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Preparation and Evaluation of Mucin-Gelatin Mucoadhesive Microspheres for Rectal Delivery of Ceftriaxone Sodium

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ABSTRACT  Soluble mucin (S-mucin) processed from the small intestines (ileal region) of freshly slaughtered pigs via homogenization, dialysis, centrifugation and lyophilization and its admixtures with type A gelatin were dispersed in an aqueous medium and used to formulate ceftriaxone sodium-loaded mucoadhesive microspheres by the emulsification cross-linking method using arachis oil as the continuous phase. The release profile of ceftriaxone sodium from the microspheres was evaluated in both simulated gastric fluid (SGF) without pepsin (pH 1.2) and simulated intestinal fluid (SIF) without pancreatin (pH 7.4). The microspheres were further evaluated as possible novel delivery system for rectal delivery of ceftriaxone sodium in rats. Release of ceftriaxone sodium from the microspheres in both release media was found to occur predominantly by diffusion following non-Fickian transport mechanism and was higher and more rapid in SIF than in SGF. The results obtained from this study may indicate that ceftriaxone sodium could be successfully delivered rectally when embedded in microspheres formulated with either type A gelatin alone or its admixtures with porcine mucin; hence providing a therapeutically viable alternative route for the delivery of this acid-labile third generation cephalosporin.

KEYWORDS  Type A gelatin-porcine mucin admixtures, microspheres, Rectal delivery, Ceftriaxone sodium

INTRODUCTION

Mucins or mucus glycoproteins, are a family of very high molecular weight, carbohydrate rich polydisperse molecules, which are believed to perform various physiological functions at the mucosal surfaces of the body (Mantle & Allen, 1980; Brian et al., 1974). Until recently, it was assumed that mucus is an inert blanket, serving as a mechanical barrier against potentially injurious chemicals, bacteria and enzymes (Jun-Ji et al., 1989; Stephen et al., 1978). In recent years, however, it has become apparent that mucins or mucus glycoproteins are
capable of interacting in various ways with many biologically important entities such as enzymes, polymers, cations, drugs, viruses, cell surfaces and bacteria (Forstner & Forstner, 1994; Mortazari et al., 1993), whereupon they elicit diverse effects some of which may influence the delivery and action of drugs.

Biologically adhesive drug delivery systems such as microspheres offer important advantages over conventional drug delivery systems. In the pharmaceutical arena, microspheres have been intensively studied for use as drug delivery systems, where they have been shown to protect sensitive macromolecules from enzymatic and acid degradation, and allow controlled release and tissue targeting of the formulated drug (Davis & Illum, 1983; Alpar et al., 1989; Illum et al., 1989; Nail, 1997; Coombes et al., 1997; Bartus et al., 1998). Thus, once loaded with compounds of therapeutic interest, microspheres could be developed as delivery systems to transfer biologically active molecules to the systemic circulation. The properties of bioadhesive microspheres such as their surface characteristics, force of bioadhesion, release pattern of incorporated drug and biodegradability are determined by the nature of the polymers used in the formulation as well as their swelling and solvent regaining characteristics (Mathiowitz & Langer, 1987; Brannon-Peppas, 1995; Langer et al., 1997; Paul et al., 1997). The use of specific polymers or their admixtures and the design of new drug delivery systems, such as microspheres, are currently perhaps one of the most exciting areas in pharmaceutical formulation. The major aim is to improve the efficiency of drugs in the treatment of diseases and to decrease their side effects (Uhlich et al., 1999).

There are on-going research efforts aimed at improving the potential for use of gelatin in controlled delivery of certain drugs (Yin et al., 1996). Microspheres prepared from admixtures of gelatin and cross-linked chitosan demonstrated some advantage, in terms of better controlled release rate of cimetidine, over that prepared from gelatin alone (Yin et al., 1996). The search for alternative routes of delivery of many drugs including insulin is continuing; hence our efforts to explore the rectal route for the delivery of an acid labile cephalosporin (ceftriaxone sodium), which hitherto, could be administered only via the parenteral route.

The reported interaction of mucin with many biologically important entities including polymers prompted the preparation of microspheres from admixtures of mucin and gelatin (a widely used pharmaceutical adjuvant). The objective of this study, therefore, was to prepare microspheres from admixtures of gelatin and mucin and to evaluate the in vitro and in vivo delivery of ceftriaxone sodium from these microspheres.

MATERIALS AND METHODS

Materials

Ceftriaxone sodium (Roche, Basel, Switzerland), sodium hydroxide (Merck, Germany), diethyl ether, concentrated hydrochloric acid, sodium chloride, glutaraldehyde (BDH, England), type A gelatin, monobasic potassium phosphate (Sigma Chemical Company, St. Louis, MO) were used in the study. Distilled water was obtained from an all-glass still. All other reagents were analytical grade and used as such.

Isolation and Purification of Pig Small-Intestinal Mucus Glycoprotein

The small intestines of freshly slaughtered pigs were obtained from the abattoir of the Animal Science Department in our University. The isolated ileum was dissected starting from the jejunum to the ileocaecal sphincter. The intestines, sectioned into short lengths, were flushed through with chilled saline, and the mucosal surface was exposed by longitudinal dissection. By using a microscope slide, the mucus layer was gently scraped off and diluted with four times its volume of distilled water. The gel was homogenized by stirring for 2 hr at 4°C and then exhaustively dialyzed against distilled water. The dialysate was centrifuged at 10,000 rpm for 30 min to give a supernatant of water soluble mucosal glycoprotein and lower layer of insoluble mucosal glycoprotein. The supernatants were collected separately, pooled and lyophilized to obtain flakes of soluble (S) mucin, which were further powdered and used for study.

Preparation of Mucin-Gelatin Admixtures

A 1 g quantity of gelatin was weighed out and dispersed in 100 mL of citrate/phosphate buffer of pH 3.4 by gently stirring with a glass rod at room temperature (28°C) for a period of 1 hr in order to obtain a
homogenous dispersion. Soluble mucin (1 g) was similarly weighed out and mixed thoroughly with the dispersion of gelatin in a beaker. The combination was left to stand for 24 hr in order to attain maximum hydration. It was then homogenized by gently stirring with a glass rod for 1 hr to obtain the polymer admixture. Thus admixtures of S-mucin and gelatin in ratios of 1:1, 1:2, 1:3 and 1:4, were prepared.

**Preparation of Stabilized Mucin-Gelatin Microspheres**

A 25% v/v dispersion of each of mucin-gelatin admixture and gelatin alone in arachis oil was used. The mucin-gelatin dispersion was preheated to 40°C and further extruded drop wise into pure arachis oil at 40°C on a thermostatically controlled hot plate magnetic stirrer. The mixture was stirred at a speed of 500 rpm for 30 min. Enough glutaraldehyde to produce about 1% v/v concentration was added and stirring continued for further 1 hr. The resulting mixture was centrifuged at 5000 rpm for 5 min to collect the microspheres. The microspheres collected were washed with diethylether to remove excess oil and then dried at the ambient temperature of 28 ± 2°C.

**Swelling Studies**

The initial weight of the microspheres was recorded and placed in 100 mL of simulated intestinal fluid (SIF) without pancreatin, prepared by dissolving 2.0 g of monobasic potassium phosphate in 190 mL of 0.2M sodium hydroxide and adding sufficient distilled water to bring the final volume to 1000 mL (Ofoefule et al., 2004), and allowed to swell. The temperature of the medium (SIF) was maintained at 37°C with the aid of a thermostated hot plate. The pH of the SIF was adjusted to 7.4 by adding sodium hydroxide in drops. At regular time intervals, the swollen microspheres were carefully removed using forceps, blotted dry with filter paper and weighed. Water sorption was calculated from the difference between the initial weight and the weight at the time of determination. The total time the microspheres spent outside the swelling medium in between each determination was less than a minute. The experiment was repeated five times and the mean was calculated. The swelling experiment was further repeated using simulated gastric fluid (SGF) without pepsin (pH 1.2), prepared by dissolving 2.0 g of sodium chloride in 7.0 mL of concentrated hydrochloric acid and adding enough distilled water to bring the final volume to 1000 mL (Ofoefule et al., 2004), as the swelling medium.

**Mucoadhesive Properties**

The apparatus used for the study was designed to give reproducible measurements following the procedure of Attama and Adikwu (1999). The test was carried out at the ambient temperature (28°C) using a freshly excised hog ileum. The ileum was cut into pieces measuring 12.0 cm (length) × 1.5 cm (internal diameter) and each was gently rinsed with chilled saline to remove intestinal waste materials and quickly pinned unto the polythene support. A known quantity (10 g) of the different mucin-gelatin microspheres was weighed out and placed on the trough of the mucus surface and allowed to hydrate for 15 min to allow for microsphere-mucus interaction to take place. A 250 mL volume of SIF contained in a separatory funnel was allowed to flow over the hydrated microspheres at a rate of 30 mL/min. The weight of microspheres detached (washed out) calculated as a percentage of the original weight of the microspheres was used as a measure (index) of mucoadhesion. Preliminary studies carried out with ceftriaxone sodium-loaded microspheres showed that the mucoadhesive properties of the formulated microspheres were not significantly affected by the presence of the drug (Ofokansi, 2004). The experiment was repeated using SGF. Five replicates were taken and the mean values recorded.

**Mean Diameter**

Particle size of the microspheres was determined by optical microscopy using a projection microscope (Olympus, Tokyo, Japan). At least, 150 microspheres were dispersed on a slide in a mineral oil plus 1% of a nonionic surfactant and their diameter was then sized using suitable objectives (Esposito et al., 2004).

**Drug Loading**

A known quantity of the dried mucin-gelatin microspheres was incubated at 37 ± 1°C with a concentrated solution of ceftriaxone sodium (50 mg/mL)...
in citrate/phosphate buffer (pH 7.4) for 1 hr with the aid of a thermostated hot plate. The microspheres, in each case, were carefully removed from the buffer solution after incubation and allowed to dry at ambient temperature. To determine the drug contents, a quantity (20 mg) of ceftriaxone sodium loaded microspheres was weighed out and allowed to completely swell in a beaker containing 100 mL of the buffered citrate/phosphate medium (pH 7.4). A period of 24 hr was allowed for complete hydration of the microspheres after which the dispersion was vortexed repeatedly to break up the microspheres completely and cause them to discharge their contents (Dandagi et al., 2004; Ofokansi et al., 2005). The concentration of ceftriaxone sodium in the microspheres was then determined spectrophotometrically at 240 nm using a digital UV-Vis spectrophotometer (Spectronic 21D). Four replicate determinations were done for each batch of microspheres.

In Vitro Drug Release

The USP paddle method (USP, XXVII) was adopted in this study. The release medium consisted of 500 mL of freshly prepared simulated intestinal fluid (SIF), without pancreatin (pH 7.4) maintained at 37 ± 0.5°C. A known quantity (100 mg) from each batch of the ceftriaxone sodium loaded microspheres was placed into the appropriate chamber of the release apparatus and agitated at 100 rpm. At predetermined time intervals, 1 mL portions of the release medium were withdrawn, appropriately diluted and their absorbance determined at a wavelength of 240 nm using a digital UV-Vis spectrophotometer. The volume of the release medium was kept constant by replacing it with 1 mL of fresh SIF after each withdrawal. The release study was repeated using freshly prepared simulated gastric fluid (SGF) without pepsin (pH 1.2) as the release medium. Four replicate release studies were carried out in each case.

Pharmacokinetic Study

Male Wistar rats aged two months with a mean weight of 200 g were obtained from the Department of Veterinary Pathology and Microbiology of our University. The rats were allowed to acclimatize to the new environmental conditions of our laboratories for one week before use. Three groups of animals (with each group comprising eight rats) were used for the study. An amount of the microspheres containing ceftriaxone sodium was weighed to achieve a dose level of 100 mg/kg body weight in the rats and carefully transferred into empty hard gelatin capsule (No. 3). A positive control was set up by similarly encapsulating amounts of pure ceftriaxone sodium equivalent to that in the microspheres. By means of the capsules, therefore, the drugs were administered rectally to the rats. At regular time intervals of 1 hr, 0.5 mL of blood was sampled from the orbital sinus of the rats and then analysed for plasma levels of ceftriaxone sodium.

Analysis of Ceftriaxone Sodium in Protein-Free Rat Plasma

The method of Tietz (1970) was adopted to prepare a protein-free filtrate. From each of the 0.5 mL of blood sampled from the rats, 0.2 mL was added to a test-tube containing 1.8 mL of 3% trichloroacetic acid (TCA). The test-tube was shaken gently to ensure a proper homogenization of the TCA and the blood sample and then allowed to stand for 5–10 min. The test-tube was further centrifuged at 3000 rpm for 10 min after which 1 mL of the clear supernatant layer was collected. The collected portion was analyzed spectrophotometrically without dilution at a wavelength of 240 nm. An absorption spectrum previously run for a solution of ceftriaxone sodium in TCA did not show any shift from the earlier wavelength of maximum absorption, an indication that no significant interaction occurred between the two compounds.

Statistical Data Analysis

Statistical data analyses were performed using the Student’s t-test with p=0.05 as the minimal level of significance.

RESULTS AND DISCUSSION

The results of the mucoadhesion of the microspheres to hog everted intestinal tissue as evaluated in both SIF and SGF are presented in Figs. 1 and 2, respectively. It is evident from both figures that the microspheres formulated showed good mucoadhesive properties and exhibited percentage mucoadhesion as high as 85% for microspheres prepared from
Microspheres for Rectal Delivery of Ceftriaxone Sodium

mucin-gelatin in the ratio of 1:1. Mucoadhesion to hog everted intestinal tissue was found to be higher in SIF than in SGF only for 1:1 (mucin:gelatin) microspheres. Apart from the 1:1 (mucin:gelatin) microspheres, other combinations, as are evident in Figs. 1 and 2, showed comparatively higher mucoadhesion in SGF than in SIF; an indication that those combinations may be preferable as carriers for drugs targeted to have long residence time in the stomach. Undoubtedly, this might be a new approach to prolong the release of such drugs. It is evident from Figures 1 and 2 that in comparison with microspheres formulated with gelatin alone, those formulated with admixtures of S-mucin and gelatin showed higher mucoadhesion. It is also evident that the percentage mucoadhesion seem to vary with the mucin-gelatin ratios used in formulating the microspheres. Microspheres prepared with mucin-gelatin in the ratio of 1:1 exhibited a consistently high percentage mucoadhesion in both SIF and SGF. This may indicate that 1:1 is the optimal ratio of combination of S-mucin and gelatin for enhanced mucoadhesiveness especially when a drug is targeted to adhere to the small intestine for an extended period of time.

The mean particle diameters of the microspheres formulated are presented in Table 1 and ranged from 159.0–253.0 μm. This range of particle diameter for microspheres is useful in oral, Intramuscular and intravenous delivery of various classes of drugs since the size of microspheres is known to play a critical role in determining the route of delivery of various drugs (Sokoloski & Royer, 1984; Tomlinson & Burger, 1987). The microspheres formulated in this study might be suitable for all purpose delivery of various classes of drugs.

The absolute drug contents of the microspheres are represented as a bar chart (Fig. 5). It is evident from

**TABLE 1** Particle Size Distribution of the Bioadhesive Microsphere

<table>
<thead>
<tr>
<th>Mucin-gelatin ratio</th>
<th>Mean diameter* (μm ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:1</td>
<td>183.0 ± 1.15</td>
</tr>
<tr>
<td>1:2</td>
<td>201.4 ± 2.50</td>
</tr>
<tr>
<td>1:3</td>
<td>205.0 ± 2.55</td>
</tr>
<tr>
<td>1:4</td>
<td>253.4 ± 2.70</td>
</tr>
<tr>
<td>Gelatin alone</td>
<td>159.0 ± 2.05</td>
</tr>
</tbody>
</table>

*Each measurement represents the mean ± SD (n=30).
SD=standard deviation.
this chart that the drug contents were dependent on the composition of the microspheres, which also showed a relationship to the degree of swelling of the microspheres. Swelling of the microspheres in an aqueous environment containing the drug and the adsorption of the drug into the microspheric network were considered the principal mechanisms of loading of ceftriaxone into the microspheres.

Preliminary liquid uptake studies carried out in two different media (SIF and SGF) indicated that microspheres prepared from combinations of gelatin and S-mucin showed greater swelling tendency especially in SGF when compared to those prepared from gelatin alone and that the swelling was higher in SIF than in SGF (Figs. 3 and 4). Water absorption and the rate of water absorption by the microspheres followed the order: 1:4 > 1:1 > 1:2 > 1:3 > gelatin alone in SGF while the order in SIF was 1:4 > gelatin alone > 1:3 > 1:1 > 1:2. The water sorption behavior in the two media further confirms a modification of the gelatin microspheres by the mucin. The higher amount and rate of water absorption in SIF than in SGF may also be attributable to the type of gelatin used in preparing the microspheres. Type A gelatin is known to be prepared from acid hydrolysis and would, therefore, be expected to swell more in an alkaline environment than in an acidic one (Jones et al., 1988). There seems to be a correlation between the swelling and mucoadhesive properties of the microspheres formulated. It is, therefore, expected that microspheres prepared from admixtures of gelatin and S-mucin adsorbed greater amounts of ceftriaxone ($p=0.05$) in comparison with those prepared from gelatin alone (Fig. 5). This may have resulted from the higher swelling of the microspheres in the slightly alkaline medium (pH 7.4) in which the drug loading was carried out. It is equally reasonable to infer from this observation that in the presence of mucin, the intermolecular network and, possibly other characteristics of gelatin, were modified.

The release profiles of ceftriaxone sodium from the mucoadhesive microspheres in two different release
media (SIF and SGF) are shown in Figs. 6 and 7, respectively. Each point is the mean value of a quadruplicate study. There was high percentage and rapid release of ceftriaxone from the microspheres in SIF within 30 min. The highest release, ranging between 60 and 85%, was achieved from microspheres containing gelatin alone or a much higher proportion of gelatin relative to mucin in SIF. The higher and more rapid release of ceftriaxone may be a consequence of the higher rate of hydration and swelling of the microspheres in SIF than in SGF, which, in turn, may be attributable to the type of gelatin (type A) used in the formulation. Type A gelatin, as earlier noted, is known to be prepared from acidic precursors and consequently swells more in an alkaline environment such as SIF than in an acid medium. The low percentage release of ceftriaxone sodium in SGF could possibly be a result of the limited swelling of the microspheres in that acidic medium. This situation may have interesting implications in the protection of ceftriaxone sodium from the acidic environment of the stomach when administered in vivo via the oral route.

Drug release from monolithic spheres has been reported variously as taking place by numerous differing mechanisms, which include surface erosion, total sphere disintegration, microsphere hydration (or swelling), drug diffusion and desorption, particulate diffusion and leaching (Tomlinson & Burger, 1987). However, drug release from the microspheres in this study was observed to take place by a combination of mechanisms involving microsphere hydration/swelling, drug diffusion, desorption and surface erosion. A characteristic feature of the release profiles of ceftriaxone sodium from the microspheres as is evident in Figs. 6 and 7 is the biphasic pattern of release. There was an initial rapid release within 10 min, referred to as “burst” effect, followed by a much slower first-order release. This is in agreement with reported pattern of in vitro release of incorporated drugs from microspheres (Tomlinson & Burger, 1987). This rapid release of ceftriaxone sodium may also be attributable to its high aqueous solubility since water soluble molecules are generally known to be released quicker than hydrophobic and less soluble molecules (Tomlinson & Burger, 1987). The high release of ceftriaxone especially in SIF (Fig. 6) could
give an indication of the rate and extent of in vitro bioavailability, which may suggest that ceftriaxone, an acid labile drug, could be successfully delivered orally when embedded in mucin-gelatin microspheres.

An attempt was made to determine the mechanism of release of ceftriaxone from the microspheres using the Fickian diffusion model. To understand the release mechanism of ceftriaxone from the microspheric network, the release rate was described with the following equations:

\[ \frac{M_t}{M_i} = K t^n \]  
\[ \log \frac{M_t}{M_i} = \log K + n \log t \]

\( M_t/M_i \) is the fraction of released drug at time \( t \), \( K \) is a kinetic constant (with units of per min) that incorporates the structural and geometric characteristics of the release device and \( n \) is the release exponent indicative of the mechanism of release. In an attempt to assign release kinetics models to drugs being released from polymeric matrices using the above equations, Peppas (1985) has established that an \( n \) value of 1 corresponds to zero-order release kinetics (case-II transport); \( 0.5 < n < 1 \) means an anomalous (non-Fickian) diffusion release model, \( n = 0.5 \) indicates Fickian diffusion and \( n > 1 \) indicates a super case-II transport relaxational release. The kinetic parameters, \( n \) and \( K \) calculated from plots of \( \log M_t/M_i \) versus \( t \) are presented in Table 2. It is evident from Table 2 that the values of the release exponent, \( n \), ranged between 0.4896 and 0.9113. This indicates that the release of ceftriaxone from the microspheres in both SIF and SGF occurs by diffusion following non-Fickian transport mechanism.

The plasma level-time curve for the rectally administered ceftriaxone loaded mucoadhesive microspheres is shown in Fig. 8. The areas under the plasma concentration versus time curves (AUC) were determined using the trapezoidal rule based on a non-compartmental

### TABLE 2  Release Kinetic Parameters of Ceftriaxone Sodium from the Microspheres in Two Release Media

<table>
<thead>
<tr>
<th>Mucin-gelatin ratio in microsphere</th>
<th>SIF</th>
<th></th>
<th></th>
<th>SGF</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( n )</td>
<td>( k )</td>
<td>( r )</td>
<td>( n )</td>
<td>( k )</td>
<td>( r )</td>
</tr>
<tr>
<td>1:1</td>
<td>0.7950</td>
<td>0.7882</td>
<td>0.9800</td>
<td>0.7812</td>
<td>0.8113</td>
<td>0.9946</td>
</tr>
<tr>
<td>1:2</td>
<td>0.6341</td>
<td>0.8002</td>
<td>0.9945</td>
<td>0.9113</td>
<td>0.7821</td>
<td>0.9954</td>
</tr>
<tr>
<td>1:3</td>
<td>0.5352</td>
<td>0.9291</td>
<td>0.9974</td>
<td>0.6212</td>
<td>0.9123</td>
<td>0.9977</td>
</tr>
<tr>
<td>1:4</td>
<td>0.5112</td>
<td>1.3323</td>
<td>0.9909</td>
<td>0.6002</td>
<td>1.1912</td>
<td>0.9958</td>
</tr>
<tr>
<td>Gelatin alone</td>
<td>0.5061</td>
<td>1.8204</td>
<td>0.9950</td>
<td>0.4896</td>
<td>1.9615</td>
<td>0.9936</td>
</tr>
</tbody>
</table>

\( n = \) Release exponent; \( k = \) Release kinetic constant; \( r = \) Correlation coefficient.
pharmacokinetic analysis. The pharmacokinetic parameters as calculated from Fig. 8 are presented in Table 3. It is noteworthy that the bioavailability of ceftriaxone sodium via the rectal route was highest (AUC=44.4 μg·h/mL) from microspheres prepared from equal portions of S-mucin and gelatin (1:1). Microspheres prepared from gelatin alone gave much lower AUC value in comparison with those prepared from its admixtures with S-mucin. Remarkably, the peak plasma concentration followed a trend closely similar to the area under the curve and this gave indication as to the bioavailability of the drug studied. The generally high AUC values obtained for the microspheres may suggest that the absorption of ceftriaxone sodium from the rectal mucosa was both rapid and complete and that the drug must have bypassed the hepatic first pass metabolism. It is necessary to point out that adequate precautions were taken to deposit the encapsulated microspheres on the lower part of the rat’s rectum with the expectation of causing the absorbed drug to drain directly into the general circulation via either the lower or middle haemorrhoidal veins. This target may well have been achieved considering the high AUC values obtained for all the microspheres.

It is equally discernible from Fig. 8 that the bioavailability of ceftriaxone was generally higher from the mucoadhesive microspheres in comparison with that of the control. The Student’s t-test was used to ascertain if there was any significant difference in the AUC values of ceftriaxone from the microspheres and that from the control. At 5% level of significance, the AUC values of ceftriaxone from the mucoadhesive microspheres were found to be significantly different from that of the control. The longer t\text{max} values for mucin-gelatin microspheres may further corroborate our earlier observation that the mucin samples may have modified the characteristics of gelatin microspheres. This modification may have resulted in the prolongation of the in vivo release of ceftriaxone sodium from the microspheres.

**CONCLUSION**

Mucoadhesive microspheres were successfully prepared from type A gelatin alone and its admixtures with porcine mucin and evaluated in vitro and rectally for the delivery of an acid-labile cephalosporin, ceftriaxone sodium. Water sorption by the microspheres in both alkaline and acidic media was found to be reasonably high. The microspheres showed considerably high mucoadhesive capacities. Release of ceftriaxone sodium from the microspheres was found to occur by diffusion following non-Fickian transport mechanism.
It may be concluded from this study, that the rectal route could provide a therapeutically viable alternative for the delivery of ceftriaxone sodium, which hitherto, is administered only parenterally owing to its instability in the acidic environment of the stomach. Further in vivo studies using selected admixtures of porcine mucin and type A gelatin in higher animals such as dogs are currently in progress to explore possibilities of obtaining more predictable results.

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