Formulation and evaluation of pectin-HPMC mesalamine tablets coated with eudragit L 100 for ulcerative colitis

Sandina Swetha, Ravi Teja Allen & D V Gowda

ABSTRACT

The potential of Eudragit L 100 as protective for drug in acidic environment and effectiveness of pectin for the sustained drug release has been demonstrated. Due to solubility and swelling properties of pectin in aqueous media, it is frequently coated with acid resistant polymers for targeting drugs to the colon. The aim of this study was to prepare and evaluate mesalamine matrix tablets containing pectin as bacterially-degradable and bioactive polysaccharide in combination with HPMC K4M which acts agonistically in the drug release. Wet granulation method was used for the preparation of tablets. 60% of pectin was used and different combinations were prepared with polymers. Optimised formulation was selected and another same formulation was prepared and tried without Eudragit L 100 coat. Then the formulations were evaluated for various parameters like weight variation, friability, drug content, drug release etc. Formulations containing highest amount of pectin exhibited sustained drug release than the remaining formulations. Formulation without Eudragit L 100 coat has released the entire drug within 4 h as it had no protective coat for acidic pH. Formulations with highest amount of HPMC K4M showed poor flow properties due to sticking property caused by hydrophilic polymer. Formulation with highest amount of HPMC K4M showed highest swelling than the other formulations. Formulation containing pectin and HPMC K4M in the ration of 6:1 coated with Eudragit L 100 was a promising formulation for the targeted and sustained drug delivery to the colon.

Keywords: Colon targeted, HPMC K4M, Mesalamine, Pectin, Ulcerative Colitis, Wet granulation.

INTRODUCTION

The most convenient and important method of administering drugs for systemic effect is the oral route of drug administration. Nearly 50% of drug delivery systems available in the market are oral drug delivery systems and these systems have more advantages due to patient acceptance and ease of administration.[1,2] Colonic drug delivery has gained increased importance not just for the delivery of drugs for the treatment of local diseases associated with colon like Crohn’s disease, ulcerative colitis, irritable bowel syndrome and constipation but also for the systemic delivery of proteins, therapeutic peptides, anti-asthmatic drugs, antihypertensive drugs and anti-diabetic agents.[3-7] These diseases can be treated effectively when the drugs are targeted to the colon. There are various methods or techniques through which colon drug targeting can be achieved. These include, formation of prodrug, coating with pH sensitive polymers, coating with biodegradable polymers, designing formulations using polysaccharides, timed released systems, pressure-controlled drug delivery systems, osmotic pressure controlled systems.[8, 9]

Mesalamine, an anti-inflammatory agent used in the treatment of ulcerative colitis and in mild to moderate Crohn’s disease undergoes rapid & extensive hepatic first-pass metabolism following oral administration, with a reported systemic bioavailability between 20% and 30%. It has a half-life of 5 h after initial dose and 7 h at steady state, so patients are advised to administer Mesalamine formulation for several times a day. Such frequent drug administration may lead to patient non-compliance and reduced therapeutic efficacy. Hence formulations containing
Mesalamine which target the drug release to colon with sustained drug release have been formulated in this study for the treatment of ulcerative colitis.

The objective of the present study was to develop controlled release matrix formulations of Mesalamine and to evaluate various parameters like drug content, drug release etc. In the present study, Mesalamine matrix formulations were prepared by using bioactive polymer pectin and hydrophilic polymer HPMC. The main aim of the present study was to increase the bioavailability of the drug by decreasing first pass metabolism which leads to decreased dose and also to reduce the dosing interval by sustained action for improved patient compliance.

MATERIALS AND METHODS

Mesalamine was kind gift sample from Wallace Pharma, Goa. Pectin was purchased from Loba Chemie, Mumbai. Pectin with 65% esterification was used in this study. Eudragit L 100 was purchased from Evonik Industries, Germany. Hydroxypropyl methylcellulose (HPMC K4M) was purchased from Shreeji chemicals, Mumbai, India. Starch 1500 was purchased from Colorcon, Goa. All other chemicals and reagents used were of analytical grade.

Preparation of Mesalaminetablets

Matrix tablets of mesalamine were formulated by wet granulation process. Accurately weighed quantities of drug, polymers (pectin & HPMC) and binder (Starch, 6% w/w) were mixed in a mortar. Required quantity of the solvent (ethanol) was added to the above mixture and mixed thoroughly to form a mass suitable for formation of granules. The dough mass formed was passed through sieve # 22 to form granules which were dried in an oven at 50 ºC. Required quantities of diluent (lactose) and lubricant (magnesium stearate, 2% w/w) were added to the granules and mixed well. The granules were then compressed to form tablets by using a Rimek, Minipress-1 (model-1674, India) machine with flat face punches & dies (12 mm in diameter) at an optimum pressure [10]. Six formulations were prepared with different polymer (pectin & HPMC) concentrations and the last formulation was prepared without coating. The prepared matrix tablets were coated with Eudragit L 100 by solution coating.

Preparation of coating solution

Using glycerol as plasticizer, coating solution (10% w/v) was prepared in hot water. Conventional coating pan (Ram Scientific Suppliers, Bangalore) was used to coat the tablets at an inlet temperature of 55º, pan rotation speed of 15 rpm, spray pressure of 4 kg/cm² and a spray rate of 10 ml/min. The solution was sprayed using a pilot type spray gun (Bullows 630) fitted with a 1 mm atomizing nozzle. Formulation table is given in Table 1.

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>F1</th>
<th>F2</th>
<th>F3</th>
<th>F4</th>
<th>F5</th>
<th>F6</th>
<th>F7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug (mg)</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
<td>300</td>
</tr>
<tr>
<td>Pectin (mg)</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>50</td>
<td>100</td>
<td>150</td>
<td>150</td>
</tr>
<tr>
<td>HPMCK4M (mg)</td>
<td>50</td>
<td>100</td>
<td>150</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Eudragit L 100 (% w/v)</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>10</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Lactose (mg)</td>
<td>125</td>
<td>75</td>
<td>25</td>
<td>125</td>
<td>75</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Starch (% w/w)</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Magnesium stearate(%)</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Total weight (mg)</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>500</td>
<td>500</td>
</tr>
</tbody>
</table>

*Excluding Magnesium stearate & Starch

PREFORMULATION STUDIES

Compatibility study

The integrity and compatibility of mesalamine and polymers used in the tablets was studied by using Fourier transform-infrared (FT-IR- 8400, Shimadzu Co., Japan) spectroscopy. The pellatization was done by the KBr press. The FT-IR spectra were recorded in the wavelength region between 4000 and 400 cm⁻¹. The spectra obtained for pure mesalamine and formulation were compared for compatibility.
Differential scanning calorimetry (DSC)
About 5 mg of sample was weighed and crimped into an aluminium pan and analyzed at a scan range from 0 °C – 300 °C at the heating rate of 5 °C / min under nitrogen flow of 25 ml/min. It was measured using DSC Q200 V24.4 Build 116, Universal V4.7A TA Instruments, USA.

Scanning electron microscopy (SEM)
Morphological characteristics of the tablets in pH 1.2HCl buffer and in pH 7.4 phosphate buffer were determined by using a scanning electron microscope (SEM). It was measured using Joel SEM analysis Instrument, Model JSM 840A, Japan.

Bulk density
5 g of mesalamine powder was weighed and gently poured through a short stemmed glass funnel into 100 ml graduated glass cylinder. The volume occupied by granules was read and the bulk density of the powder can be determined by the formula given below. It was measured in terms of g/cm³. [11]

\[ \text{Bulk density} = \frac{\text{Weight of the powder}}{\text{Bulk volume}} \]

Tapped density
Tapped density was determined by USP method II. Tablet blend was filled in 100 ml graduated cylinder of tap density tester ETD - 1020 which was operated for fixed number of taps until the powder bed volume has reached a minimum. It was calculated by the following formula. It was measured in terms of g/cm³.

\[ \text{Dt} = \frac{M}{V_b} \]

Where, \( M = \) Weight of powder taken; \( V_b = \) tapped volume.

Compressibility index and Hausner’s ratio
Compressibility index was measured for the property of powder to be compressed, as such they are measured for relative importance of inter particulate interactions. Compressibility index and was calculated by the following equation.[12]

\[ \text{Compressibility index} = \left( \frac{\text{Dt} - \text{Db}}{\text{Dt}} \right) \times 100 \]

Where, \( \text{Dt} = \) tapped density; \( \text{Db} = \) bulk density;

Hausner ratio was calculated by following equation

\[ \text{Hausner’s ratio} = \frac{\text{Dt}}{\text{Do}} \]

Where, \( \text{Dt} = \) tapped density; \( \text{Do} = \) bulk density

Angle of repose
Circumference of the pile of powder was drawn with a pencil and height of the pile was measured without disturbing the pile. The radius of the pile was noted as ‘r’ cm. and angle of repose was calculated by the following formula,

\[ \tan \theta = \frac{h}{r} \]

\[ \theta = \tan^{-1} \frac{h}{r} \]

Where, \( h = \) height of the pile; \( r = \) radius of the pile

TECHNOLOGICAL CHARACTERISTICS OF TABLETS
Weight variation
20 tablets were randomly selected from every batch and average weight was calculated. (As per Indian pharmacopoeia, limits is ± 7.5 % for 80 to 250 mg tablet). Then the deviation of individual weights from the average weight and standard deviation were calculated.
Hardness
The crushing strength was determined using an Erweka, IHT 100, Ahmedabad, India. Ten tablets were randomly selected from each batch. In tablets, the crushing strength is additionally transformed into a tensile strength. It was measured in terms of Kg. [13]

Friability
20 tablets are weighed and placed in the plastic chamber which revolves at 25 rpm for 4 min. The tablets are then reweighed to find out the % loss in weight. The friability of the tablets was determined by the formula given below. Then average hardness and standard deviation were calculated.

\[
\% \text{ Friability} = \frac{\text{Final weight-initial weight}}{\text{Initial weight}} \times 100
\]

Determination of thickness
Thicknesses of five randomly selected tablets from each batch were measured with digital Vernier calipers. Then the average thickness and standard deviation were calculated. Tablet thickness should be controlled within 5 % variation of a standard value.

Swelling studies
The swelling behaviour of the tablets was determined in triplicate. Tablet was weighed and placed in a glass beaker, containing 200 ml of 0.1 N HCl, maintained in a water bath at 37 ± 0.5 °C for 10 h. The tablet was removed at every two hour interval up to 10 h and the excess surface liquid was carefully removed by a filter paper and then reweighed. [14, 15]

Swelling index (SI) = \{(Wt-Wo) / Wo\} x 100

Where, SI = swelling index
Wt = Weight of tablet at time ‘t’
Wo = Weight of tablet before immersion.

Drug content
Five tablets were randomly selected from every batch, weighed and powdered in a mortar. An accurately weighed quantity of powdered tablets equivalent to 100 mg was taken in standard flask and make up the volume of flask with 0.1 N HCl and the solution was filtered through 0.45 µ membrane paper. Each extract was suitably diluted and analysed spectrophotometrically at 303 nm. Concentration of solution was calculated from the standard calibration curve. [16]

In vitro release studies
The dissolution test for the tablets was carried out using USP apparatus II Electrolab EDT 08 L, Mumbai. 900 ml of 1.2 pH HCl buffer was used as dissolution medium for the first 2 h and 7.4 pH of phosphate buffer is used as dissolution medium for the next 10 h. The paddle was rotated at 50 rpm for 12 h. 5 ml of sample was withdrawn at predetermined time intervals and 5 ml of fresh medium was replaced to maintain the sink condition. The collected samples were analyzed at 303 nm UV spectrophotometrically. Cumulative percentage drug release was calculated from the standard calibration curve of mesalamine. [17]

Kinetics and mechanism of drug release
To analyse the in vitro release data various kinetic models were used to describe the release kinetics.

Zero order equation
This equation describes the systems where the drug release rate is independent of its concentration and a graph is plotted between cumulative % drug release vs. time.

\[ C = k_0 t \]

Where, \( k_0 \) is zero-order rate constant expressed in units of concentration / time and \( t \) is the time. [18]

First order equation
This equation describes the release from system where release rate is concentration dependent and a graph is plotted between log cumulative of % drug remaining vs. time.
Log C = Log C₀ - kt/ 2.303

Where, C₀ is the initial concentration of drug and K is first order constant. [19]

**Higuchi equation**
Higuchi described the release of drugs from insoluble matrix as a square root of time dependent process based on fickian diffusion and a graph is plotted between cumulative % drug release vs. square root of time.

\[ Q = K \sqrt{t} \]

Where, K is the constant reflecting the design variables of the system. [20]

**Hixson and Crowell equation**
This equation describes the release from systems where there is a change in surface area and diameter of particles or tablets and a graph is plotted between cube root of drug (%) remaining in matrix vs. time.

\[ Q₀^{\frac{1}{3}} - Qₜ^{\frac{1}{3}} = K_{HC} t \]

Where, Qₜ is the amount of drug released in time t, Q₀ is the initial amount of the drug in tablet and K_{HC} is the rate constant for hixson-crowell rate equation. [21]

**KorsmeyerPeppa’s equation**
Korsmeyer et al (1983) derived a simple relationship which described drug release from a polymeric system. To find out the mechanism of drug release, first 60% drug release data was fitted in korsmeyer – peppa’s model and a graph is plotted between log cumulative % drug release vs. log time.

\[ M_t / M_∞ = Kt \]

Where Mₜ / Mₜ is fraction of drug released at time t, k is the rate constant and n is the release exponent. [22, 23, 24]

**Stability studies**
Stability studies were carried out for optimized formulation at 40 °C / 75 % RH in a humidity chamber for 90 days. After 90 days the samples were analyzed for drug content and drug release.[25]
RESULTS AND DISCUSSION

Compatibility studies
Compatibility studies were performed by Fourier transform infrared spectrophotometer. The spectra indicated that there was no drug – polymer interaction. Polymers like pectin and HPMC K4M were selected on the basis of their biodegradability and adhering property respectively. Physical or chemical interaction between drug and polymers were determined by FTIR study. IR spectra were recorded for pure mesalamine and the physical mixture. Pure mesalamine spectra showed sharp characteristic peaks at 3408, 2960, 2932, 2860, 1544 cm$^{-1}$ due to the presence of OH phenolic group, the aliphatic and aromatic $\equiv$CH bond in protected methyl groups and C=C bond of aromatic group respectively. FTIR characteristic peaks of physical mixture appeared at the same wave number indicating no interaction between the drug and the polymers used. This proves the fact that there was no potential incompatibility of the drug with the polymers used in the formulations. The graph for the pure drug and physical mixture is given in Figure 1.

Comparative DSC thermograms of pure mesalamine and physical mixture were shown in Figure 2. The DSC thermogram of mesalamine displayed the characteristic peak at 283 $^\circ$C corresponding to its melting point. The drug peak appeared in the thermogram at 281.8 $^\circ$C, confirming the chemical integrity of the drug. A slight shift in the formulation peak could be due to the presence of HPMC K4M which is hydrophilic in nature.

Surface morphology of the tablets in pH 1.2 HCl buffer showed that there were no cracks in the tablets which indicated that the tablet was stable in acidic pH (stomach) and in pH 7.4 phosphate buffer the tablets showed cracks which indicated that the dosage form was stable in acidic pH and drug was released in the colon and the drug release might be by slight swelling and erosion of the polymer. SEM photographs were shown in Figure 3.

Preformulation studies
The preformulation studies of mesalamine were evaluated for various physical properties and the results were shown in the Table 2. Bulk density of powder indicated good packaging character of the tablets. The carr’s index of F1 was found to be below 15 % which indicated excellent flow properties and this might be due to low amount of HPMC K4M used. Out of all formulations F3 had highest carr’s index of 27.27 which indicated poor flow properties and this might be due to the highest amount of HPMC K4M which resulted in sticky nature. The hausner’s ratio for all the formulation was less than 2 %, which also indicates good flow property and packaging characters of powders. Angle of repose observed was within the range of 25-35$^\circ$ and showed that the flow property of the powder was excellent and within the acceptable limits.
Table 2. Preformulation studies of Physical mixture

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Bulk Density (g/cm³)</th>
<th>Tapped density (g/cm³)</th>
<th>Carr’s index</th>
<th>Hausner’s ratio</th>
<th>Angle of repose (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.316 ± 0.19</td>
<td>0.370 ± 0.52</td>
<td>14.55 ± 0.15</td>
<td>1.17 ± 0.07</td>
<td>27.85°</td>
</tr>
<tr>
<td>F2</td>
<td>0.333 ± 0.12</td>
<td>0.403 ± 0.41</td>
<td>17.33 ± 0.26</td>
<td>1.20 ± 0.11</td>
<td>28.19°</td>
</tr>
<tr>
<td>F3</td>
<td>0.324 ± 0.18</td>
<td>0.546 ± 0.47</td>
<td>27.27 ± 0.18</td>
<td>1.37 ± 0.05</td>
<td>33.24°</td>
</tr>
<tr>
<td>F4</td>
<td>0.357 ± 0.13</td>
<td>0.432 ± 0.59</td>
<td>17.42 ± 0.37</td>
<td>1.21 ± 0.10</td>
<td>27.97°</td>
</tr>
<tr>
<td>F5</td>
<td>0.312 ± 0.17</td>
<td>0.383 ± 0.48</td>
<td>18.43 ± 0.19</td>
<td>1.22 ± 0.04</td>
<td>29.44°</td>
</tr>
<tr>
<td>F6</td>
<td>0.416 ± 0.23</td>
<td>0.524 ± 0.42</td>
<td>20.50 ± 0.14</td>
<td>1.25 ± 0.02</td>
<td>28.75°</td>
</tr>
<tr>
<td>F7</td>
<td>0.384 ± 0.21</td>
<td>0.487 ± 0.54</td>
<td>21.07 ± 0.23</td>
<td>1.26 ± 0.09</td>
<td>27.38°</td>
</tr>
</tbody>
</table>

Physical evaluation of mesalamine coated tablets

Tablets were selected randomly from all the seven batches and physical evaluation of tablets were studied and tabulated in Table 3. The average weight of tablet was found to be 0.498 ± 0.12 to 0.524 ± 0.71 mg. The hardness was found to be 5.11 ± 0.13 to 5.41 ± 0.29 kg and % friability was found to be 0.36 ± 0.21 to 0.47 ± 0.14%. The thickness of the tablet was found to be 4.15 ± 0.05 to 4.48 ± 0.05 mm. From the above discussion it was found that all parameters were within the acceptable limits.

Table 3. Physical evaluation of tablets

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Weight variation (%)</td>
</tr>
<tr>
<td>F1</td>
<td>1.217 ± 0.22</td>
</tr>
<tr>
<td>F2</td>
<td>1.506 ± 0.13</td>
</tr>
<tr>
<td>F3</td>
<td>1.513 ± 0.72</td>
</tr>
<tr>
<td>F4</td>
<td>0.924 ± 0.43</td>
</tr>
<tr>
<td>F5</td>
<td>0.701 ± 0.26</td>
</tr>
<tr>
<td>F6</td>
<td>1.411 ± 0.72</td>
</tr>
<tr>
<td>F7</td>
<td>1.207 ± 0.92</td>
</tr>
</tbody>
</table>

Swelling studies

Swelling studies revealed that tablets of all formulations did not show much swelling. Out of these, F3 formulation showed more swelling in 0.1 N HCl because of swelling nature of HPMC K4M and % swelling observed was 89.25 ± 1.64%, followed by F2 formulation which contains next highest amount of HPMC K4M. Results were tabulated in Table 4 and the comparative graph was shown in Figure 4.

Drug content

Drug content observed was very good in all the formulations and the highest was observed in case of F6 with highest pectin concentration and the value observed was 99.95 ± 2.08%. This might be due to the highest amount of pectin which entrapped the drug efficiently. Second highest was observed in case of F7 with 99.81 ± 1.99%. It also contains the same amount of pectin as of F6 which also might be the reason for highest drug content. Least drug content was observed in case of F1 with lowest polymer concentrations. The results were tabulated in Table 4.
Table 4. Table showing drug content and swelling studies

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Drug Content (%)</th>
<th>Swelling (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>97.23 ± 1.59</td>
<td>69.23 ± 1.57</td>
</tr>
<tr>
<td>F2</td>
<td>98.49 ± 2.05</td>
<td>75.33 ± 1.05</td>
</tr>
<tr>
<td>F3</td>
<td>99.37 ± 1.95</td>
<td>89.25 ± 1.64</td>
</tr>
<tr>
<td>F4</td>
<td>97.26 ± 1.86</td>
<td>70.44 ± 2.09</td>
</tr>
<tr>
<td>F5</td>
<td>98.48 ± 2.31</td>
<td>66.87 ± 1.94</td>
</tr>
<tr>
<td>F6</td>
<td>99.95 ± 2.08</td>
<td>65.61 ± 1.67</td>
</tr>
<tr>
<td>F7</td>
<td>99.81 ± 1.99</td>
<td>24.80 ± 2.19</td>
</tr>
</tbody>
</table>

**Swelling Studies**

![Swelling Studies Graph]

**Figure 4. Swelling studies of all formulations**

**In vitro release studies**

Seven different formulations (F1-F7) were prepared in different polymer concentrations and the release characteristics were studied for 12 h. Among all formulations, F6 showed least amount of drug release for the first 2 h in the acidic pH and highest in phosphate buffer with a drug release of 99.54 ± 1.35 % at the end of 12th h. This might be due to presence of eudragit coat which prevents degradation of drug in acidic pH and due to high concentrations of pectin which enabled drug targeting due to its bioactivity. Formulations with insufficient amount of pectin failed in exhibiting the drug release upto 12 h. F5 with next highest amount of pectin showed drug release of 99.93 ± 0.91 % at the end of 10 h. The same was observed with F4 formulation and it showed a drug release of 98.15 ± 1.21 % at the end of 8 h. As the concentration of pectin decreased the drug release time decreased. Considering F6 as optimised formulation, F7 was prepared without eudragit polymer coat to evaluate whether coating helps to protect the drug from acidic pH. The formulation without coat i.e., F7 showed a drug release of 97.24 ± 2.09 % at the end of 4th h. This clearly proved the efficiency of eudragit coat in preventing the drug from degradation in acidic pH. Comparative dissolution graph for formulations F1-F7 was shown in **Figure 5**.

**Stability studies**

Stability studies were performed for all batches to observe physico-chemical changes like colour, appearance, flexibility, drug content. As per the ICH guidelines, temperature and humidity conditions were maintained and tests were carried out. Tablets were analysed at different time intervals for 15, 30, 45, 60 and 90 days. The drug content was found to be in the range of 97.98 ± 2.19 to 99.05 ± 2.73 %. The results indicate that all the formulations were stable upon storage. Stability graph of optimized formulation is shown in **Figure 6**.
Figure 5. Comparative *in vitro* drug release profile of Mesalamine matrix tablet.

Figure 6. Shelf life analysis for formulation F6

Table 5. Drug release kinetics data

<table>
<thead>
<tr>
<th>Formulation</th>
<th>Zero order $R^2$</th>
<th>First order $R^2$</th>
<th>Korsmeyer-Peppa’s $n$</th>
<th>Higuchi $R^2$</th>
<th>Best fit model</th>
</tr>
</thead>
<tbody>
<tr>
<td>F1</td>
<td>0.926</td>
<td>0.698</td>
<td>0.948</td>
<td>0.421</td>
<td>0.718</td>
</tr>
<tr>
<td>F2</td>
<td>0.941</td>
<td>0.713</td>
<td>0.936</td>
<td>0.475</td>
<td>0.747</td>
</tr>
<tr>
<td>F3</td>
<td>0.918</td>
<td>0.690</td>
<td>0.919</td>
<td>0.637</td>
<td>0.710</td>
</tr>
<tr>
<td>F4</td>
<td>0.955</td>
<td>0.826</td>
<td>0.920</td>
<td>0.449</td>
<td>0.807</td>
</tr>
<tr>
<td>F5</td>
<td>0.957</td>
<td>0.680</td>
<td>0.903</td>
<td>0.567</td>
<td>0.849</td>
</tr>
<tr>
<td>F6</td>
<td>0.932</td>
<td>0.841</td>
<td>0.893</td>
<td>0.391</td>
<td>0.875</td>
</tr>
<tr>
<td>F7</td>
<td>0.965</td>
<td>0.943</td>
<td>0.975</td>
<td>0.910</td>
<td>0.954</td>
</tr>
</tbody>
</table>
Mechanism of drug release

From the release kinetics it revealed that the best fit model for formulation F6 was zero order, with release exponent value (n) 0.391, which showed that the release mechanism of tablet followed fickian diffusion. According to the models considered, K values represent release rate constants and R^2 values were represent determination coefficient; and n value represents the release exponent. The results were shown in Table 5.

CONCLUSION

Pectin HPMC K4M matrix tablets targeting colon were successfully prepared and coated with Eudragit L 100. From the results we can conclude that eudragit coat is very essential for the drug to prevent its degradation in acidic pH. We can also conclude that minimum quantity of pectin is essential for effective sustained drug release. For the treatment of diseases such as ulcerative colitis and for the drugs following highest first pass metabolism, this method will be highly effective.

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REFERENCES