of the polymers K15 conc is 20 (F6) Batch , The drug release is 72.74% .
7. The conc. Of the polymers K15 conc is 30 (F7) Batch , The drug release is 71.70% .
8. The conc. Of the polymers K15 conc is 50 (F8) Batch , The drug release is 70.76% .

**SUMMARY AND CONCLUSION****Summary:**

Diclofenac exerts its action via inhibition of prostaglandin synthesis by inhibiting cyclooxygenase-1 (COX-1) and cyclooxygenase-2 (COX-2) and Chlorzoxazone (INN) is a centrally acting muscle relaxant used to treat muscle spasm and the resulting pain or discomfort. It acts on the spinal cord by depressing reflexes. In combination of this drug are used to treat the irritable bowel syndrome Due to its shorter half- life and frequent administration, this drug was selected as candidate for developing sustain released matrix tablets. The oral route is the route most often used for administration of drugs. Tablets are the most popular oral formulations available in the market and are preferred by patients and physicians alike. Sustain release dosage forms have been demonstrated to improve therapeutic efficiency by maintenance of a steady drug plasma concentration 2-3 times.

The use of polymers in sustaining the release of drugs has become an important tool in the formulation of pharmaceutical dosage forms. Sustain release can be achieved by using HPMC K15 & HPMC K35 cross-linking agents and other excipients used were MCC as a direct compressible agent, talc and magnesium stearate as a glidant and lubricating agent respectively.

- Drug and excipients were subjected for compatibility study using FT-IR, which suggested that there was no interaction between drug and excipients.
- All the formulations were subjected for various pre-compression studies such as angle of repose, bulk density, tapped density, Carr's index, Hausner's ratio and results revealed that the powder mixtures showed good to acceptable flow and compressibility properties.
- All the formulations were subjected for various post-compression studies such as weight variation, hardness, thickness, friability, drug content and *in-vitro* dissolution studies. The hardness and thickness of prepared tablets were found in the range of 6.0 to 8.0 kg/cm<sup>2</sup> and 7.8-8.0 mm and all other parameters were within the standard official specifications.
- The results of *in-vitro* dissolution study indicated that the drug release from formulation F<sub>1</sub> and F<sub>8</sub> showed 70.76% and 85.11% respectively at the end of 12 hours in sustain manner.
- To analyze the mechanism of drug release from the matrices, the *in-vitro* drug release data were fitted to

Zero order, First order, Higuchi and Korsmeyer's-Peppas model.

It was observed that the release of drug followed first order and the mechanism was found to be non-Fickian.

## CONCLUSION:

The following conclusions can be drawn from the result obtained. The pre-formulation studies like angle of repose, bulk density, tapped density Hausner's ratio and Carr's index of all formulations were found to be within the standard limits. FTIR studies revealed that there was no chemical interaction between drug and other excipients. The powder mixtures were compressed into tablet and evaluated for post-compression parameters like weight variation, thickness, hardness, friability and drug content. All the formulation batches showed acceptable results.

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