Research Article

FORMULATION AND EVALUATION OF MUCOADHESIVE TABLET OF PANTOPRAZOLE SODIUM

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ABSTRACT

Pantoprazole sodium (PAS) is a proton pump inhibitor, with an anti-ulcer activity. Due to the short elimination half-life and poor bioavailability, it’s rapidly degrades in gastro intestinal tract (GIT). An objective of work, to formulate mucoshesive tablets for prolongation of drug release and preventing GI degradation. PAS tablets formulated using different concentration of HPMC and Xanthan gum by wet granulation technique and evaluated characterizations. Prepared granules were subjected to the pre-compression and post-compression evaluations, and there is no significant variation of tablets. PAS 3 showed better ex-vivo mucoadhesive strength (31.44±1.06g), and force (3.08±0.072N), highest in-vitro mucoadhesion time (476±0.596 min) and good swelling index (82.07%). PAS 3 had proven 79.48% drug release at end of dissolution studies and the mechanism of drug release kinetics was analyzed. Overall, optimized EPAS 3 formulation was evaluated the relevant parameters. GRDDS mucoshesive tablets were shown satisfactory sustained release and suitable for potential therapeutic effects.

INTRODUCTION

Controlled drug delivery systems (CDDS) is extend the existence of dosage form in GI absorption site (Debijit Bhowmik et al, 2012) and shown benefits like maintenance of optimum therapeutic drug concentration in blood (Chien YW, 1985). But several difficulties are faced in designing CDDS for better absorption and an inability to confine dosage form in GIT (Hirtz J, 1985). It can be achieved by Gastro-retentive drug delivery systems (GRDDS), which can remain in the desired area of gastric region for several hours and hence significantly prolong the gastric residence time (GRT) of drug. Such systems utilize the property of mucoadhesion of certain polymers which become an adhesive on hydration and used for extending retention time to the particular region of mucosal surfaces and the flexibility for interpenetration with mucous which enable continuous input of drug into an upper part of GIT (Kavitha et al, 2010). Thus provides possibility of avoiding destruction by GI contents, decrease dosing frequency and prolonged effect which better than conventional therapy (Chowdary et al, 2000). Based on the above concept, mucoadhesive drug delivery systems (Deshpande et al, 1997; Kawashina et al, 1992; Washington N, 1990; Ponchel et al, 1998; Rednick et al, 1970; Hwang et al, 1998) has received a significant degree of attention due to lengthened period of contact time with absorbing membrane and proven an expected bioavailability, high drug loading capacity, good mucoadhesive properties and controlled release (Timmermans and Moes, 1990). Also mucoadhesive polymers could be used as therapeutic agents in their own right, to coat, protect and soothe injured tissues. These polymers can be naturally occurring e.g. chitosan and pectin (or) synthetic e.g. polyacrylic acid derivatives and cellulose derivatives. They are classified as anionic, cationic/non-ionic and are water soluble / insoluble in nature (Nafee et al, 2004; Rossi et al, 2005; Punitha and Girish, 2010). Pantoprazole sodium (PAS) is chemically known as sodium-5- (difluoromethoxy) – 2 – [[(3, 4- dimethoxy-2- pyridinyl) methyl][sulfinyl]-1H, is a substituted benzimidazole derivative (Fig 1), that targets gastric acid proton pumps, used for the treatment of peptic ulcer, gastroesophageal reflux disease and control of Zollinger-Ellison syndrome (Ganesh et al, 2011; Devi and Basavaiah, 2010; Choi et al, 2000). However, it's
completely absorbed after oral administration (Dose: 40mg once/twice daily), short elimination half-life (1-2h), low bioavailability (77%), undergoes hepatic first pass metabolism and have short stability due to rapidly degrades in the stomach. So an improve the bioavailability, preventing gastric rapid degradation and maintain blood level concentration, favors the development of mucoadhesive formulations may solve the stability properties of drug in the stomach and an improve gastric residence with an efficient absorption especially in GI mucosal layer, which can provide an extended drug release in constant level without waste (Randip Chaudhary and Basavaraj, 2016). So present studies, an attempt to prepare gastro-retentive mucoadhesive pantoprazole sodium in tablet form using natural and synthetic polymers which expect to retain in the stomach for sufficient hours and reduce dosing frequency fluctuation for management of peptic ulcer. Thus mucoadhesive tablet tend to formulate using HPMC and xanthan gum with different ratios and determine the characterizations. An optimized formulation was also subjected to an enteric coating property and analyzes the relevant parameters.

MATERIALS AND METHODS

Materials

Pantoprazole Sodium (PAS) received from Aurobindo Pharma Pvt Ltd, Hyderabad. Hydroxy propyl methyl cellulose, Xanthan gum, Magnesium Stearate and Potassium Bromide obtained from Qualigens Fine Chem Pvt Ltd, Mumbai, Avicel PH 102 from Research Lab Fine Chem Industries, Mumbai, Eudragit L100 from Balaji Chemicals, Surat and Titanium dioxide from Nice Chemicals Pvt Ltd, Ernakulam, Kerala. All other chemicals used were analytical grade.

IR spectral analysis

The Fourier-transform infrared (FT-IR) spectrum of PAS and polymers was recorded using KBr mixing method on the FT-IR instrument (Schimadzu). The drug alone and in combination with polymers (mixed in ratio of 1:1) was taken and subjected to FT-IR studies (Rajamanickam et al, 2010).

Methods

Preparation of Pantoprazole sodium mucoadhesive tablets

Pantoprazole sodium (PAS) granules for tabletting were prepared by wet granulation method. Specified quantity of PAS and polymers such as Hydroxy propyl methyl cellulose (HPMC) and Xanthan gum, Avicel pH 102 were weighed (Table 1) and transferred into a mortar and pestle, and mixed thoroughly. The dry powder mass (previously passed through sieve no. 40) was mixed with adequate quantity of starch paste to obtain a sluggy mass and it’s passed through sieve no.10 to obtain the wet granules which was dried at 50°C for 4h. And the dried granules were screened through sieve no.16 and 44 and then the specified quantity of magnesium stearate and talc were also added finally and mixed. Then an ideal mixture of granules were directly punched into tablets weighing about 180 mg equivalent 40mg of drug, using multi station rotary tablet compression machine (8 stations). The different batches of PAS mucoadhesive tablets (Photograph 1&2), were collected, stored in air tight containers and used for further studies (Badoni et al, 2012).

Characterization of Mucoadhesive Tablets

Micromeric Properties of granules (Pre-compression)

PAS granules were characterized by their micromeric properties like Bulk density, Tapped density, Carr’s index, Hausner’s ratio and Angle of repose (Aulton ME and Wells, 1988; Martin A, 1988; Liberman 1991).

Thickness, Hardness, Weight variation and Friability (Post-compression)

Prepared Tablets were evaluated for their thickness, hardness and weight variation using Varnier calipers, Monsanto hardness tester and Digital balance (Schimadzu) and average determined. The friability test done by using Roche’s friabilator which was carried out at 25 rpm and percentage loss was calculated (Guda et al, 2010; Ali-Marzouqi et al, 2006; Shivanand S Shiralashetti et al, 2010).

Friability (%)) = (1- W/ Wo) × 100

Determination of Drug content uniformity

An accurately weighed quantity of tablets was finely powdered and kept in 100ml volumetric flask containing phosphate buffer (pH 6.8). After it’s completely dissolved then the solution is allowed to filter. Then 1ml filtrate was taken and absorbance measured by using UV spectrophotometer at 288nm (Davashala V Bhave et al, 2017).

Ex-vivo Mucoadhesion Strength and Force

Modified physical balance was used to determine ex-vivo mucoadhesive strength of tablets by Detachment force measurement method. Initially sheep intestine mucosa membrane (2×2) was cut into pieces and washed with PBS (pH 6.8) and tied to a block which moistened with PBS. The both pans were balanced by adding an appropriate weight on left side pan. The block was then lowered into the glass container, which was filled with an isotonic PBS and kept at 37°±10°C, such that buffer just reaches the surface of mucosal membrane and keeps it moist. This was kept below the left hand set-up of balance. Mucoadhesive strength was also assessed in terms of weight (gm) required to detach the tablets from mucosal membrane. The force of adhesion was calculated from mucoadhesive strength (Perioli et al, 2007; Pethe et al, 2014).

Force of adhesion (N) = (Mucoadhesive strength × 9.81) ÷ 100

In-vitro Mucoadhesive Time

Mucoadhesive properties of prepared formulations were evaluated by an in-vitro adhesion testing known as wash-off method. Pieces of intestinal mucosa were mounted on to glass slides were connected with suitable support. A tablet is attached on to the slide and the support was hung on to the arm of a USP tablet disintegration apparatus. By operating an apparatus, it was given a slow regular up and down movement in test fluid (pH 6.8) at 37°C temperatures and time of detachment of tablets was counted (Dhruba Sankar Goswami et al, 2010).

Swelling Index Analysis

For conducting swelling study, tablets was weighed (Wo) and placed in a petridish containing 5ml of phosphate buffer (pH 6.8) for 8 hours. After each interval, the tablets were taken out...
from petridish and excess water was removed carefully and weighed again (Wt). The swelling index was calculated using following formula (Paul et al, 2012).

Swelling index (SI) = (Wt-Wo) / Wo × 100,
where SI = Swelling index, Wt = Weight of tablets after time (t), Wo = Weight of tablet before placing in the Petri dish.

In–vivo Dissolution Study

USP dissolution apparatus type II (Lab India, Thane, India) was employed for in vitro drug release studies. The dissolution medium used was 900 mL of acidic buffer (pH 1.2) for first 2h and phosphate buffer (pH 6.8) were used for remaining hours. The formulated tablets were kept into the basket before proceeding on the study. The temperature was maintained at 37±0.5°C and stirring rate fixed at 100 rpm. Samples were withdrawn at regular time intervals and same volume was replaced with fresh dissolution medium. The samples were measured by UV spectrophotometer at 283 nm (pH 1.2) and 288 nm (pH 6.8) against a blank. The dissolution release studies were conducted and mean values were plotted versus time (Sumi et al, 2009) and percentage drug release was calculated. To understand the mechanism and kinetics of in–vivo drug release studies of all formulations was subjected to goodness of fit test by linear regression analysis according to Zero order, First order kinetics equation.

Micromeritic Properties

Bulk Density, Tapped Density, Carr’s Index, Hausner’s Ratio
From Table 2, it was observed that the bulk and tapped density values were lies between 0.308 to 0.347 and 0.346 to 0.398g/cm³ and confirming that the value less than 1.2g/cm³, indicating good packing. The Carr’s index was lies between 10.09% to 12.63%, which indicate excellent flow characteristics of the granules. The Hausner’s ratio was lies between 1.123 to 1.146 which indicating good flow. Also it was observed that, an angle of repose of various proportions of granules is found to be less than 30° indicate free flow properties.

Thickness, Hardness, Average weight, Friability and Drug content
From Table 3, the thickness of all formulated tablets was found in the range of 2.53±0.059 to 2.80±0.056 mm. The hardness of tablets found from 5.2±0.054 to 5.8±0.051 kg/cm² and concludes that the strength increased based on the polymer proportions. From an average weight, 170mg to 180mg was found in all formulations and there is no significant variation observed. The friability of tablets was also found less than 1% indicates that, the test complied with an official test as per IP and good mechanical resistance. The drug content was found from 96.85±0.68% to 99.42±0.48%, indicating uniform distribution of drug over an area of the surface of tablets.

Ex-vivo Mucoadhesion Strength and Force
Mucoadhesion strength of tablets (Photograph 3) to be a function of nature and concentration of polymers. From Table 4, mucoadhesive strength of formulations (PAS 1 to PAS 3) was found from 27.37±1.15g to 31.44±1.06g and
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mucoadhesion force from 2.68±0.069N to 3.08±0.072N. The strength of formulation (PAS 4 to PAS 6) found 26.42±1.12g to 28.33±1.21g and force from 2.59±0.063N to 2.77±0.063N respectively. It’s observed that, HPMC formulations have good strength and greater force (16-19%) than xanthan gum batches. Overall, PAS 3 proved better in both mucoadhesive strength and force.

In-vitro Mucoadhesive Time (In-vitro wash off test)
From results (Fig 5), the mucoadhesive time of tablets were found in the ranges from 371±0.521 to 476±0.596 min (PAS 1 to PAS 6) and indicates that all formulated tablets had fairly good mucoadhesive properties in PBS (pH 6.8) and the rapid wash-off reduces an adhesive strength. Overall, PAS 3 exhibited 476±0.596 min than other tablets due to the increase in polymer solubility in turn to produce a viscous gel which increases the mucoadhesion property.

Swelling Index
In swelling studies, all mucoadhesive formulations were hydrated by keeping tablets in contact with PBS (pH 6.8) upto 8h. This indicates the hydrophilic property of polymers with establishing fundamentals that an increase in degree of swelling depends on the polymer concentrations. HPMC formulated tablets had shown greater percentage and good degree of swelling index than PAS 4 to PAS 6 (Fig 6). The highest swelling was observed in PAS 3 formulation which may due to quick hydration of polymers. The images of swelling behavior are shown in Photograph 4 respectively.

In–vivo Dissolution Profile
The results of comparative in-vitro dissolution plots (Fig 7&8), PAS 1, PAS 2 and PAS 3 had shown the percentage drug release from 89.83%, 84.78% and 79.48% using HPMC and xanthan gum formulated tablets (PAS 4, PAS 5 & PAS 6) was also exhibited 96.89%, 93.58% & 90.53% drug release respectively. Among all formulations, PAS 3 had proven better release (79.48%), and drug release rates over 12h due to an increased the polymer concentration. In similar manner, PAS 6 has shown 90.53% drug release at end of intervals due to an increased level of xanthan gum. Overall comparative results, higher concentration of HPMC tablets were shown a least percentage release than other formulations due to the basis for hydrophilic matrices for oral delivery.

In order to understand the mechanism and kinetics of an in-vitro drug release (Table 5) and coefficient of correlation (r) values were computed. From results, co-efficient of determination indicated that, release data was best fitted with first order kinetics. When drug release data was put into Higuchi’s equation, good correlation coefficient (r) values 0.965 to 0.994 were obtained, which indicating diffusion controlled release mechanism. The release data were also substitute in Korsmeyer-Peppas model in order to find out n values which describe the drug release mechanism. From the kinetics data results, the n values were found in the range between 0.633 to 0.789 with correlation coefficient values ranging from 0.979 to 0.995, indicating non-fickian diffusion mechanism. Hence, an above observation, the release of drug from the formulated tablets using HPMC and Xanthan gum was proven a sustained release pattern for a period of sufficient hours and kinetics study shows that ‘r’ values of all batches indicate compliance with Higuchi’s plot.

Mucoadhesive Tablets Behavior
Based on an in-vitro drug release performance, the best formulations (PAS 3 & PAS 6) were taken for mucoadhesive strength test and crushing analysis which was evaluated by Microsystems Texture analyzer.

Mucoadhesive strength test
PAS-3 tablet exhibited more mucoadhesiveness (180 sec) compared than PAS 6 (Photographs 5&6). In both formulations, the time period contact of tablets with the mucoadhesive layer of goat intestine (adhesiveness) increases upto 2 min beyond that it decreases.

Hardness / crushing strength
From images of crushing strength test (Photographs 7&8), PAS 3 have good crushing strength than PAS 6. This was reflected in increased hardness and work of penetration readings. Overall, among two formulations, PAS 3 was proven good hardness and mucoadhesive strength.

Enteric Coated Mucoadhesive Tablets
For enteric coating (EC), best formulation (PAS 3) was selected based on their characterizations and the selected tablets were subjected to the required coating as per composition ratios. From the results of evaluated parameters of coated tablet (EPAS 3), drug content was found be 99.56% and shown promising mucoadhesion strength (34.34g). Mucoadhesion time is performed using USP disintegration apparatus and it was found in 480min which nearly higher than plain mucoadhesive tablet (PAS 3). Swelling index behaviour of coated tablets was also performed in PBS (pH 6.8) upto the required intervals and proven good swelling index (85.01%) (Table 6).

The comparative in-vitro drug release plots of plain and EC mucoadhesive tablets (Fig 9) results, EPAS 3 exhibited not more than 67.87% drug release at end of appropriate hours and didn’t much amount release in an acidic medium and also further expecting to release at additional hours using PBS. Overall comparative dissolution behavior studies (Photograph 9), EPAS 3 formulation were proven greatest strength and exhibited sustained effects than plain PAS 3 tablet, so it’s concluded that, an in-vitro release of coated tablets was delayed by barrier coating, which until it reaches intestinal environment especially in ulcer patients.

CONCLUSIONS
From research studies, developed gastro retentive mucoadhesive PAS tablets expected to retain in GIT and have potential sustained effective release over a sufficient and long period of time. Hence an optimized formulation (PAS 3) and enteric coated tablets (EPAS 3) had proven good mucoadhesive and better in-vitro drug release. So designing GRDDS for novel drugs of narrow absorption window, found suitability for the treatment of an acid-related disease of stomach especially upper parts of GIT and may reduce dose intake, avoid drug degradation, minimize blood level oscillations and adverse effects with an improvement of the patient compliance.
Acknowledgements

The authors are thankful to the Management, Devaki Amma Memorial College of Pharmacy, Chelenbra, Malappuram Dt, Kerala, for providing support and necessary facilities to carry out this research work.

Table 1 Composition of formulations of Pantoprazole sodium Mucoadhesive tablets

<table>
<thead>
<tr>
<th>Ingredients*</th>
<th>Formulations Code</th>
<th>PAS 1</th>
<th>PAS 2</th>
<th>PAS 3</th>
<th>PAS 4</th>
<th>PAS 5</th>
<th>PAS 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pantoprazole sodium</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Hydroxy propyl methylcellulose</td>
<td>40</td>
<td>60</td>
<td>80</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Xanthan gum</td>
<td>94</td>
<td>74</td>
<td>54</td>
<td>94</td>
<td>74</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>Avicel PH 102</td>
<td>q.s</td>
<td>q.s</td>
<td>q.s</td>
<td>q.s</td>
<td>q.s</td>
<td>q.s</td>
<td></td>
</tr>
<tr>
<td>Starch paste</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Talc</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

* (Equivalent to mg)

Table 2 Bulk density, Tapped density, Carr’s index, Hausner’s ratio and Angle of repose of Pantoprazole sodium Mucoadhesive tablets

<table>
<thead>
<tr>
<th>Form. Code</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>PAS 1</td>
<td>0.30±0.003</td>
<td>0.34±0.002</td>
<td>10.9±0.43</td>
<td>1.12±0.13</td>
<td>26.9±0.14</td>
</tr>
<tr>
<td>PAS 2</td>
<td>0.31±0.002</td>
<td>0.35±0.004</td>
<td>11.2±0.58</td>
<td>1.12±0.21</td>
<td>28.7±0.56</td>
</tr>
<tr>
<td>PAS 3</td>
<td>0.34±0.001</td>
<td>0.39±0.003</td>
<td>11.4±0.54</td>
<td>1.12±0.03</td>
<td>29.5±0.72</td>
</tr>
<tr>
<td>PAS 4</td>
<td>0.31±0.002</td>
<td>0.35±0.001</td>
<td>11.7±0.59</td>
<td>1.12±0.25</td>
<td>27.4±0.07</td>
</tr>
<tr>
<td>PAS 5</td>
<td>0.32±0.004</td>
<td>0.37±0.005</td>
<td>11.8±0.60</td>
<td>1.13±0.29</td>
<td>25.8±0.43</td>
</tr>
<tr>
<td>PAS 6</td>
<td>0.34±0.005</td>
<td>0.39±0.007</td>
<td>12.6±0.63</td>
<td>1.14±0.32</td>
<td>30.5±0.82</td>
</tr>
</tbody>
</table>

Results are mean ± S.D of three trials (n=3)

Table 3 Thickness, Hardness, Average weight, Friability and Drug content of Pantoprazole sodium mucoadhesive tablets

<table>
<thead>
<tr>
<th>Formulations Code</th>
<th>Thickness (mm)</th>
<th>Hardness (kg/cm²)</th>
<th>Average weight (mg)</th>
<th>Friability (%)</th>
<th>Drug content (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAS 1</td>
<td>2.8±0.056</td>
<td>5.6±0.057</td>
<td>173±0.447</td>
<td>0.01±0.02</td>
<td>97.8±0.42</td>
</tr>
<tr>
<td>PAS 2</td>
<td>2.73±0.054</td>
<td>5.4±0.053</td>
<td>170±0.548</td>
<td>0.01±0.015</td>
<td>98.8±0.64</td>
</tr>
<tr>
<td>PAS 3</td>
<td>2.53±0.059</td>
<td>5.8±0.051</td>
<td>176±0.567</td>
<td>0.01±0.025</td>
<td>99.4±0.48</td>
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<tr>
<td>PAS 4</td>
<td>2.58±0.058</td>
<td>5.2±0.054</td>
<td>180±0.668</td>
<td>0.02±0.034</td>
<td>96.8±0.68</td>
</tr>
<tr>
<td>PAS 5</td>
<td>2.72±0.050</td>
<td>5.4±0.052</td>
<td>176±0.623</td>
<td>0.02±0.015</td>
<td>97.4±0.69</td>
</tr>
<tr>
<td>PAS 6</td>
<td>2.78±0.056</td>
<td>5.6±0.058</td>
<td>176±0.479</td>
<td>0.00±0.017</td>
<td>98.5±0.61</td>
</tr>
</tbody>
</table>

Results are mean ± S.D of three trials (n=3)

Table 4 Ex-vivo mucoadhesive strength and force of Pantoprazole sodium tablets

<table>
<thead>
<tr>
<th>Formulations Code</th>
<th>Mucoadhesive strength (g)</th>
<th>Mucoadhesive force (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAS 1</td>
<td>27.37±1.15</td>
<td>2.68±0.069</td>
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<tr>
<td>PAS 2</td>
<td>29.61±1.16</td>
<td>2.90±0.066</td>
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<tr>
<td>PAS 3</td>
<td>31.44±1.06</td>
<td>3.08±0.072</td>
</tr>
<tr>
<td>PAS 4</td>
<td>26.42±1.12</td>
<td>2.59±0.063</td>
</tr>
<tr>
<td>PAS 5</td>
<td>27.03±1.21</td>
<td>2.65±0.065</td>
</tr>
<tr>
<td>PAS 6</td>
<td>28.33±1.21</td>
<td>2.77±0.063</td>
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</tbody>
</table>

Results are mean ± S.D of three trials (n=3)

Table 5 Kinetics analysis of in-vitro drug release data of Pantoprazole sodium mucoadhesive tablets

<table>
<thead>
<tr>
<th>Formulations Code</th>
<th>Zero order</th>
<th>First order</th>
<th>Higuchi’s</th>
<th>Korsmeyer &amp; peppa’s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
<td>S</td>
<td>R</td>
<td>S</td>
</tr>
<tr>
<td>PAS 1</td>
<td>0.907</td>
<td>10.55</td>
<td>0.979</td>
<td>-0.064</td>
</tr>
<tr>
<td>PAS 2</td>
<td>0.913</td>
<td>12.94</td>
<td>0.970</td>
<td>-0.083</td>
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<tr>
<td>PAS 3</td>
<td>0.935</td>
<td>10.72</td>
<td>0.966</td>
<td>-0.063</td>
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<tr>
<td>PAS 4</td>
<td>0.896</td>
<td>10.60</td>
<td>0.909</td>
<td>-0.059</td>
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<tr>
<td>PAS 5</td>
<td>0.857</td>
<td>10.80</td>
<td>0.904</td>
<td>-0.059</td>
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<tr>
<td>PAS 6</td>
<td>0.894</td>
<td>10.79</td>
<td>0.940</td>
<td>-0.055</td>
</tr>
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</table>

Correlation coefficient (R), Slope(S)

Table 6 Evaluated Parameters of Enteric coated mucoadhesive tablet

<table>
<thead>
<tr>
<th>Evaluated Parameters</th>
<th>PAS 1</th>
<th>PAS 2</th>
<th>PAS 3</th>
<th>PAS 4</th>
<th>PAS 5</th>
<th>PAS 6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Drug content (%)</td>
<td>99.56±0.76</td>
<td>34.34±1.15</td>
<td>480.0±0.590</td>
<td>85.01</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Results are mean ± S.D of three trials (n=3)
Figure 5 *In-vitro* mucoadhesion time of Pantoprazole sodium tablets

Figure 6 Swelling index Plot of mucoadhesive tablets

Figure 7 Comparative *in-vitro* drug release plot of mucoadhesive tablets (PAS 1 to PAS 3)

Figure 8 Comparative *in-vitro* drug release plot of mucoadhesive tablets (PAS 4 to PAS 6)

Figure 9 Comparative *in-vitro* drug release plot of mucoadhesive tablets (PAS 3 & EPAS 3)

Photograph 1 Pantoprazole sodium mucoadhesive tablets containing HPMC

Photograph 2 Pantoprazole sodium mucoadhesive tablets containing Xanthan gum

Photograph 3 Ex-vivo mucoadhesion strength of Pantoprazole sodium tablet
Photograph 4 Swelling behaviour of Pantoprazole sodium mucoadhesive tablet

Photograph 5 Mucoadhesive strength of Pantoprazole sodium tablet (PAS 3)

Photograph 6 Mucoadhesive strength of Pantoprazole sodium tablet (PAS 6)

Photograph 7 Hardness strength of of Pantoprazole sodium tablet (PAS 3)

Photograph 8 Hardness strength of of Pantoprazole sodium tablet (PAS 6)

Photograph 9 Dissolution behaviors of enteric coated mucoadhesive tablet (EPAS 3)

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