FORMULATION AND EVALUATION OF COMPRESSION COATED TABLETS BASED ON MODIFIED OKRA MUCILAGE

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ABSTRACT
Recently there has been greater interest in modified release systems like extended release or delayed release systems to deliver required amount of drug at specific site for duration of therapy. These systems play an important role in the chronotherapy of asthma, angina and arthritis. Compression coated tablets are advantageous as they do not require solvents, and prevent the drug release in gastric region due to presence of coating layer. In the present study fast disintegrating core tablets of model drug diclofenac sodium were coated with coating material granules containing okra mucilage or cross linked okra mucilage in combination with HPMC K15M and evaluated for pre and post compression parameters. The in-vitro disintegration time for core tablets was 64.66 ±0.575sec; % friability was 0.76 % whereas the wetting time was found to be 41.66 ±0.57 sec. All other parameters were found to be satisfactory for core and coated formulations. Formulations CP1, CP2 and CP3 showed drug release of 96.789 ± 0.6699 %, 100.86 ± 0.42729 % and 95.15 ±0.7180 % in 24 hrs respectively. The prepared formulations showed greater drug release after 6 hrs indicating a burst release in intestinal environment, making the formulations suitable candidates for colonic drug release. All the prepared formulations followed first order kinetics with release exponent n>1. There was no significant difference in in-vitro dissolution in presence and absence of rat caecal content indicating drug release depends on pH, swelling and erosion. The formulations were found to be stable for duration of study.

Keywords: Okra mucilage, Compression coated, Diclofenac sodium, Cross linked okra mucilage.

INTRODUCTION
Recently there has been greater development in the field of modified release systems. An ideal drug delivery system should deliver the drug at a rate dictated by the needs of the body over the period of treatment and should provide spatial targeting to specific sites. These prerequisites lead to development of modified release technologies, which can improve the therapeutic efficacy and safety of a drug by targeting the drug to specific site in the body, thereby reducing both the size and number of doses required. The various modified release dosage forms available, include: extended release dosage forms that are designed to achieve a prolonged therapeutic effect by continuously releasing drug over an extended period of time. Delayed release dosage form is designed to release the drug at a time other than promptly after administration. The modified release systems with barrier coating are beneficial for the drugs having chrono-pharmacological behavior, first pass effect and having specific site of absorption in gastro intestinal tract (GIT). Diseases where the modified release systems are promising include asthma, cardiovascular diseases, arthritis, peptic ulcers and hypercholesterolemia.

Diclofenac sodium (DS) is a non-steroidal anti-inflammatory drugs widely used to control pain and inflammation. The conventional therapy may result in local GI toxicity varying from minor gastric discomfort to ulceration and bleeding of the mucosa. In an attempt to reduce side effects and achieve high local drug concentration at the absorption site in the colon, thereby enhancing therapeutic effectiveness and patient compliance. Colon targeted extended release formulations are thus warranted to promote patient compliance and to reduce upper GI toxicity to some extent. DS was selected as a model drug since it is well absorbed in the colon. Colon-specific drug delivery system was developed to reduce side effects and achieve high local drug concentration at the absorption site in the colon, thereby enhancing therapeutic effectiveness and patient compliance. The various approaches that have been studied for targeting orally administered drugs to the colon include use of pro-drugs, pH-sensitive polymers, time-dependent dosage forms and the use of carriers degraded by enzymes produced by colonic bacteria. Among the strategies, compression coated systems seem to be superior in preventing premature drug release in stomach and small intestine, and release the active agents at the proximal colon. The polysaccharides due to hydrophilic nature dissolve in the aqueous dissolution medium and show higher drug release. To overcome this problem, additional excipients like HPMC or retardants like ethyl cellulose are required to be included.

In the present study it is proposed to use the okra mucilage and cross linked okra mucilage with chitosan in combination with HPMC K15M as coating polymer in compression coated formulations to achieve the colon specific release of diclofenac sodium for chronotherapy of arthritis.

MATERIALS AND METHODS
Okra pods obtained from local market, diclofenac sodium as a gift sample from Emcure Pharmaceuticals Ltd, Pune, HPMC K15M and chitosan were obtained from SD Fine Chem, Mumbai and Sigma Aldrich, USA respectively. 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) obtained from Spectrochem Ltd Mumbai. All other chemical are of analytical grade.

Extraction of okra mucilage8: Fresh unripe pods of okra (Ladies finger) were obtained from the local market. The pods were cut into very thin slices and the seeds were removed and then soaked in the distilled water (pH 8) for 24 hrs, the swollen slices were then squeezed through muslin bags to obtain aqueous extract. To the aqueous extract twice the volume of alcohol (90%) was added to precipitate the mucilage. The mucilage was defatted and final precipitation was carried out with acetone.

Preparation of chemical cross linked okra mucilage
Okra mucilage is a acidic polysaccharide containing repeating units of (1→4)-β-[(D-galactopyranosyluronic acid)-1→2]-O-α-L-rhamnopyranose.8
Hydrolysis of okra mucilage revealed that the polysaccharide was composed of galacturonic acid, galactose, rhamnose and glucose (1:3:1:0:0.1:0.1). The free –COOH group of Okra mucilage was...
reacted with cationic polymer chitosan which is composed repeating units of N-acetylglucosamine-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC) was used as a zero length cross linking agent.

Optimized Conditions for cross linking

Ratio of okra mucilage: chitosan: 1:0.5, 1:2, 1:1, 2:1, 0.5:1
Concentration of EDC used: 10mM -40mM
Time of cross linking: 1 hr- 24 hrs
pH of reaction: ≤5 adjusted with 0.1 N HCl

Purification: soaked in deionised distilled water for 5hrs with occasional shaking and dialysis against deionised distilled water for 24hrs to remove unreacted EDC.

<table>
<thead>
<tr>
<th>Ratio</th>
<th>OM mg</th>
<th>PH</th>
<th>EDC mM</th>
<th>Time hr</th>
<th>Chitosan mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:2</td>
<td>100</td>
<td>≤5</td>
<td>10</td>
<td>1</td>
<td>200</td>
</tr>
<tr>
<td>1:2</td>
<td>100</td>
<td>20</td>
<td>1</td>
<td>2</td>
<td>200</td>
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<tr>
<td>1:2</td>
<td>100</td>
<td>30</td>
<td>1</td>
<td>2</td>
<td>200</td>
</tr>
<tr>
<td>1:1</td>
<td>150</td>
<td>≤5</td>
<td>10</td>
<td>1</td>
<td>150</td>
</tr>
<tr>
<td>1:1</td>
<td>150</td>
<td>20</td>
<td>1</td>
<td>1</td>
<td>150</td>
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<tr>
<td>1:1</td>
<td>150</td>
<td>30</td>
<td>1</td>
<td>1</td>
<td>150</td>
</tr>
<tr>
<td>1:1</td>
<td>150</td>
<td>40</td>
<td>1</td>
<td>1</td>
<td>150</td>
</tr>
<tr>
<td>2:1</td>
<td>200</td>
<td>≤5</td>
<td>10</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>2:1</td>
<td>200</td>
<td>20</td>
<td>1</td>
<td>1</td>
<td>100</td>
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<tr>
<td>2:1</td>
<td>200</td>
<td>30</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
<tr>
<td>2:1</td>
<td>200</td>
<td>40</td>
<td>1</td>
<td>1</td>
<td>100</td>
</tr>
</tbody>
</table>

Method used for cross linking.

The okra mucilage was dispersed uniformly in deionised distilled water and shaken for 24 hrs using rotary shaker (Remi instruments Ltd, Mumbai, India). The pH of the reaction was adjusted to value of 5 using 0.1N hydrochloric acid. And then the EDC was added in required concentration as per table 1 and stirred on the rotary shaker for 1 hr to activate the carbonyl groups. Then the specified quantity of chitosan was added and stirred on the rotary shaker for 24 hrs to complete cross linking. Cross linked polymer was soaked in deionised distilled water for 5 hrs and then exhaustively dialysed against deionised distilled water for 24 hrs to remove unreacted EDC.

Evaluation parameters for cross linked polymer.

Percent yield

The yield of the dried modified polymers was determined. The ratio of polymers that gave highest yield was selected for further studies.

Swelling study

The modified polymers 100 mg were press molded into tablets using 7.0 mm flat punches (Cadmach machinery Co. Pvt, Ltd. Ahmedabad, India) and the swelling index in phosphate buffer pH 6.8 was determined. Discs were weighed individually (designated as W₁) and placed separately in a petri plate containing 15 ml of phosphate buffer pH 6.8 incubated at 37°C ± 1°C. At regular 1hr time intervals until 8hr, the disc was removed from beaker, and the excess surface liquid was blotted carefully using the filter paper. The swollen disc was then reweighed (W₂) and swelling index (SI) was calculated using the following formula,

$$ S.I = \frac{W_2 - W_1}{W_1} \times 100 $$

Where W₁= Weight of dry disc, W₂= weight of swollen disc (n=3).

Preparation of core tablets of diclofenac sodium

The fast disintegrating core tablets of diclofenac sodium were prepared by direct compression (table 2). The drug, polymer and the super-disintegrant were stirred through sieve # 85. Then they were mixed in a plastic pouch for 10 min to get uniform mixture. The lubricants were added to the mixture and again mixed. The drug excipient blend was compressed on a single station rotary tablet machine (Karnavati Engg. Ltd, Gujarat, India) using 7mm convex punches.

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Ingredients</th>
<th>Composition/tablet(mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Diclofenac sodium</td>
<td>100 mg</td>
</tr>
<tr>
<td>2</td>
<td>Okra mucilage</td>
<td>05 mg</td>
</tr>
<tr>
<td>3</td>
<td>Sodium starch glycolate</td>
<td>9 mg (6%)</td>
</tr>
<tr>
<td>4</td>
<td>Lactose</td>
<td>33 mg</td>
</tr>
<tr>
<td>5</td>
<td>MgS+Talc</td>
<td>3 mg</td>
</tr>
</tbody>
</table>

MgS= Magnesium stearate, Weight of core tablets=150mg.

Preparation of coating material and compression coated tablets

The formulations of compression coating, for coating of core tablets are shown in table 3. The coating granules were prepared by wet granulation technique using 2% w/v ethyl cellulose in isopropyl alcohol as a binder. The powders were blended in a plastic pouch to get uniform mixture and granulated with solution of ethyl cellulose. Then the granules were obtained by passing the wet mass through sieve #16. The granules were dried at 50°C for 1hr in a hot air oven (Sunshine industries, Coimbatore India). The dried granules were resized by passing through sieve # 22 and were lubricated with a mixture of talc and magnesium stearate. Then 45% weight of coating material granules were then kept in die cavity and then core tablet was placed carefully on it in centered position and then remaining 55% of coating material granules were added to cavity and compressed into tablets, by using convex punches of 10.05 mm diameter after optimizing the hardness and die cavity of rotary tablet machine, so that the tablets will be of uniform hardness and with minimal weight variation.

<table>
<thead>
<tr>
<th>Table 3: Composition of coating material</th>
</tr>
</thead>
<tbody>
<tr>
<td>Form Code</td>
</tr>
<tr>
<td>-----------</td>
</tr>
<tr>
<td>H</td>
</tr>
<tr>
<td>M1</td>
</tr>
<tr>
<td>M2</td>
</tr>
<tr>
<td>M3</td>
</tr>
<tr>
<td>CP1</td>
</tr>
<tr>
<td>CP2</td>
</tr>
<tr>
<td>CP3</td>
</tr>
</tbody>
</table>

2% w/v EC in isopropyl alcohol was added to each coating material as a binder, weight of coated tablets = 300 mg

(OM Okra mucilage, CP cross linked polymer, MCC Microcrystalline cellulose, MgS Magnesium stearate)

Evaluation of core and coated tablets

Compatibility study

Fourier Transform Infra Red (FTIR) of okra mucilage: The mixture of sample powders and KBr prepared in the form of potassium bromide pellets by applying a pressure of 7 tons for 5 min in a KBr press. The pellet was placed in the light path and the spectrum was obtained by scanning from 4000 cm-1 to 400 cm-1 using FT-IR spectrophotometer (FT-IR-BR400S, Shimadzu, Japan).

Differential scanning Calorimeter study

Samples were subjected to Differential Scanning Calorimeter (DSC) for compatibility study (Mettler Toledo, USA). For DSC, aluminum pans are employed to place the samples which are then sealed with aluminum caps and kept under nitrogen purging (atmosphere). The
heating rate was kept at 10°C rise per min up to 300 °C to better integrate the information.

Physical evaluation of core and coated tablets
The core and coated tablets were evaluated for pre-compression\textsuperscript{9} parameters like loose bulk density, tapped density, Carr’s index, Hausner’s ratio and angle of repose using standard procedures. Mean of three readings was recorded

The thickness of the diclofenac sodium matrix tablets was determined by using dial micrometer (Mitutoya, Japan). Montecarlo hardness tester was used to determine the tablet crushing strength. Percent friability was determined using Roche Friabilator.\textsuperscript{10} Weight variation test was performed for 20 tablets and percent weight deviation was calculated.\textsuperscript{11}

**In-vitro Disintegration time**

In-vitro disintegration time was determined for core tablets using disintegration test apparatus. A tablet was placed in each of the six tubes of the apparatus and one disc was added to each tube. The phosphate buffer pH 6.8 was maintained at a temperature of 37±0.5°C and time taken for complete disintegration of the tablet with no palpable mass remaining in the apparatus was measured in seconds.

**Wetting time**

A piece of tissue paper folded twice was placed in a small petri dish containing 10 ml of phosphate buffer pH 6.8. A core tablet was put on the paper, and the time required for complete wetting was measured. Three trials were performed; average time for wetting with standard deviation was recorded.

**Drug Content**

Drug content uniformity test was performed to check dose uniformity in the formulation. Randomly ten tablets were weighed and powdered. A quantity equivalent to 100 mg of diclofenac sodium was placed in a 100 ml volumetric flask and dissolved in 60 ml methanol, sonicated for 10 minutes and made up to the mark and filtered through 0.45μ membrane filter. After appropriate dilutions with phosphate buffer pH 6.8, the drug content was determined by UV spectrophotometer at 276 nm against suitable blank using standard plot equation.

**In-vitro release studies for core tablets**

The core tablets were subjected to in-vitro dissolution studies in 900 ml phosphate buffer pH 6.8 for 1 hr using an USP XXIII dissolution apparatus II at 50 rpm maintained at 37 ± 0.5°C. The aliquot was withdrawn after every 10 min and filtered through 0.45μ membrane filter and diluted suitably and analyzed using UV-visible double-beam spectrophotometer (Shimadzu-UV 1601, Japan) at 276 nm. Equal amounts of fresh dissolution medium were replaced immediately after withdrawing an aliquot.

**In-vitro release studies for coated tablets**

The in-vitro drug release study was carried out using an USP XXIII dissolution apparatus II at 500 ml of dissolution medium maintained at 37 ± 0.5°C for 24 hrs at 50 rpm. 0.1N hydrochloric acid of pH 1.2 was used as dissolution medium for first 2 hrs as average gastric emptying time is 2 hrs. The dissolution medium was replaced by phosphate buffer pH 7.4 for further 3 hrs as small intestinal transit time is 3 hrs. Once again the dissolution medium was replaced by phosphate buffer pH 6.8. A 5ml aliquot was withdrawn at predetermined time intervals, filtered through 0.45μ membrane filter and diluted suitably and analyzed using UV-visible double-beam spectrophotometer (Shimadzu-UV 1601, Japan) at 276 nm. Equal amounts of fresh dissolution medium were replaced immediately after withdrawing an aliquot. Samples were assayed in triplicate.

**In-vitro drug release studies with and without 2% rat caecal contents**

The rat caecal content (anaerobic in nature) was collected and immediately transferred into buffer saline solution pH 6.8 to obtain 2% w/v concentration. Solution was previously bubbled with carbon dioxide gas to maintain an anaerobic environment. The tablets of formulations CP2 were tested for drug release for 2 hours in pH 1.2 (100 ml) as the average gastric emptying time is about 2 hours. Then, the dissolution medium was replaced with phosphate buffer pH 7.4 (100 ml) and tested for 3 hours as the average small intestine transit time is about 3 hours, again the medium was replaced with 100 ml of pH 6.8 phosphate buffer with 2% w/v rat caecal contents and also with the same medium phosphate buffer pH 6.8 but without rat caecal content as control.

**Release kinetics**

The in-vitro dissolution data was fitted into different kinetic models like zero and first order, Korsemeyer peppas and Weibull model to find out the drug release profile.\textsuperscript{12}

\[
Q_t = K_st ---- Zero order
\]

\[
Q_t = Q \cdot (1-e^{-kt}) ---- First order
\]

\[
\frac{Q_t}{Q_{\infty}} = K_i^{b'} ---- -Korsemeyer Peppas
\]

In Peppas model \(Q_t/Q_{\infty}\) is the fraction of drug released at time \(t\), \(K_i\) is constant and \(n\) is release exponent respectively.

**Weibull model:**

The data obtained were also fit to Weibull model to further elucidate mechanism of release. The Weibull equation expresses the accumulated fraction of the drug, \(m\), in solution at time, \(t\), by

\[
m = 1 - e\left(-\frac{(t-T_i)^b}{a}\right)
\]

In this equation, the scale parameter, \(a\), defines the time scale of the process. The location parameter, \(T_i\), represents the lag time before the onset of the dissolution or release process and in most cases will be zero and \(b'\) is the shape parameter.\textsuperscript{13}

**Statistical analysis**

The formulation CP2 was subjected to in-vitro drug release study with or without rat caecal content. The data obtained from the dissolution studies were statistically analyzed by one way ANOVA followed by post hoc Tukey method. The statistical analysis was performed using Graphpad Prism software Inc (USA Version 4.0). A probability value of \(P <0.05\) was considered as statistically significant.

**Stability studies**

The stability studies were performed for the selected formulation CP2 which was maintained at 40±2°C and 75 ± 5 % RH and also at room temperature in a desiccator at 25±2°C and 60 ± 5 % RH for a period of six months. At the end of every month the formulations were observed for physical changes. After six months the formulations were tested for hardness, drug content and drug release profiles.

**RESULTS AND DISCUSSION**

**Percent yield**

The okra mucilage was modified by reaction with chitosan at different ratios (1:0.5, 1:1, 1:2, 2:1 and 0.5:1) using 1-(3-dimethylaminopropyl)3-ethylcarbodiimide hydrochloride (EDC) as a cross linking agent at different concentration of 10, 20, 30 and 40 mM. The results of preliminary studies showed that at the ratio of 1:0.5 and 0.5:1 the % yield was negligible, hence only 1:1, 1:2 and 2:1 ratio were selected for further study.

The % yield of cross linked polymer was higher (72.57 to 83.10\textsuperscript{11}) at 2:1 ratio were selected for further study. The formulation CP2 was subjected to in-vitro drug release study with or without rat caecal content. The data obtained from the dissolution studies were statistically analyzed by one way ANOVA with or without rat caecal content. The data obtained from the dissolution studies were statistically analyzed by one way ANOVA followed by post hoc Tukey method. The statistical analysis was performed using Graphpad Prism software Inc (USA Version 4.0). A probability value of \(P <0.05\) was considered as statistically significant.
remove the traces of unreacted chemicals. Carbodimides unlike gluteraldehyde or polyepoxide do not remain as a part of that linkage but simply change to water soluble urea derivative that have very low cytotoxicity.\textsuperscript{14} This urea can be removed by above treatment. It was reported that the supernatant solutions were not toxic when the polymers synthesized with 50mM EDC were sonicated for 30 sec in distilled water for five times to remove residual EDC.\textsuperscript{15} From this it can be stated with exhaustive washing cycle the modified polymer was devoid of any residual EDC, hence not toxic.

**Swelling index**

The swelling study was performed for cross linked polymers synthesized at different polymeric ratios and 40 mM concentration of cross linking agent in phosphate buffer pH 6.8. The swelling was highest and more sustained for modified polymers C3 (40mM, 2:1). The polymer C3 showed suitable properties to be used for modified release formulations.

**FTIR studies**

OM is characterized by several IR absorption bands. The absorption at 3442.94 cm\(^{-1}\) is characteristic of free OH - groups, 1637.56 cm\(^{-1}\) of symmetrical and asymmetrical oscillations is characteristic of ionized carboxyl groups, and 2922.16 cm\(^{-1}\) is attributed to the –CH\(_2\) groups of OM. In addition, the minor absorption peak at 2123.63 cm\(^{-1}\) is attributed to CO\(_2\) and H\(_2\)O. The occurrence of cross linking is ascertained by the slight increase in the amide bands at 1633.94 cm\(^{-1}\), 1537.72 cm\(^{-1}\), 1412.50 cm\(^{-1}\) and 1017.35 cm\(^{-1}\) (figure 1).

The FTIR spectra of formulations H, M1 and CP2 showed the presence of peaks associated with diclofenac sodium. The results indicated that no interaction has taken place between drug and the excipients.
Fig. 1: FTIR spectra of okra mucilage (A), diclofenac sodium (B), cross linked okra mucilage at 2:1 ratio and 40 mM (C), formulation H (D), M1 (E) and CP2 (F)

Differential scanning calorimeter

The DSC thermograms of formulations M1 and CP2 showed endothermic peaks at 79.96°C and 272.31°C and 84.05°C and 277.01°C (figure 2). The slight decrease in temperatures of the endothermic peaks and melting point of diclofenac sodium may be due to mixing of drug with excipients and change in thermal behavior of drug in presence of excipients. The results indicated that the drug and the excipients were compatible.

Fig. 2: DSC thermograms of diclofenac sodium (A), formulations M1 (B) and CP2(C).
Evaluation of core tablets
The fastest disintegrating core tablets showed the in-vitro disintegration time of 64.6 ± 0.57 sec, friability 0.76 % and the wetting of 41.66 ± 0.57 sec. All other parameters were found to be satisfactory.

Physical evaluation of compression coated tablets
The results of pre-compression study showed good compressibility and flow property of prepared granules (table 4). The coating materials contained okra mucilage, cross linked okra mucilage with HPMC in the ratios of 4:1, 1:1 and 1:4. The compression coated formulations were prepared at core to coat ratio of 1:1. The post compression parameters of prepared formulations were evaluated and the results are shown in table 5. The results indicated good mechanical strength. The formulations showed drug content of 99.550 ± 0.5945 % to 98.5018 ± 0.5655 %. The percent deviation in weights of the prepared formulations was found to be within the specified limits. The results indicated satisfactory physical properties of prepared formulations.

Table 4: Pre-compression parameters for coated tablets

<table>
<thead>
<tr>
<th>Form Code</th>
<th>Bulk Density (gm/ml)</th>
<th>Tapped Density (gm/ml)</th>
<th>Carr’s Index %</th>
<th>Hausner’s Ratio</th>
<th>Angle of Repose °</th>
</tr>
</thead>
<tbody>
<tr>
<td>CORE</td>
<td>0.537 ± 0.012</td>
<td>0.608 ± 0.015</td>
<td>11.716 ± 0.255</td>
<td>1.132 ± 0.003</td>
<td>30.80 ± 0.057</td>
</tr>
<tr>
<td>M1</td>
<td>0.389 ± 0.008</td>
<td>0.482 ± 0.007</td>
<td>19.993 ± 0.823</td>
<td>1.238 ± 0.042</td>
<td>31.11 ± 0.1</td>
</tr>
<tr>
<td>M2</td>
<td>0.408 ± 0.006</td>
<td>0.460 ± 0.012</td>
<td>11.374 ± 0.826</td>
<td>1.118 ± 0.039</td>
<td>30.80 ± 0.152</td>
</tr>
<tr>
<td>M3</td>
<td>0.391 ± 0.011</td>
<td>0.452 ± 0.025</td>
<td>13.450 ± 0.732</td>
<td>1.154 ± 0.031</td>
<td>30.49 ± 0.2</td>
</tr>
<tr>
<td>CP1</td>
<td>0.422 ± 0.010</td>
<td>0.520 ± 0.009</td>
<td>17.104 ± 0.615</td>
<td>1.232 ± 0.035</td>
<td>30.04 ± 0.288</td>
</tr>
<tr>
<td>CP2</td>
<td>0.383 ± 0.006</td>
<td>0.464 ± 0.006</td>
<td>17.393 ± 0.198</td>
<td>1.210 ± 0.002</td>
<td>30.80 ± 0.057</td>
</tr>
<tr>
<td>CP3</td>
<td>0.382 ± 0.007</td>
<td>0.451 ± 0.009</td>
<td>15.309 ± 0.692</td>
<td>1.180 ± 0.009</td>
<td>30.04 ± 0.115</td>
</tr>
<tr>
<td>H</td>
<td>0.322 ± 0.010</td>
<td>0.360 ± 0.014</td>
<td>12.306 ± 0.263</td>
<td>1.155 ± 0.032</td>
<td>30.64 ± 0.1</td>
</tr>
</tbody>
</table>

Table 5: Post-compression parameters for coated tablets

<table>
<thead>
<tr>
<th>Form Code</th>
<th>Thickness (mm)</th>
<th>Hardness (Kg/cm²)</th>
<th>Friability %</th>
<th>Drug Content Weight ± % Deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Core</td>
<td>2.666 ± 0.02</td>
<td>3.233 ± 0.01</td>
<td>0.76</td>
<td>100.224 ± 0.449</td>
</tr>
<tr>
<td>M1</td>
<td>4.27 ± 0.01</td>
<td>5.673 ± 0.046</td>
<td>0.3513</td>
<td>99.17 ± 0.3432</td>
</tr>
<tr>
<td>M2</td>
<td>4.22 ± 0.003</td>
<td>5.933 ± 0.0577</td>
<td>0.085</td>
<td>99.101 ± 0.979</td>
</tr>
<tr>
<td>M3</td>
<td>4.09 ± 0.03</td>
<td>6.3 ± 0.1</td>
<td>0.2134</td>
<td>99.550 ± 0.594</td>
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<tr>
<td>CP1</td>
<td>4.23 ± 0.02</td>
<td>5.766 ± 0.152</td>
<td>0.1982</td>
<td>98.876 ± 0.449</td>
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<tr>
<td>CP2</td>
<td>4.163 ± 0.0125</td>
<td>5.466 ± 0.1154</td>
<td>0.2154</td>
<td>98.876 ± 0.2247</td>
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<tr>
<td>CP3</td>
<td>4.156 ± 0.0923</td>
<td>5.333 ± 0.1527</td>
<td>0.185</td>
<td>98.951 ± 0.7223</td>
</tr>
<tr>
<td>H</td>
<td>4.25 ± 0.005</td>
<td>5.31 ± 0.0953</td>
<td>0.3720</td>
<td>99.475 ± 0.6866</td>
</tr>
</tbody>
</table>
In-vitro drug release in presence and absence of rat caecal content

The effect of rat caecal enzymes on the drug release was investigated by performing in-vitro dissolution studies in presence of 2% w/v rat caecal content and in absence of the same (figure 5). The difference in the in-vitro drug release profile was found to be less significant (p>0.05).

Stability study

The stability study for the selected formulations CP2 and H was performed as per ICH guidelines. The results of the stability study indicated there was less significant decrease in the hardness of the formulations. The change in the % drug content and % drug release was also found to be less significant (p>0.05). This indicated satisfactory stability of the prepared formulations for the duration of study.

CONCLUSION

Okra mucilage and modified okra mucilage were successfully used as coating materials in combination with HPMC K15 M to deliver model drug diclofenac sodium to colon for chronotherapy of arthritis. The drug release was extended for 24 hrs in colon. The formulations followed first order kinetics with pH dependent swelling, polymer relaxation and erosion as release mechanisms.

REFERENCES


