Exploiting the interaction of polymethacrylates with iron oxide for the enhancement of mucoadhesive strength

Inderbir Singh and Vikas Rana*
Pharmaceutics Division, Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, Punjab, India

Abstract: The present investigation was aimed at preparation of polymethacrylate(s)- iron oxide conjugates and to evaluate mucoadhesive performance using texture analyzer. Eudragit RL-iron oxide or Eudragit RS-iron oxide conjugate granules were prepared by solvent evaporation technique. The mucoadhesive strength of pure Eudragit RL and RS was found to be 11.25±2.02 and 7.78±0.92 g respectively, whereas the same was found to be 36.42±4.01 and 24.32±4.44 for the iron oxide conjugates of Eudragit RL and RS respectively. Hence, mucoadhesive strength of polymethacrylates was found to be enhanced by this technique while, retaining their pH resistant property. A correlation (p>0.05) of 0.97 between mucoadhesive strength and zeta potential indicated conjugation of iron oxide contributed positive surface charge that causes enhancement of mucoadhesion. Further, the ATR-FTIR spectral analysis as well as DSC analysis supported existence of ionic interactions between conjugates (Eudragit RS or RL with iron oxide) and the tissue surface. Hence, the findings point out toward the expected potential use and application of Eudragit RL-iron oxide conjugate in mucoadhesive drug delivery systems, gastro retentive drug delivery systems, etc.

Keywords: Eudragit RS, Eudragit RL, iron oxide, conjugates, mucoadhesive strength, texture analysis, work of adhesion.

INTRODUCTION

Amongst various polymethacrylate polymers, Eudragit RS-100 and Eudragit RL-100 are the only protonated polymeric material. The protonation could be due to quaternary ammonium moieties attached to acrylic acid and methacrylic acid esters backbone. Eudragit RL-100 and Eudragit RS-100 contained 10% and 5% functional quaternary ammonium groups, respectively (Rowe et al., 2006). Interestingly, the ammonium groups present as salts, were found to show pH independent permeability of the polymers. Hence, both polymers are water-insoluble and pH resistant which is essential property of a polymer for its use as mucoadhesive polymeric material. However, these materials are lacking in weak adhesive strength. Therefore, adsorption of iron oxide (water insoluble metal oxide) over the surface of Eudragit RS or Eudragit RL was expected to enhance mucoadhesive component of the polymers, which are otherwise non mucoadhesive.

Adhesion of drug delivery systems to mucosal membranes leads to an increased drug concentration gradient at the absorption site and therefore improved therapeutic effect of administered drugs. Prolongation of gastric residence time of oral sustained release formulations can be used to improve the bioavailability especially for drugs having narrow absorption window in the upper part of the GI tract (Vasir et al., 2003; Nagai and Machida 1985). Mucosal-adhesive formulations generally use polymers as the adhesive component. For these applications, polymers need to be inert, non absorbable, stable and easy to process. For sufficient bioadhesion intimate contact must exist between the polymer of the drug delivery system and the mucosal surface that has arisen due to mechanical, electrostatic or chemical bond formation. Generally adhesion of polymers to biological tissues may involve physical or mechanical bonds (resulting from the deposition or inclusion of adhesive polymers in the cervices of mucosa), primary or covalent bonds and secondary or chemical bonds (resulting from Vander Waals interactions, hydrogen bonding, ionic interactions) (Peppas and Sahlin 1996; Smart 2005).

The present study was aimed at preparation of Eudragit (RS or RL) adsorbed iron oxide conjugate that could improve mucoadhesive potential of the polymer. Texture analyzer was employed for quantifying mucoadhesive performance of Eudragit RS 100 and RL 100 and iron oxide conjugates of the polymers. Further, the effect of texture analyzer parameters (contact force, contact time, test speed and probe return distance) on mucoadhesive properties was explored. Furthermore, the mechanism of mucoadhesion was studied through FTIR, DSC and zeta potential investigations.

MATERIALS AND METHODS

Materials
Eudragit RS 100, Eudragit RL 100 were received as gift samples from Evonik, Mumbai, India. Iron oxide, ethanol and dichloromethane were procured from Loba Chem., Mumbai, India. All other chemicals were of analytical grade and were used as received.
Preparation of Eudragit-iron oxide conjugate granules

The Eudragit-iron oxide conjugate granules were prepared by solvent evaporation method. Various combination of granules were prepared by mixing Eudragit polymer : iron oxide in the different ratios as shown in table 1. For the preparation of conjugate granules, Eudragit RS 100 or Eudragit RL 100 was dissolved in ethanol: dichloromethane (4:1). Iron oxide (60%) was then added with stirring at 400 rpm into clear solution of polymer to obtain uniform suspension. The solvent was then evaporated on water bath with stirring speed of 300 rpm to obtain uniform size granules. The control granules were prepared by omitting iron oxide in the above process.

Preparation of Eudragit-iron oxide conjugate tablets

The prepared Eudragit-iron oxide conjugate granules were used for preparing tablets to be employed in the study. The conjugate granule and/or pure Eudragit polymer were mixed with glidant, colloidal silica (2 %w/w) by tumbling method and compressed directly using 6 punch rotary tablet making machine (A.K Industries, Nakoda, India) fitted with round shaped die punch tooling (8 mm diameter) for preparing 250 mg weight tablets. After preparation the tablets were kept in a desiccator until further used.

Differential scanning calorimetry

A sample of iron oxide, Eudragit RS, Eudragit RL, Eudragit RS-iron oxide physical mixture, RS-iron oxide conjugate, Eudragit RL-iron oxide physical mixture and Eudragit RL-iron oxide conjugate were subjected to DSC analysis (Mettler Toledo Star System, 305, Switzerland) at a heating rate of 10°C/min in aluminium pans under nitrogen atmosphere.

ATR-Fourier transform infrared spectroscopy

The Fourier transform infrared (FTIR) spectra of samples were obtained using FTIR-ATR spectrophotometer (Alpha, Bruker, Japan) in the spectral region of 4000 cm\(^{-1}\) to 400 cm\(^{-1}\).

Zeta potential determination

The zeta potential is representative of particle charge. Zeta potentials were measured by electrophoresis in phosphate buffer with pH 7.0 (0.001 M) environment, after suspending the sample in the buffer followed by ultrasonication for 30 minutes. The concentration of the suspension was kept 2% w/v. The cell was filled with a measured amount of sample and inserted with its integral gold electrodes close to the lid. The zeta potential was measured using Malvern Zetasizer nanoZS apparatus (Malvern, United Kingdom).

Preparation of GI tissue

Porcine stomach tissue was obtained from local slaughter house (Patiala, Punjab, India) immediately after slaughtering of the animal. The tissue was washed with deionized water to remove the non-digested food from the lumen followed by placing the tissue in normal saline at 4°C and used within 6 h. The tissue should be washed carefully so as to avoid any damage to the underlying mucosal membrane.

Estimation of mucoadhesive strength employing texture analyzer

Mucoadhesion testing of the prepared polymeric tablets was carried out using texture analyzer (TA.XT plus, Stable Micro Systems, UK) with 50 N load cell equipped with mucoadhesive holder. Sample tablet was attached to the cylindrical probe (10 mm in diameter) using a double side adhesive tape. The tissue (about 20 x 20 mm) was equilibrated for 15 min at 37.0 ± 0.5°C before placing onto the holder stage of mucoadhesive holder cavity filled with test medium (pH 7.4). The parameters selected for studying the mucoadhesive detachment force were contact force, contact time, test speed of the probe removal from the tissue and probe return distance of the probe with the tissue. Four test speeds (0.1, 0.3, 0.5 and 1.0 mm/s) were studied at the contact force of 1.0 N, contact time of 60 s and return distance of 15 mm. The effects of contact force (i.e. 0.1, 0.2, 0.5, 1.0 and 2.0 N) and contact time (i.e. 30, 60, 180 and 300 s) were investigated using test speed of 0.5 mm/s and return distance of 15 mm. Four return distances (10, 15, 20 and 40 mm) were further studied using test speed of 0.5 mm/s, contact force of 1.0 N and contact time of 60 seconds. The maximum detachment force (F\(_{\text{max}}\)) required to separate the tablet side probe from the tissue could be detected directly from Texture Exponent 32 software and the total amount of forces involved in the probe withdrawal from the tissue (work of adhesion; W\(_{\text{ad}}\)) could be calculated from the area under the force versus distance curve.

RESULTS

Correlation of mucoadhesive strength with zeta potential

Various batches of Eudragit-iron oxide conjugates were prepared and evaluated for mucoadhesive strength and electrical performance. The results suggested increase in concentration of iron oxide from 1 to 20% in RL-iron oxide conjugate and RS-iron oxide conjugate enhanced the mucoadhesive strength as well as zeta potential (table 1). However, mucoadhesive strength was found to decrease with further increase in concentration of iron oxide from 20 to 30% in Eudragit RL-iron oxide conjugates. A similar decrease in zeta potential was observed with increase in concentration of iron oxide (from 20 to 30% w/w) in Eudragit RS-iron oxide conjugates. Interestingly, iron oxide alone did not show any zeta potential. However, interaction of iron oxide with Eudragits to form Eudragit-iron oxide conjugates bears net positive potential. In addition, a high level correlation (p>0.05) was obtained between zeta potential and mucoadhesive strength suggesting ionic interactions could be the possible cause of mucoadhesion (fig. 1). Further, the lower magnitudes of mucoadhesive strengths of...
Eudragit RS-iron oxide conjugates as compared to Eudragit RL-iron oxide conjugates was found to be due to lower zeta potential of Eudragit RS-iron oxide conjugates. Hence, the findings suggested Eudragit-iron oxide conjugate bears positive zeta potential that had interacted with negatively charged mucin present at the surface of porcine stomach and enhanced mucoadhesive strength.

Influence of texture analyzer parameters on mucoadhesive strength

Contact force, contact time, test speed and return distance of probe movement were the texture analyzer parameters identified during preliminary studies for evaluating their effect on mucoadhesive strength. Contact force indicates the force with which tablet adhere to the tissue surface. Contact time is the duration for which tablet remain adhered to the tissue surface. Test speed correlates the time taken by probe from the upper surface of solvent/buffer present above the surface of the tissue to the time when the tablet adheres to the tissue surface. Higher the test speed, faster is the tablet adherence to the tissue surface or vise-a-versa. Return distance depicts position at which stop returning with post test speed. The results suggested increase in contact force from 0.1 N to 1 N, increases the mucoadhesive strength as well as work of adhesion (W_{ad}) (fig. 2). However, further increase in contact force from 1 N to 2.5 N decreased the mucoadhesive strength and W_{ad} to near zero. This unusual behavior could only be possible when linkages are destroyed physical deformation of the polymeric material (Eudragit RL-iron conjugate/Eudragit RS-iron conjugate) and/or disruption of the mucosal lining. Thus, optimum value of contact force without destroying tissue was found to be 1 N. Similar findings were reported by Wong et al., 1999 suggesting that too much contact force may not be advantageous but may damage the mucosa without achieving better contact. They observed no significant increase in W_{ad} if the contact force is increased above 0.5 N. Thirawong et al., 2007 also reported proportionate increase in F_{\text{max}} and W_{ad} with increase in contact force in mucoadhesion studies on pectin discs using texture analyzer. Further, increase in contact time and test speed keeping contact force constant (1 N) was found to increase the mucoadhesive strength and W_{ad} (figs. 3, 4).

**Fig. 1**: Correlation between zeta potential and mucoadhesive strength for (a) Eudragit RL and conjugates (b) Eudragit RS and conjugates.

**Fig. 2**: Effect of contact force on (a) mucoadhesive strength, and (b) work of adhesion (n=5).
Both contact time and test speed are interconnected parameters and provides the pre-adhesion time for charge activation/generation RL-iron conjugate/RS-iron conjugate. Thus, high level of contact time and lowest level of test speed was selected to obtain accurate magnitude mucoadhesive strength and $W_{ad}$. A substantial decrease in mucoadhesive strength and $W_{ad}$ was found with the increase in probe return distance (fig. 5). This could probably be due to extensive distancing of mucin and polymethacrylate polymeric chains, originating a loose structure that limits the electrostatic interactions between the mucin and polymer leading to establishment of weak adhesive bonds and ultimately decrease in mucoadhesive strength.

**Molecular Attributes**

**Spectral Attributes**

The FTIR-ATR analysis was conducted to explore the possibilities of chemical interaction between Eudragit RL and Eudragit RS with iron oxide that leads to positive zeta potential and promoted mucoadhesion. The results are depicted in fig. 6. The ATR-FTIR analysis of Eudragit RL showed characteristic bands of the ester group (C-O-C) at 1150-1190 cm$^{-1}$, 1240-1270 cm$^{-1}$ and the C=O ester vibrations at 1730 cm$^{-1}$. In addition a peak at 1719 cm$^{-1}$ of quaternary ammonium group and C=O symmetric stretch at 1436.67 cm$^{-1}$ (fig. 6A). However antisymmetric stretch at 1500 cm$^{-1}$ was found to be absent in pure Eudragit RL, indicating absence of C-O moieties in the sample. A pure sample of iron oxide showed strong bands in the low frequency region (1000 cm$^{-1}$-500cm$^{-1}$) due to iron oxide skeleton (fig. 6B). Sample of physical mixture of Eudragit RL and iron oxide showed all those peaks as seen in their individual FTIR spectra, suggesting absence of any interaction in the physical state (fig. 6C). The ATR-FTIR spectra of Eudragit RL-iron conjugate indicated a peak at 1719 cm$^{-1}$ indicated for quaternary ammonium group and C=O symmetric stretch at 1436.67 cm$^{-1}$, however appearance of antisymmetric stretch at 1516.44 cm$^{-1}$ along with symmetric stretch at 1436.67 cm$^{-1}$ suggested chemical linkage of iron oxide with C=O moieties present in Eudragit RL (fig. 6D). The FTIR analysis of pure Eudragit RS sample showed characteristic peaks at 1140 cm$^{-1}$, 1234 cm$^{-1}$ of ester group.
Inderbir Singh and Vikas Rana


347

However, the peak at 1720 cm$^{-1}$ representing quaternary ammonium moieties present in Eudragit RS was found to be less in magnitude as compared to peak in pure sample of Eudragit RL, suggesting less number of quaternization in Eudragit RS compared to Eudragit RL. Fig. 6F showed FTIR spectra of Eudragit RS-iron oxide physical mixture, indicating no new peaks as observed in their individual FTIR spectra. The FTIR spectra of Eudragit RS-iron oxide conjugate showed additional peak at 1516 cm$^{-1}$ depicting antisymmetric stretching along with band at 1451 cm$^{-1}$ of symmetric stretching (fig. 6G). These results indicated the bonding of iron oxide with C=O moieties of Eudragit RS or Eudragit RL.

Tao (1993) interpreted the results in the light of bonding pattern of the carboxylic acid on the surface of the amorphous iron, was a combination of molecules bonded symmetrically and molecules that are bonded at an angle to the surface. Thus, the deposition of carboxylic acids on metal differ in IR results in the C=O absorption region. Hence, the main difference is whether the symmetric and asymmetric C=O stretching modes are both observed in the spectra. Ahn et al., 1994 observed only the symmetric stretching mode at 1440 cm$^{-1}$ when stearic acid as deposited on silver. However, Tao 1993 and Kataby et al., 1999 obtained symmetric C=O stretching at 1441 cm$^{-1}$ and asymmetric stretching at 1557 cm$^{-1}$ for the deposition of carboxylic acid on Cu. The presence of both symmetric and asymmetric stretching modes was an indication that part of carboxylic head group is bonded to the surface at an angle. On the other hand, if only the symmetric stretching mode was observed in the spectrum, the bonding pattern was such that both the carboxylic oxygens are symmetrically bonded to the surface. Overall, the finding suggested bonding of C=O moieties of Eudragit RL or Eudragit RS with iron oxide could be at an angle to the surface of the iron oxide. This bonding additionally generated positive charge over the surface of RL-iron or RS-iron oxide conjugate. This probably enhanced the zeta potential and hence the mucoadhesive strength. Further, it could be envisaged that the lower magnitude of zeta potentials in RS-iron oxide conjugate as compared to Eudragit RL-iron oxide conjugate (table 1) was due to low quaternization of Eudragit RS.

Thermal attributes

The DSC analysis was conducted to understand the interaction between Eudragit RS/Eudragit RL and iron oxide. The results of thermotropic transition obtained are depicted in fig. 7. The DSC thermogram of pure RS sample showed three endothermic transitions respectively at 62.85°C, 310.7°C and 395.41°C. Weak endothermic transitions below 100°C could be ascribed to the moisture present in the samples (fig. 7A). The second and third transitions could be attributed to the transformation of metastable amorphous form to more stable crystalline form. A similar three transitions had appeared in the pure RL sample at 92.55°C, 252.82°C and 380.5°C (fig. 7B). Fig. 7C showed DSC thermogram of pure iron oxide indicating peaks at 78.23°C (endothermic, due to moisture), 204.55°C (exothermic, due to dehydroxylation of the sample), 260.51°C (exothermic, due to crystallization of $\gamma$-Fe$_2$O$_3$ phase) and 320.6°C (exothermic, due to $\gamma$ to $\alpha$ phase transition). Similar peaks were observed by Phu et al., 2011, Schimanke and Martin 2000, Ennas et al., 1999, Kido et al., 2004 and Zhao et al., 2007. The physical mixture of Eudragit RL with iron oxide and Eudragit RS with iron oxide showed peaks similar to those seen in their individual thermograms (fig. 7D, 7E) indicating the absence of any interaction in the physical state. The DSC thermogram of Eudragit RS-iron oxide conjugate showed three endothermic transitions respectively at 62.46°C (due to moisture), 290.97°C (Phase transition) and 380.98°C (interaction peak) (fig. 7F). However the $\Delta H$ of the third endothermic transition at 380.98°C was found to increase from 120.23 J/gm to...
Exploiting the interaction of polymethacrylates with iron oxide

150.63 J/gm suggesting interactions occurred between Eudragit RS and iron oxide. However, the endothermic transition at 378.95°C corresponds to the interaction between Eudragit RL and iron oxide indicated two-fold increase in ∆H, i.e. from 140.23 J/gm (pure Eudragit RL) to 271.40 J/gm (Eudragit RL-iron conjugate) suggesting higher interaction of iron oxide with Eudragit RL as compared to Eudragit RS (fig. 7G). This further indicated the reason for higher mucoadhesive strength of Eudragit RL-iron conjugates. Thus, the results were in consonance with the findings of FTIR-ATR analysis.

DISCUSSION

Polymethacrylates are well accepted polymeric materials for the site specific as well as modified delivery of drugs due to their low toxicity, safety, acceptable in vivo/in vitro performance and reproducible results of formulations prepared using them. However, the use of polymethacrylates for the development of mucoadhesion based drug delivery systems is still at the research level. Therefore, present study was aimed at modification and evaluation of polymethacrylates for their acceptance in the development of mucoadhesive drug delivery systems. The results of correlation of mucoadhesive strength with zeta potential are in accordance with the findings of Bogataz and co workers which revealed that the lower values of the detachment force are correlated well with more negative zeta potential of the polymer (Bogataj et al., 2003). Takeuchi et al., 2001b reported that positively charged liposomes had a higher adhesion than negatively charged ones due to negatively charged mucin layer of the intestine. Therefore, RL5 and RS5 were considered as optimum composition batches for developing mucoadhesion based drug delivery systems.

The results of optimizing various parameters of texture analyzer viz. contact force, contact time, test speed and return distance are in line with the findings reported by Das Neves et al., 2008. The findings suggested to apply intermediate values of contact time, contact force, test speed, probe return distance for obtaining optimum results of mucoadhesive parameters (F max, W ad).

The correlation behavior of mucoadhesive parameters (F max, W ad) obtained with different contact time, contact force, test speed, probe return distance were examined to fit in simple mathematical models (linear, nonlinear (logarithmic, polynomial)). The results are summarized in table 2. W ad to be better adjusted into mathematical models as compared to F max. W ad was obtained from area under the force vs distance curve that constitutes overall behavior of mucoadhesive strength between tissue and substrate. Further, the chances of maximum detachment force in a run may vary within a sample. However, the overall area under the curve will take minimum variation arisen during a run that leads to better fitment into different mathematical models. Further, the analysis of data suggested better correlation of experimental data of contact time and probe return distance with F max and/or W ad in polynomial model. However, contact force better adjusted into logarithmic and polynomial models whereas test speed follows linear mathematical model. Hence, the appearance of polynomial model fitting suggested the cause of origination of plateau region for mucoadhesive parameters (F max, W ad) at higher values of contact time, contact force, test speed and probe return distance.
Table 2: Comparison of different mathematical models for evaluating relationship between mucoadhesive detachment force (F_{max})/Work of adhesion (W_{ad}) and contact time, contact force, probe withdrawal speed and probe return distance.

<table>
<thead>
<tr>
<th>Texture analyzer parameter</th>
<th>Linear</th>
<th>Logarithmic</th>
<th>Polynomial</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F_{max}</td>
<td>W_{ad}</td>
<td>F_{max}</td>
</tr>
<tr>
<td>Contact time</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RS</td>
<td>0.95</td>
<td>0.98</td>
<td>0.99</td>
</tr>
<tr>
<td>RS 5</td>
<td>0.93</td>
<td>0.96</td>
<td>0.95</td>
</tr>
<tr>
<td>RL</td>
<td>0.90</td>
<td>0.99</td>
<td>0.99</td>
</tr>
<tr>
<td>RL 5</td>
<td>0.83</td>
<td>0.95</td>
<td>0.92</td>
</tr>
<tr>
<td>Contact force</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RS</td>
<td>0.87</td>
<td>0.99</td>
<td>0.96</td>
</tr>
<tr>
<td>RS 5</td>
<td>0.87</td>
<td>0.98</td>
<td>0.94</td>
</tr>
<tr>
<td>RL</td>
<td>0.89</td>
<td>0.96</td>
<td>0.97</td>
</tr>
<tr>
<td>RL 5</td>
<td>0.93</td>
<td>0.98</td>
<td>0.88</td>
</tr>
<tr>
<td>Test speed</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RS</td>
<td>0.95</td>
<td>0.99</td>
<td>0.97</td>
</tr>
<tr>
<td>RS 5</td>
<td>0.99</td>
<td>0.98</td>
<td>0.93</td>
</tr>
<tr>
<td>RL</td>
<td>0.99</td>
<td>0.99</td>
<td>0.92</td>
</tr>
<tr>
<td>RL 5</td>
<td>0.98</td>
<td>0.97</td>
<td>0.82</td>
</tr>
<tr>
<td>Probe return distance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RS</td>
<td>0.77</td>
<td>0.99</td>
<td>0.88</td>
</tr>
<tr>
<td>RS 5</td>
<td>0.82</td>
<td>0.97</td>
<td>0.94</td>
</tr>
<tr>
<td>RL</td>
<td>0.77</td>
<td>0.99</td>
<td>0.88</td>
</tr>
<tr>
<td>RL 5</td>
<td>0.98</td>
<td>0.98</td>
<td>0.90</td>
</tr>
</tbody>
</table>

Fig. 6: FTIR spectra of: A, Eudragit RL; B, Iron oxide; C, Eudragit RL-iron oxide physical mixture; D, Eudragit RL-iron oxide conjugate; E, Eudragit RS; F, Eudragit RS-iron oxide physical mixture; G, Eudragit RS-iron oxide conjugate.

Fig. 7: DSC spectra of: A, Eudragit RS; B, Eudragit RL; C, Iron oxide; D, Eudragit RS-iron oxide physical mixture; E, Eudragit RL-iron oxide conjugate; F, Eudragit RS-iron oxide physical mixture; G, Eudragit RL-iron oxide conjugate.
CONCLUSIONS

Polymethacrylates are well known and useful polymeric materials for pharmaceuticals in various areas such as sustained, controlled, transdermal etc drug delivery systems. However, their use in mucoadhesive devices was not been reported. The present study revealed Eudragit-iron oxide conjugates had a great potential for mucoadhesion. The results suggested generation of high zeta potential on Eudragit by their conjugation with iron oxide could be the cause of mucoadhesion. The findings obtained from FTIR-ATR as well as DSC analysis further indicated bonding of C=O moieties of Eudragit RL or RS with iron oxide could be at an angle to the surface of the iron oxide that had produced positive charge over the surface of conjugates. This positive charge resulted in mucoadhesion. This suggesting overwhelming influence of iron oxide on Eudragit RL or RS that leads to mucoadhesive nature of polymer. Hence, revealed potential of Eudragit RL-iron oxide conjugate to be used for development of mucoadhesive drug delivery system, gastro retentive drug delivery systems, etc.

ACKNOWLEDGEMENTS

We kindly acknowledge Dr. A. K Tiwary Professor and Coordinator UGC-SAP programme, Department of Pharmaceutical Sciences and Drug Research, Punjabi University, Patiala, Punjab, India for extending the facility of texture analyzer.

REFERENCES