Development and Evaluation of a Novel Drug Delivery of Rosiglitazone by Mucous Route

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ABSTRACT

The objective of the present study was to extend the GI residence time of the dosage form and control the release of rosiglitazone using mucoadhesive tablet to achieve controlled plasma level of the drug which is especially useful after 8 to 12 weeks of monotherapy. Direct compression method using simplex lattice design, followed by optimization of the evaluation parameters was employed to get final optimized formulation. The tablets were evaluated for weight variation, hardness, thickness, drug content uniformity mucoadesion and swelling index. Mucoadhesive strength and mucoadhesion time, in-vitro drug release study and subjected to stability study. The stability studies shown that all the formulation were stable as there was no significant change in any values under study. Formulation (F4) containing Drug, Carbopol 934P and HPMC in the ratio of (1:6.5:18.5) shown good buccoadhesive force and maximum drug release of 99.0219% in 8 hours. The surface pH of all tablets was found to be satisfactory (pH = 5.13 – 6.19), close to buccal pH, hence no irritation would observe with these tablets. It was observed that the best formulation F4 shown surface pH 6.12 and follows release kinetics First order >Higuchi order >Korsemeyer-Peppas> zero order > Hixson Crowell order. Although majority of the formulations followed non-fickian (anomalous) diffusion mediated drug release, the release exponent ‘n’ for formulation F8 is 0.964 (i.e., > 0.89), which indicates that when the Carbopol934P and HPMC ratio is 0.8, the release mechanism is undergoing a change from non-Fickian to Case II transport. The results indicate that the mucoadhesive buccal tablets of Rosiglitazone may be a good choice to bypass the extensive hepatic first pass metabolism with an improvement in the bioavailability of Rosiglitazone maleate through buccal mucosa for the treatment of type II Diabetes Mellitus.

Keywords: Mucoadhesive drug delivery, Buccal tablets Rosiglitazone, HPMC K4M, PEG 940
Introduction

The effect of new formulations can be enhanced by the development of newer release systems. The main controlled drug delivery systems currently available include matrices, pellets, floating systems, liposomes, microemulsions, liquid crystals, solid dispersions, nanosuspensions, transdermal systems, cyclodextrin inclusion complexes, osmotic pumps and bioadhesive systems. The potential use for mucoadhesive systems as drug carriers lies in its prolongation of the residence time at the absorption site, allowing intensified contact with the epithelial barrier. When adhesion is restricted to the mucosal membrane it is called as mucoadhesion. Mucous membrane is the main administration site for bioadhesive systems. Mucous membranes of human organism are relatively permeable and allow fast drug absorption. They are characterized by an epithelial layer whose surface is covered by mucus. This approach to confer bioadhesion properties has been widely applied in the development of a number of drug delivery systems.

The Mucosal Buccal Delivery has brought about a great change in the pharmaceutical arena. It produces a sustained release of drug over a prolonged time, thereby reducing frequent dosing. The area is well suited for a retentive device and appears to be acceptable to the patient. With the right dosage form design and formulation, the permeability and the local environment of the mucosa can be controlled and manipulated in order to accommodate drug permeation. Buccal drug delivery is a promising area for continued research with the aim of systemic delivery of orally inefficient drugs as well as a feasible and attractive alternative for non-invasive delivery of potent peptide and protein drug molecules.

Preformulation and Drug Characterization

Drug Polymers compatibility study

Drug-polymer compatibility studies were done by FTIR study which gave conformation about their purity of the drug and chemical interaction between drug and selected polymers. Drug-excipients interactions, initial tablets and accelerated condition tablets were assessed by FTIR spectroscopy. The drug and polymer mixtures of rosiglitazone with various polymers prepared at different ratio. A base line correction was made using dried potassium bromide and then the
spectra of the dried mixture of drug, formulation mixture and potassium bromide and then the spectra of the dried mixture of drug, formulation mixture and potassium bromide were recorded. The resultant disc was mounted in a suitable holder in Perkin Elmer IR spectrophotometer and the IR spectrum was recorded from 4000 per cm to 450 per cm. The resultant spectra were compared for any spectral changes.

**Preparation of Standard Curve for Rosiglitazone using pH 6.8 phosphate buffer**

**Preparation of phosphate buffer pH 6.8**

About 28.80 g of disodium hydrogen phosphate and 11.45 g of potassium dihydrogen phosphate was weighed accurately and dissolved in sufficient water to produce 1000m

**Determination of absorption maximum of Rosiglitazone maleate**

The various concentration of samples were taken one by one and the maximum peak of UV graph was analyzed. From the UV spectrophotometric analysis, it was conclude that the drug Rosiglitazone maleate showed a λ max at 311 nm. Therefore the observed λ max was used for further work to analyze the test samples

**Standard curve of pure drug Rosiglitazone at phosphate buffer pH 6.8**

**Procedure:**

1. Preparation of stock solution: 100 mg of drug was dissolved in 1000 ml of media purified phosphate buffer to give 100 µg/ml.

2. Preparation of dilutions: The different dilutions were made using stock solution prepared. 0.2 ml, 0.4 ml, 0.6 ml, 0.8 ml, 1.0 ml of stock solution was taken and made up to 10 ml purified water to get 2, 4, 6, 8, 10 µg/ml concentrations. Absorbance of diluted
solutions were taken by using UV – Spectrophotometer at 308 nm wave length, using phosphate buffer as blank. The data is shown in Table 8.1 and figure 8.2

Procedure for preparation of Rosiglitazone buccal tablet

- Mucoadhesive buccal tablets, each containing 4mg Rosiglitazone, were prepared by direct compression method. Composition of various formulations employing Carbopol 934P, HPMC are shown in Table-1.
- All the ingredients of tablets were blended in mortar with a pestle for 15 min to obtain uniform mixture. The blended powder was then compressed into 150 mg tablets (at 5-7 kg/cm²) on a single stroke, 10station rotary tablet machine (Rimek Mini Press-I, Ahmedabad, India) with 8mm round shaped flat punch.

Table 2 Formulation of Rosiglitazone

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>F1(mg)</th>
<th>F2(mg)</th>
<th>F3(mg)</th>
<th>F4(mg)</th>
<th>F5(mg)</th>
<th>F6(mg)</th>
<th>F7(mg)</th>
<th>F8(mg)</th>
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<tbody>
<tr>
<td>Drug</td>
<td>4</td>
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<td>4</td>
</tr>
<tr>
<td>CP934</td>
<td>10</td>
<td>15</td>
<td>20</td>
<td>25</td>
<td>30</td>
<td>35</td>
<td>40</td>
<td>35</td>
</tr>
<tr>
<td>HPMC</td>
<td>90</td>
<td>85</td>
<td>80</td>
<td>75</td>
<td>70</td>
<td>65</td>
<td>60</td>
<td>55</td>
</tr>
<tr>
<td>Spray Dried Lactose</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Mannitol</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Magnesium Stearate</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
</tbody>
</table>
Characterization of Rosiglitazone and tablet properties

Preformulation Parameters

Preformulation involves the application of biopharmaceutical principles to the physicochemical parameters of a drug with the goal of designing an optimum drug delivery system. Characterization of drug molecule is a very important step at the preformulation phase of product development. Following studies are conducted as basic preformulation studies, special studies are conducted depending on the type of dosage form and the type of drug molecule.

In-Vitro Swelling Studies

Five Buccal tablets were individually weighed ($W_1$) and placed separately in petridishes with 5 ml of phosphate buffer (pH 6.8). At time intervals of 1, 2, 4, 8, and 12h, each tablet was removed from the Petri dish and excess surface water was removed from the Petri dish carefully with filter paper. The swollen tablet was then reweighed ($W_2$) and the swelling index (SI) was calculated using the following formula:

Swelling Index = \[\frac{(W_2 - W_1)}{W_1}\] \times 100

The average values were calculated.

Bioadhesion Studies

Selection of model mucosal surface

| Talc | 2 | 2 | 2 | 2 | 2 | 2 | 2 | 2 |
|------|---|---|---|---|---|---|---|
| Total| 150mg | 150mg | 150mg | 150mg | 150mg | 150mg | 150mg | 150mg |

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In evaluation of adhesion, it is important to use uniform surfaces that allow the formation of reproducible adhesive bonds. In the present study, sheep buccal mucosa was used as a model mucosal surface for bioadhesion testing. Immediately after slaughtering, the buccal mucosa was removed from the sheep and transported to laboratory in Tyrode solution. The composition of Tyrode solution is (g/L): sodium chloride - 8, potassium chloride - 0.2, calcium chloride dehydrate - 0.134, sodium bicarbonate - 1.0, sodium dihydrogen phosphate - 0.05 and glucose - 1.0.

**Fabrication of assembly**

The two sides of balance were made equal before study by keeping 5 g of weight on the right hand side pan. The sheep buccal mucosa was cut into strips/pieces and washed with Tyrode solution. The mucosal surface facing upward side was tied to support. The tablet was stuck to lower side of left hand side stainless steel pan by using bilayered adhesive tap, adhesive side facing downward. The pan was then lowered on to the buccal mucosa, which was tied to support. The weight on the right hand side was removed which lowered the left pan along the tablet over the mucosa, with the weight of 5 gm.

The balance was kept in this position for 3 minutes and then slowly weights were increased in the right pan, till the tablet separated from the mucosal surface.

The excess weight on the pan was total weight minus 5 gm was force required to separate the tablet from the mucosa. This gave bioadhesion strength of tablet in gm. The average values were calculated.

**In vitro dissolution study**

The *In-vitro* dissolution study was conducted as per the United States Pharmacopoeia (USP) XXIV. The rotating paddle method was used to study the drug release from the tablets. The dissolution medium consisted of 900 ml of phosphate buffer (pH 6.8). The release was performed at 37°C ± 0.5°C, at a rotation of speed of 50 rpm. Five ml samples were withdrawn at predetermined time intervals (1 to 8 h) and the volume was replaced each time with fresh medium. The samples were filtered through What man filter paper No 40 and analyzed for
Rosiglitazone after appropriate dilution by UV spectrophotometer at 311 nm. The drug release was calculated using the calibration curve. The average values were calculated. The results are shown in table no. 8.5-8.12

**Determination of drug content**

Ten randomly selected tablets from each formulation (F1 to F8) were finely powdered and powder equivalent to 4 mg of Rosiglitazone was accurately weighed and transferred to 100 ml volumetric flasks containing 50 mL of phosphate buffer pH 6.8. The flasks were shaken to mix the contents thoroughly. The volume was made up to the mark with phosphate buffer pH 6.8 and filtered. One ml of the filtrate was suitably diluted and Rosiglitazone content was estimated at 216.0 nm using a double beam UV-visible spectrophotometer. This procedure was repeated thrice and the average value was calculated.

**Drug release kinetics**

- To examine the release mechanism of Rosiglitazone from the prepared buccoadhesive tablets, the results were analyzed according to the following equation:

- Where $\frac{M_t}{M_\infty}$ is the fractional drug released at time $t$, $k$ is a kinetic constant incorporating structural and geometrical characteristics of the drug/polymer system [device], and $n$ is the diffusional exponent that characterizes the mechanism of drug release. It is known that for non-swelling tablets, the drug release can generally be expressed by the Fickian diffusion mechanism, for which $n = 0.5$, whereas for most erodible matrices, a zero-order release rate kinetics is followed, for which $n = 1$. For non-Fickian release, the $n$ value falls between 0.5 and 1.0 ($0.5 < n < 1.0$); whereas in the case super case II transport $n > 1$.

- The data of the *in-vitro* release was fit into different equations and kinetic models to explain the release kinetics of Rosiglitazone from buccal tablets. The kinetic models used were zero-order equation $^{11}$ (eq. 1), first-order equation $^{12}$ (eq. 2), Higuchi equation $^{13}$ (eq. 3), Krosmeyer-Peppas equation $^{14}$ (eq. 4), and Hixon- Crowell equation $^{15}$ (eq. 5)

$$Q_t = K_0 t \quad \text{------------------- (1)}$$
\[ Q_t = Q_0 \left(1 - e^{-k_1 t}\right) \quad (2) \]

\[ Q_t = K_{H} t^{1/2} \quad (3) \]

\[ Q_0^{1/3} - Q_t^{1/3} = K_{HC} t \quad (4) \]

\[ \frac{Q_t}{Q_\infty} = K_k t^n \quad (5) \]

Where,

- \( Q_t \) is the amount of drug release in time \( t \)
- \( Q_0 \) is the initial amount of the drug
- \( F \) is the fraction of drug release in time \( t \)
- \( n \) is the exponent value

And \( K_0, K_1, K_H, K_{HC}, \) and \( K_k \) are release rate constants for Zero-order, First-order, Higuchi, Hixon-Crowell, and Korsmeyer-Peppas model respectively.

Zero order represents an ideal release profile in order to achieve the pharmacological prolonged action. This is applicable to dosage forms like transdermal systems, coated forms, osmotic systems, as well as matrix tablets with low soluble drugs. First order is applicable to study hydrolysis kinetics and to study the release profiles of pharmaceutical dosage forms such as those containing water-soluble drugs in porous matrices. Higuchi Matrix is applicable to systems with drug dispersed in uniform swellable polymer matrix as in case of matrix tablets with water-soluble drug.

Hixson-Crowell Equation applies to pharmaceutical dosage form such as tablets, where the dissolution occurs in planes that are parallel to the drug surface if the tablet dimensions diminish proportionally, in such a manner that the initial geometrical form keeps constant all the time. When this model is used, it is assumed that the release rate is limited by the drug particles dissolution rate and not by the diffusion that might occur through the polymeric matrix. Korsmeyer-Peppas equation is widely used; when the release mechanism is not well known or when more than one type of release phenomena could be involved. Data of the \textit{in-vitro} release
was fit into different equations and kinetic models to explain the release kinetics of Rosiglitazone from buccal tablets.

**Results & Discussion**

**Drug –polymers compatibility study**

FTIR spectroscopy study was carried out to find out the possibility interaction between selected drugs and polymers and excipient. The infrared spectra of pure drug Rosiglitazone and mixture of polymer and excipients were studied by FTIR spectroscopy using suitable solvent KBR. The results indicate that there was no chemical incompatibility between drug –polymer, polymer–polymer and polymer – excipients.

![FTIR study of Rosiglitazone tablet](image-url)

**Fig 1 FTIR study of Rosiglitazone tablet**
Fig 2 FTIR study of Rosiglitazone pure drug

Fig. 3 FTIR study of Rosiglitazone and Carbopol 934
Fig. 4 FTIR study of Rosiglitazone and HPMC K4M

**Standard curve of pure drug**

The $C_{max}$ was found to be 308 nm

*Linear Regression Equation:*

Linear regression analysis was performed to obtain equation for straight line.

Equation for calibration curve of drug in water is $y = 0.045x - 0.004$.

Linear regression coefficient = 0.998

**Table 3 Standard curve of pure drug**

<table>
<thead>
<tr>
<th>Concentration(µg/ml)</th>
<th>Absorbance</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>0.089</td>
</tr>
<tr>
<td>4</td>
<td>0.166</td>
</tr>
<tr>
<td>6</td>
<td>0.254</td>
</tr>
<tr>
<td>8</td>
<td>0.368</td>
</tr>
<tr>
<td>10</td>
<td>0.44</td>
</tr>
<tr>
<td>12</td>
<td>0.538</td>
</tr>
</tbody>
</table>
Fig 6 Standard curve of Rosiglitazone pure drug

Physicochemical evaluation of Rosiglitazone

Table 5 Physicochemical evaluation of Rosiglitazone

<table>
<thead>
<tr>
<th>Formulation Code</th>
<th>Bulk density (mg/ml)</th>
<th>Tapped density (mg/ml)</th>
<th>Carr’s Index (%)</th>
<th>Hauser’s ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.614</td>
<td>0.788</td>
<td>22.2</td>
<td>1.28</td>
</tr>
<tr>
<td>F2</td>
<td>0.658</td>
<td>0.724</td>
<td>15.4</td>
<td>1.08</td>
</tr>
<tr>
<td>F3</td>
<td>0.698</td>
<td>0.774</td>
<td>9.92</td>
<td>1.11</td>
</tr>
</tbody>
</table>
**Bulk density**: The bulk density for the formulations F1-F8 lies in range of 0.614-0.698 mg/ml. The bulk density of formulation F6 is minimum whereas the bulk density of formulation F3 is the maximum. All pass the optimum range.

**Tapped density**: The tap density for formulation F1-F8 lies in range of 0.710-0.788 mg/ml. The tap density is minimum for formulation F4 and maximum for formulation F1. All pass the optimum range.

**Carr’s Index**: The Carr’s index for formulation lies in range of 9.14-9.92%. The Carr’s index of formulation F8 is minimum and formulation F1 is maximum. All pass the optimum range.

**Hausner’s Ratio**: The Hausner’s Ratio of formulation F1-F8 lies in range of 1.08-1.28. The formulation F2 has minimum value whereas formulation F1 has maximum value. All pass the optimum range.

Table 6 Physiochemical evaluation of Rosiglitazone buccal tablet

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Average weight of tablet (mg ±SD)</th>
<th>Hardness (Kg/cm²)</th>
<th>Friability (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>149.89±0.04</td>
<td>3.0±0.14</td>
<td>0.51±0.03</td>
</tr>
</tbody>
</table>
Weight variation test:-

The weight variation test was conducted for each batch of all formulations F1 to F8 as per I.P and the results are shown in Table 8.3. All the tablets passed weight variation test. None of the formulations showed deviation (I.P limit ± 10%) for any tablet tested.

Hardness test:-

The adequate tablet hardness is necessary requisite for consumer acceptance and handling. The measured hardness of the tablets of each batch of all formulations i.e. F1 to F8 were ranged between 3.0 to 6.5 kg/cm² and the results are shown in Table 8.3. This ensures good handling.

Friability test:-

The friability test for all the formulations were done as per the standard procedure I.P. The results of the friability test were tabulated in Table 8.3. The measured hardness of the tablets of each batch of all formulations i.e. F1 to F8 were ranged between 0.35 to 0.65 %. The data indicates that the friability was less than 1% in all formulations ensuring that the tablets were mechanically stable.
Thickness, Content uniformity, surface pH and Bioadhesive strength: The above parameters were evaluated and the results are shown in Table 8.4

**Table 7 Thickness, Content Uniformity, surface pH and bioadhesive strength**

<table>
<thead>
<tr>
<th>Formulation code</th>
<th>Thickness in mm</th>
<th>%drug content</th>
<th>Surface pH</th>
<th>Bioadhesive strength (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>2.7</td>
<td>97.00</td>
<td>5.1</td>
<td>26.6</td>
</tr>
<tr>
<td>F2</td>
<td>2.9</td>
<td>98.78</td>
<td>5.9</td>
<td>29.5</td>
</tr>
<tr>
<td>F3</td>
<td>2.5</td>
<td>97.00</td>
<td>6.12</td>
<td>32.4</td>
</tr>
<tr>
<td>F4</td>
<td>2.6</td>
<td>99.25</td>
<td>6.18</td>
<td>35.5</td>
</tr>
<tr>
<td>F5</td>
<td>2.7</td>
<td>94.65</td>
<td>6.04</td>
<td>32.7</td>
</tr>
<tr>
<td>F6</td>
<td>2.9</td>
<td>96.00</td>
<td>6.25</td>
<td>33.5</td>
</tr>
<tr>
<td>F7</td>
<td>3.0</td>
<td>95.00</td>
<td>6.09</td>
<td>35.2</td>
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<tr>
<td>F8</td>
<td>2.6</td>
<td>101.00</td>
<td>6.26</td>
<td>36.5</td>
</tr>
</tbody>
</table>

Swelling study:

Swelling index of the tablets of formulation F1 to F8 was evaluated and the results are provided in Table 8.4. The results indicate that after 8 hrs the tablets from the formulations F1 to F4 were hydrated to an extent of 69.7, 67.8, 60.4 and 87.6% respectively. The results indicate that after 8 hrs the tablets from the formulations F5 to F8 were hydrated to an extent of 79.8, 75.9, 73.3 and 71.1% The highest hydration (swelling) was observed with the formulation F4. This may be due to quick hydration of polymers (Carbopol 934p and HPMC K4M).

**Table 8. Percentage hydration of Rosiglitazone buccal tablets**

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Percentage Hydration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>
In-vitro Dissolution Study:

In-vitro dissolution studies were designed to carry out in such a way that they simulate in-vivo conditions. The purpose of in-vitro release study was to provide a fast, easily performed and inexpensive method that correlates with the performance of dosage form in human subjects. The conditions of in-vitro dissolution test were well defined, standardized and enable comparison among various results. For in-vitro dissolution study, it was decided to carry out the dissolution in pH 6.8 phosphate buffer.

Table 8. Dissolution profile of F1 (DRUG: CARBOPOL 934p:HPMCK4M)(1:2.5:22.5)

<table>
<thead>
<tr>
<th>S. L. No</th>
<th>Time (hrs.)</th>
<th>Log Time</th>
<th>SQRT Time</th>
<th>% CDR</th>
<th>Log %ADR</th>
<th>Log Mt/Mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>--</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>0</td>
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<tr>
<td>2</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>26.44</td>
<td>1.866</td>
<td>1.422</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td>0.3</td>
<td>1.41</td>
<td>33.87</td>
<td>1.820</td>
<td>1.529</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td>0.47</td>
<td>1.73</td>
<td>48.33</td>
<td>1.713</td>
<td>1.684</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td>0.6</td>
<td>2</td>
<td>65.42</td>
<td>1.538</td>
<td>1.815</td>
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<tr>
<td>6</td>
<td>5</td>
<td>0.69</td>
<td>2.23</td>
<td>76.98</td>
<td>1.362</td>
<td>1.886</td>
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<tr>
<td>7</td>
<td>6</td>
<td>0.77</td>
<td>2.44</td>
<td>85.49</td>
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<tr>
<td>8</td>
<td>7</td>
<td>0.84</td>
<td>2.64</td>
<td>91.019</td>
<td>0.953</td>
<td>1.959</td>
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</table>
**Fig. 7** Comparative cumulative percentage release formulations of F1 to F4 using carbopol 934p and HPMC

**Fig. 8** Comparative cumulative percentage release formulations of F5 to F8 using carbopol 934p and HPMC

**Table 9**: % Cumulative drug release from different formulation

<table>
<thead>
<tr>
<th>Time</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
<th>F8</th>
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<tbody>
<tr>
<td>0</td>
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<td>0</td>
<td>0</td>
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<td>0</td>
</tr>
</tbody>
</table>
The formulations F1, F2, F3 & F4 containing drug, Carbopol 934p and HPMCK4M polymers in the ratios of 1:2.5:22.5; 1:3.75:21.5; 1:5:20 and 1:6.5:18.5 respectively. The *in-vitro* cumulative
drug release profile of formulations F1, F2, F3 and F4 showed 91.01%, 90.19%, 98.12% and 98.52% respectively. Among these four formulations F1 was found to be highest percentage drug release. During the study it was observed that the tablets were initially swell and non-erodible over the period of 7 hrs.

Similarly the formulations F5, F6, F7 & F8 drug, containing carbopol 934p and HPMCK4M polymers in the ratios of 1:7.5:17.5; 1:8.75:16.25; 1:10:15 and 1:11.25:13.75 respectively. The in-vitro cumulative drug release profile of formulations F5, F6, F7 and F8 showed 97.58%, 98.59%, 85.0173% and 81.63% respectively. Among these four formulations F5 was found to be highest percentage drug release. During the study it was observed that the tablets were initially swell and non-erodible over the period of 7 hrs.

The drug release pattern was studied for all formulations (F1 to F8) for 8 hrs. following standard procedure and the results are provided in Table No. The release was found to be influenced by the presence of polymers – Carbopol 934P and HPMC. It was concluded that by increasing the concentration of Carbopol 934p in the formulation, the drug release rate from the tablets was found to be decreased. But when the concentration of secondary polymers (Polyethylene Oxide and HPMC K4M) increased, the drug release rate was found to be increased. This may be due to increased hydration (or) swelling characteristics of polymers with increased concentrations. From the overall data it was found that the formulation F4 showed the maximum percentage of drug release i.e. 98.5218% at the end of 7 h.

**Drug release kinetics**

**Table 10: Release kinetics of different formulations F1-F8**
In-vitro drug release data of F1 to F8 were fitted to zero order, first order, Higuchi and Korsmeyer-Peppas equations to ascertain the pattern of drug release Table 8.15. The $R^2$ values were found to be higher in zero-order followed by Korsmeyer-Peppas, Higuchi and then first order, which indicates all the formulations followed zero-order release pattern. According to Korsmeyer-Peppas equation, the release exponent “n” value is $> 0.5$, which indicates the mechanism of drug release for all formulations is non-Fickian diffusion type.

### Conclusion

The basic idea of the investigation is to define “buccal tablet “form using Carbopol 934 and HPMC polymer in sustain releasing formulation for the treatment of Type II Diabetes. Initially the standard calibration curve of rosiglitazone was developed. The powder blend for all formulation containing polymers Carbopol 934 and HPMC was prepared. The powder blend was evaluated for their properties like angle of repose, bulk density, tapped density, percentage compressibility, porosity and flowability. It was observed that all the formulation were having good flowability. It indicate its suitability for direct compression.

The tablets were prepared by direct compression using Rotary tablet punching machine. These tablets were evaluated for weight variation test, hardness test, friability, dissolution test, drug
content, surface pH, swelling test, bioadhesive strength test, and \textit{In-vitro} dissolution studies. It was observed that all the tablets passes the test for weight variation and hardness was found between 3.0-6.5 Kg/cm² was friability was found below 1%. From bioadhesive strength it was observed that formulation F4 showed the maximum bioadhesive strength i.e. 36.5 gm. The highest hydration (swelling) was observed with the formulation F4. This may be due to quick hydration of polymers (Carbopol 934p and HPMC K4M). From in vitro dissolution study it was found that the formulation F4 showed the maximum percentage of drug release i.e. 98.5218% at the end of 7 h. In-vitro drug release data of F1 to F8 were fitted to zero order, first order, Higuchi and Korsmeyer-Peppas equations to ascertain the pattern of drug release. The \(R^2\) values were found to be higher in zero-order followed by Korsmeyer-Peppas, Higuchi and then first order, which indicates all the formulations followed zero-order release pattern. According to Korsmeyer-Peppas equation, the release exponent “n” value is > 0.5, which indicates the mechanism of drug release for all formulations is non-fickian diffusion type. Further, an elaborate \textit{in vivo} study is to be carried out for the best formulation using a suitable animal model.

\textbf{References:}

4. \texttt{http://www.alzforum.org/drg/drc/detail.asp?id=116}


