FORMULATION AND EVALUATION OF SUSTAINED RELEASE MATRIX TABLETS OF GLIBENCLAMIDE
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Abstract

Treatment of diabetes mellitus (DM) with conventional dosage forms is not effective as the drugs do not reach the site of action in appropriate concentration and it also requires frequent dosing. Thus an effective and safe therapy of diabetes mellitus disorder using specific drug delivery system is a challenging task to the pharmaceutical technologists. Most commonly used method of modulating the drug release is to include it in a matrix system. The objective of the present study was to develop hydrophilic polymer (HPMC) and hydrophobic polymer (Ethyl cellulose) based Glibenclamide matrix sustained release tablet which can release the drug up to time of 14 hrs in predetermined rate. The formulation of Glibenclamide matrix tablet was prepared by the polymer combination in order to get required theoretical release profile. The influence of hydrophilic and hydrophobic polymer and granulation technique on Glibenclamide was studied. The formulated tablet were also characterized by physical and chemical parameters like drug content, hardness, friability, swelling index etc. all the formulations had shown the results within prescribed limits. The in vitro drug release study indicates that formulation GBF7 containing EC, HPMC K100M in 1:2 ratios shows good release pattern for 14 hours compared to other formulations. The in–vitro release data was well fit to Peppas and Hixon crowel release kinetics. The short term stability study proven no change in the formulation upon ageing and it indicates good stability.

Key Words: Glibenclamide, Matrix tablet, Hydrophobic, Hydrophilic, Polymer.

Introduction:

The oral route for drug delivery is the most popular, desirable, and most preferred method for administrating therapeutically agents for systemic effects because it is anatural, convenient, and cost effective to manufacturing process.
The treatment of an acute or a chronic illness by delivery of the drugs to the patients using various pharmaceutical dosage forms, including tablets, capsules, pills, suppositories, creams, ointments, injectables etc., as drug carriers started years back.¹

One of the most common approaches used for prolonging the rate of drug release is incorporating the drug in a hydrophilic colloidal matrix such as Hydroxypropylmethylcellulose, Hydroxypropyl cellulose, Carbopols, Chitosan, Alginates and Gelatinetc. The mechanism and kinetics of release of drugs incorporated in these polymer matrices is depends the type and amount of polymer as well as on the physico-chemical properties of drug substance. Generally the drug release from these matrices includes penetration of fluid, followed by dissolution of drug particles and diffusion through fluid filled pores. The diffusion of drug through a matrix is a rate-limiting step.²

Present sustained release drug delivery systems are for a maximum of 10 hours clinical effectiveness. Such systems are primarily used for the drugs with short elimination half life.

To achieve better therapeutic action various types of drug delivery systems are available, out of which sustained release systems are gaining much importance because of their wide advantages over others like ease of administration, convenience and non-invasiveness.

Oral route is the most commonly used route for drug administration. Although different route of administration are used for the delivery of drugs, oral route remain the preferred mode. Even for sustained release systems the oral route of administration has been investigated the most because of flexibility in designing dosage forms.

The term drug delivery can be defined as techniques that are used to get the therapeutic agents inside the human body. Conventional drug therapy requires periodic doses of therapeutic agents. These agents are formulated to produce maximum stability, activity and bioavailability. For most drugs, conventional methods of drug administration are effective, but some drugs are unstable or toxic and have narrow therapeutic ranges.³

**Materials and Methods**

Glibenclamide was procured from cipla pharmaceuticals, Goa, HPMC K₄M, K100M was procured from Rolex Chemical Industries, Mumbai, Ethyl cellulose was obtained from karnataka fine chemicals, Bangalore. All other chemicals and reagents used were of analytical grade.
Pre formulation Studies:

The IR spectrum of drug was recorded using Shimadzu FTIR Spectrophotometer 8400S. The observations are shown in figure 1-4.

Drug -Excipients Compatibility Studies:

The compatibility of drug and polymers under experimental condition is important prerequisite before formulation. Incompatibility between drugs and excipients can alter stability and bioavailability of drugs, thereby, affecting its safety and/or efficacy. Study of drug excipient compatibility is an important process in the development of a stable solid dosage form. Drug excipient compatibility testing at an early stage helps in the selection of excipients that increases the probability of developing a stable dosage form.

Method: IR spectra of drug and drug excipient blends were recorded on an IR spectrophotometer in the range of 4000–500 cm\(^{-1}\) using potassium bromide discs.

Preparation of matrix tablets of Glibenclamide:

Matrix tablets containing 12mg of Glibenclamide along with various amounts of polymers such as HPMC (Various grades) Ethylcellulose, and other excipients (such as magnesium stearate, Dibasic Calcium Phosphate Anhydrate and Aerosil) were used and tablets were prepared by direct compression technique. Ethyl Cellulose and HPMC were passed through mesh No.40. In the first step, the drug and ingredients with the exception of magnesium stearate were blended in a V-Cone blender for 5 minutes. Then magnesium stearate was added and formulation was mixed for an additional 2 minutes. Desired amount of blend was directly compressed into tablets using rotary tablet compression machine. Before compression, the surfaces of the die and punch were lubricated with magnesium stearate.

Table-1: Formulation of Glibenclamide Sustained Release Matrix Tablet.

<table>
<thead>
<tr>
<th>Formulation Ingredient</th>
<th>GBF1</th>
<th>GBF2</th>
<th>GBF3</th>
<th>FBF4</th>
<th>GBF5</th>
<th>GBF6</th>
<th>GBF7</th>
<th>GBF8</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glibenclamide (mg)</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Ethyl Cellulose (mg)</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>HPMC K4M</td>
<td>24</td>
<td>30</td>
<td>36</td>
<td>42</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>HPMC K100M</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>24</td>
<td>30</td>
<td>36</td>
<td>42</td>
</tr>
<tr>
<td>Dibasic Calcium Phosphate (mg)</td>
<td>93</td>
<td>87</td>
<td>81</td>
<td>75</td>
<td>93</td>
<td>87</td>
<td>81</td>
<td>75</td>
</tr>
</tbody>
</table>
Evaluation of Pre-Compressive Parameters

A) Bulk Density

It is the ratio of powder to bulk volume. The bulk density depends on particle size distribution, shape and cohesiveness of particles.

Accurately weighed quantity of powder was carefully poured into a graduated measuring cylinder through a large funnel and volume was measured which is called initial bulk volume. Bulk density is expressed in gm/cc and is given by,

$$D_b = \frac{M}{V_o}$$

Where, $D_b =$ Bulk density (gm/cc)

$M$ is the mass of powder (g)

$V_o$ is the bulk volume of powder (cc)

B) Tapped Bulk Density:

Ten grams of powder was introduced into a clean, dry 100ml measuring cylinder. The cylinder was then tapped 100 times from a constant height and tapped volume was read. It is expressed in gm/cc and is given by,

$$D_t = \frac{M}{V_t}$$

Where, $D_t =$ Tapped density (gm/cc)

$M$ is the mass of powder (g)

$V_t$ is the tapped volume of powder (cc)

C) Hausner’s factor

Hausner found that the ratio $D_t/D_o$ was related to inter particle friction and, as such, could be used to predict powder flow properties.

$$\text{Hausner’s factor} = \frac{\text{Tapped bulk density}}{\text{Poured bulk density}}$$

D) Carr’s Compressibility Index

The compressibility of the powder was determined by the Carr’s compressibility index.

$$\text{Carr’s Index} = \frac{\text{TBD- LBD}}{\text{TBD}} \times 100$$

<table>
<thead>
<tr>
<th>Magnesium stearate (mg)</th>
<th>1.5</th>
<th>1.5</th>
<th>1.5</th>
<th>1.5</th>
<th>1.5</th>
<th>1.5</th>
<th>1.5</th>
<th>1.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aerosil (mg)</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
<td>1.5</td>
</tr>
</tbody>
</table>
Angle of Repose: $8$

It is measured to find frictional forces in loose powder or granules. It is the maximum angle possible between the surface of a pile of powder or granules and horizontal plane.

$$\tan \theta = \frac{h}{r} \quad \text{or} \quad \theta = \tan^{-1} \left( \frac{h}{r} \right)$$

The values $\leq 30$ indicates the free flowing powder and values $\leq 40$ suggest poorly flowing material shown in table.

F. Total Porosity

Total porosity was determined by measuring the volume occupied by a selected weight of a powder ($V_{\text{bulk}}$) and the true volume of the powder blend (The space occupied by the powder exclusive of spaces greater than the intermolecular spaces, $V$).

$$\text{Porosity} \% = \frac{V_{\text{bulk}} - V}{V_{\text{bulk}}} \times 100$$

G. Flowrate

Flow rate of granules influences the filling of die cavity and directly affects the weight of the tablets produced.

**Method:** 5gm of the tablet granules was weighed and introduced into the hollow glass tube having length of 9 cms and diameter of 1cm, the flow of granules from one mark to another mark was noted down on the glass tube in seconds.

Average of three determinations was taken.

Evaluation of Post Compressive Parameters

a) **Thickness and diameter:**

The thickness and diameter of the tablet was measured using Vernier calipers. It is measured in mm.

b) **Hardness**

The Monsanto hardness tester was used to determine the tablet hardness. The tablet was held between affixed and moving jaw. Scale was adjusted to zero; load was gradually increased until the tablet fractured. The value of the load at that point gives a measure of hardness of the tablet. Hardness was expressed in Kg/cm$^2$.

c) **Friability (F):**

Tablet strength was tested by Friabilator USPEF-2. Pre weighed tablets were allowed for100 revolutions (4min), taken out and were deducted. The percentage weight loss was calculated by rewriting the tablets. The % friability was then
calculated by

\[ F = \frac{(W_{\text{final}}) - (W_{\text{final}})}{(W_{\text{initial}})} \times 100 \]

d) Weight variation test\(^9\)

The weight of the tablet being made is routinely measured to ensure that a tablet contains the correct amount of drug. The USP weight variation test was done by weighing 20 tablets individually, calculating the average weight and comparing the individual weights to the average. The tablets meet the USP test if not more than 2 tablets are outside the percentage limits and if not able to differ by more than 2 times the percentage limit. USP official limits of percentage deviation of tablet are presented in the following table,

\[ PD = \frac{(W_{\text{avg}}) - (W_{\text{initial}})}{(W_{\text{avg}})} \times 100 \]

Where, \( PD = \) Percentage deviation, \( W_{\text{avg}} = \) Average weight of tablet,

\( W_{\text{initial}} = \) individual weight of tablet.

(f) Swelling characteristics of matrix tablets\(^{10}\)

The swelling properties of matrix tablets were determined by placing the tablet in the dissolution medium at 37±0.5°C. The tablets were removed periodically from the dissolution medium. After draining off the free water from the surfaces, they were measured for weight gain. Swelling characteristics of matrix tablets were expressed in terms of percentage water uptake (WU %) it is calculated by using the equation,

\[ WU\% = \frac{\text{Wt. of swollen tablet} - \text{Initial wt. of tablet}}{\text{Initial wt. of tablet}} \times 100 \]

(g) Uniformity of drug content

Five tablets of various formulations were weighed individually and powdered. The powder equivalent to average weight of tablets was weighed and drug was extracted in Phosphate buffer pH 6.8, the drug content was determined measuring
(h) **In-vitro Dissolution studies**

The developed formulations of Glibenclamide were subjected in vitro dissolution studies using USP – Type I dissolution apparatus (Veego, India) with a paddle speed of 50rpm. The dissolution study was carried out in 900 ml of two different dissolution media i.e. first 2 hrs in pH 1.2 followed by SIF pH 6.8 buffer maintained at 37±0.5°C. At suitable time interval, 10 ml samples were withdrawn and replaced with equivalent amount of fresh medium to maintain sink conditions. Samples withdrawn were filtered and analyzed at 254nm using a UV spectrophotometer. After analyzing the drug content in the dissolution samples plot of cumulative percentage of drug release versus time was plotted. The general conditions for in vitro dissolution studies are as summarized.

**Results and Discussion**

Matrix tablets of Glibenclamide were developed with a view to deliver the drugs in a sustained manner. Analytical method was developed and, pre formulation studies were carried out, formulations were developed, and stability studies was done. MS-Excel and MS Word were used for calculations including graphs and word processing respectively. The details of results and discussion are given in the following sections.

**8.1 Analysis of Drug**

**i] Description:** Visual inspection of drug was done for the candidate drug and it is found to be white crystalline powder, without any characteristic odour.

**ii] Melting point:** It was found to be in the range of 166.7 ± 0.577 °C (Literature value 169 °C)

**iii] FTIR Spectroscopy:** FT-IR spectra were recorded on samples in potassium bromide disks using shimadzu FT-IR8400S spectrophotometer. Sample was prepared in potassium bromide disks by means of a hydrostatic pallet ress (typeKP919). The scanning range was 250-4000 Cm -1 and the resolution was 4 cm -1 . Figure 8 shows qualitative identification for Glibenclamide.

**Table-02: Data of FT-IR spectra.**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>-C=O, amide</td>
<td>1689 cm⁻¹</td>
</tr>
<tr>
<td>-C=O, urea</td>
<td>1661 cm⁻¹</td>
</tr>
<tr>
<td>Ar-CH stretching</td>
<td>1525 cm⁻¹</td>
</tr>
<tr>
<td></td>
<td>Value</td>
</tr>
<tr>
<td>----------------------</td>
<td>---------</td>
</tr>
<tr>
<td>Ar-CH Bending</td>
<td>1443 cm⁻¹</td>
</tr>
<tr>
<td>SO₂NH</td>
<td>1333 cm⁻¹</td>
</tr>
<tr>
<td>SO₂NH</td>
<td>1159 cm⁻¹</td>
</tr>
</tbody>
</table>

Figure No.1: IR Spectra of Pure drug Glibenclamide

Figure No.2: IR Spectra of Glibenclamide with Ethyl Cellulose

Figure No.3: IR Spectra of Glibenclamide with HPMC K4M
Evaluation of Powder Flow Properties:

Powder prepared for direct compression method was evaluated by measuring the parameters such as; bulk density, angle of repose, Hausner’s ratio, compressibility index and drug content. The results are shown in Table 02.

**Angle of Repose:** There sults of angle of repose (<30) indicate good flow properties and the values for prepared formulations ranges from 22 to 26.

**Hausner’s Factor:** The values of Hausner’s factor are under satisfactory range.

**Compressibility Index:** The values upto15% resulting ood to excellent flow properties and values for all formulation ranges from 16.352 to 21.897%.

**Drug Content:** The values for all the formulations were in the ranges from 89.68 to 94.45%.

All these results obtained indicate that the granules possess satisfactory flow properties, compressibility, and uniform drug content.

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Angle of repose</th>
<th>Loose Bulk density (g/ml)</th>
<th>Tapped Density (g/ml)</th>
<th>Hausner’s ratio</th>
<th>Carr’s Index (%)</th>
<th>Drug content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBF1</td>
<td>23.26 ±0.011</td>
<td>0.4457 ±0.005</td>
<td>0.5903 ±0.0041</td>
<td>1.182 ±0.023</td>
<td>18.367 ±1.81</td>
<td>92.87</td>
</tr>
<tr>
<td>GBF2</td>
<td>22.36 ±0.015</td>
<td>0.4367 ±0.0068</td>
<td>0.5832 ±0.0045</td>
<td>1.198 ±0.05</td>
<td>16.396 ±1.41</td>
<td>90.24</td>
</tr>
</tbody>
</table>
Evaluation of tablets:

The tablet formulations were subject to various post-compressive evaluation tests, such as thickness, diameter, and uniformity of weight, drug content, and hardness, friability, swelling characteristics, and in vitro dissolution studies. The results for all the formulations were shown in Table 3 and 4.

**Thickness:**

The results of thickness for tablets were determined using a calibrated dial calliper and results are shown in Table No.15. Tablet mean thickness (n=3) were almost uniform in all the formulations and values for core tablets ranged from 2.97±0.18mm to 3.10±0.10 mm. The standard deviation values indicated that all the formulations were within the range and show uniform thickness.

**Weight Variation Test:**

It was carried out as per official method and the average percentage deviation of all the formulation was found to be within the limit (as per Pharmacopoeial standard the deviations should not be more than 5% for tablethaving weight 150 mg). All formulations showed values within ranges.

**Content Uniformity:**

It was carried out as per official method and it was found that all batches shows good content uniformity. It was found that all batches shows percent drug content more than 97 percent.
Hardness test: states that all the formulations were found in the range 6.72 to 7.72 kg/cm².

Friability test: Another measure of tablet hardness was the friability. Compressed tablets that lose less than 1% of their weight are generally considered acceptable. For all formulation tried here the weight loss was<1 % hence acceptable.

Disintegration test: The tablet of all the batches does not disintegrated but formed swelled masses.

Swelling factor: The swelling characteristics of matrix tablets were studied and the results are shown in Table No: 04.

Table-03: Physical Characteristics of Glibenclamide Matrix Tablets.

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Thickness (mm)</th>
<th>Hardness (Kg/cm²)</th>
<th>Weight variation (%devn.)</th>
<th>Friability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBF1</td>
<td>3.00±0.18</td>
<td>7.36±0.24</td>
<td>1.517±0.126</td>
<td>0.516±0.092</td>
</tr>
<tr>
<td>GBF2</td>
<td>2.97±0.22</td>
<td>6.74±0.23</td>
<td>1.478±0.216</td>
<td>0.384±0.046</td>
</tr>
<tr>
<td>GBF3</td>
<td>3.00±0.18</td>
<td>7.25±0.23</td>
<td>1.534±0.156</td>
<td>0.486±0.087</td>
</tr>
<tr>
<td>GBF4</td>
<td>3.10±0.20</td>
<td>7.34±0.20</td>
<td>1.614±0.412</td>
<td>0.268±0.028</td>
</tr>
<tr>
<td>GBF5</td>
<td>3.00±0.18</td>
<td>7.67±0.06</td>
<td>1.524±0.624</td>
<td>0.387±0.022</td>
</tr>
<tr>
<td>GBF6</td>
<td>2.98±0.11</td>
<td>7.08±0.12</td>
<td>1.486±0.267</td>
<td>0.579±0.05</td>
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<tr>
<td>GBF7</td>
<td>3.00±0.21</td>
<td>6.95±0.21</td>
<td>1.519±0.545</td>
<td>0.446±0.05</td>
</tr>
<tr>
<td>GBF8</td>
<td>3.10±0.16</td>
<td>7.72±0.11</td>
<td>1.546±0.223</td>
<td>0.302±0.039</td>
</tr>
</tbody>
</table>

Table 4: Swelling Indices of Glibenclamide Matrix Tablets.

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Initial weight (mg)</th>
<th>Final weight (mg)</th>
<th>Swelling Index (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GBF1</td>
<td>156.21</td>
<td>230.47</td>
<td>67.77</td>
</tr>
<tr>
<td>GBF2</td>
<td>155.34</td>
<td>229.54</td>
<td>67.67</td>
</tr>
<tr>
<td>GBF3</td>
<td>154.89</td>
<td>228.43</td>
<td>67.80</td>
</tr>
<tr>
<td>GBF4</td>
<td>155.11</td>
<td>227.82</td>
<td>68.08</td>
</tr>
<tr>
<td>GBF5</td>
<td>156.14</td>
<td>233.45</td>
<td>66.88</td>
</tr>
<tr>
<td>GBF6</td>
<td>154.96</td>
<td>228.67</td>
<td>67.76</td>
</tr>
<tr>
<td>GBF7</td>
<td>155.27</td>
<td>221.96</td>
<td>69.95</td>
</tr>
<tr>
<td>GBF8</td>
<td>155.21</td>
<td>223.23</td>
<td>69.52</td>
</tr>
</tbody>
</table>
In vitro drug release study:

In vitro drug release studies of the prepared matrix tablets were conducted for a period of 14 hours using six station VDA-6DR type2apparatus (VEEGO instruments corporation, Mumbai) at 37±0.5°C the paddle speed was 100±1rpm. The dissolution medium used in each flask was 900 ml of buffer media pH 6.8.

At every 1 hour interval samples of 5 ml were withdrawn from the dissolution medium and replaced with fresh medium to maintain the volume constant and maintain sink conditions. After filtration and appropriate dilution, the sample solutions were analyzed at 229nm by using double beam UV/VIS spectrophotometer (Evolution 201) Thermo scientific, USA and dissolution medium as blank. Experiments were performed in triplicates. The amount of drug present in the samples was calculated with the help of calibration curve constructed from reference standard. Dissolution data of matrix tablets are reported in Table No:5.

Dissolution data treatment:

The dissolution of drug from tablets at different time periods was plotted as cumulative % drug release Vstime curve for prepared matrix tablets as shown in Table No.5 and in Fig 5 & 6. The dissolution data so obtained was fitted to various kinetic models like Zero Order, Firstorder, Higuchi, korsmeyer-peppas models. Model independent methods, like t 50%, t 70%, were also used to compare dissolution behavior among different formulations were shown in Table No: 6 and in Fig5 & 6.

Table-5: In-vitro cumulative % release of drug from matrix tablets (n=3).

<table>
<thead>
<tr>
<th>Time in Hrs</th>
<th>GBE1</th>
<th>GBE2</th>
<th>GBE3</th>
<th>GBE4</th>
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<tr>
<td>2</td>
<td>17.78</td>
<td>15.24</td>
<td>14.38</td>
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<td>12.43</td>
<td>12.67</td>
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<tr>
<td>3</td>
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<td>20.56</td>
<td>18.45</td>
<td>16.27</td>
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<td>18.87</td>
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<td>22.45</td>
<td>32.56</td>
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<td>92.46</td>
<td>89.42</td>
<td>88.46</td>
<td>84.61</td>
<td>87.32</td>
<td>84.21</td>
<td>82.71</td>
<td>78.25</td>
</tr>
<tr>
<td>13</td>
<td>--</td>
<td>92.43</td>
<td>94.64</td>
<td>88.32</td>
<td>91.32</td>
<td>88.38</td>
<td>86.32</td>
<td>81.36</td>
</tr>
<tr>
<td>14</td>
<td>--</td>
<td>--</td>
<td>--</td>
<td>92.46</td>
<td>94.65</td>
<td>92.31</td>
<td>89.62</td>
<td>84.92</td>
</tr>
</tbody>
</table>
Figure No:5 indicates formulation GBF-1 to GBF-4 released 94.64% and 92.46% drug respectively in 14 hrs without any lag time and F4 showed the highest release of 94.64%. Similarly the release profiles of formulation GBF-5 to GBF-8 are shown in Figure No. 6 indicates formulation GBF-5 to GBF-8 released 84.92% and 94.65% drug respectively in 14 hrs. From the figure it is seen that the drug release is directly related to the concentration of polymer and its physic chemical nature.

**Fig-05: Cumulative % drug release from Ethyl cellulose and HPMC K4M matrices.**

**Fig-06: Cumulative % drug release from Ethyl cellulose and HPMC K100M matrices.**
Kinetics of \textit{In Vitro} Drug Release:

The dosage forms most commonly release the drug either in the zero order or in the first order pattern. Sustained release dosage forms of Glibenclamide were prepared and studied for their dissolution behavior. \textit{In vitro} release data of time points between 1 to 14 hours were considered and treated for kinetic principles. The drug release from the tablets of the formulation is given in the Table No: 6.

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|c|c|}
\hline
\textbf{Formulation code} & \textbf{Coefficient of Determination ($R^2$)} & & & \\
 & \textbf{Zero Order} & \textbf{First Order} & \textbf{Higuchi square root} & \textbf{Korsmeyer-peppas} \\
\hline
GBF1 & 0.9837 & 0.9565 & 0.9364 & 0.8196 \\
\hline
GBF2 & 0.9939 & 0.9287 & 0.9235 & 0.8412 \\
\hline
GBF3 & 0.9930 & 0.8882 & 0.9122 & 0.8534 \\
\hline
GBF4 & 0.9958 & 0.9238 & 0.9149 & 0.9050 \\
\hline
GBF5 & 0.9760 & 0.9726 & 0.9406 & 0.8387 \\
\hline
GBF6 & 0.9952 & 0.982 & 0.9230 & 0.8633 \\
\hline
GBF7 & 0.9894 & 0.9624 & 0.9387 & 0.8698 \\
\hline
GBF8 & 0.9953 & 0.9585 & 0.9244 & 0.8959 \\
\hline
\end{tabular}
\caption{Coefficient of determinations for Glibenclamide matrix tablets.}
\end{table}

Fig.16 Zero order kinetic treatment for drug-EC-HPMC K4M matrices

Conclusion

Glibenclamide matrix tablets were prepared by using hydrophilic polymers such as HPMC (K4M,K100M), in different ratios, hydrophobic polymer such as Ethyl cellulose were used as release modulators. Matrix tablets were prepared by direct compression method. Total eight formulations of Matrix tablets of Glibenclamide were prepared. Prepared tablets were evaluated for pharmacopoeial and non-pharmacopoeial tests. Based on the evaluation results the formulation GBF-7 was identified as better formulation. Glibenclamide release from the tablets of GBF-1 to GBF-8 formulation follows Zero-
order kinetics. Glibenclamide release from the tablets of GBF-1 to GBF-8 formulation follows Higuchi’s model; hence, release rate was found to be swellable matrix diffusion rate controlled mechanism and directly proportional to the distance of the drug, that must travel within the matrix to the matrix surface. Release mechanism of Glibenclamide from tablets of GBF-1 to GBF-8 formulation follows Non-Fickian diffusion. After one month of accelerated stability studies developed formulation was found to be stable. The conclusions arrived in this thesis indicates the solid dispersion sustained release formulation of Glibenclamide releases drug equivalent to in-house specifications and formulation is cost effective. Further studies are needed to investigate these formulations for its performance in vivo.

References


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