Research Article

Dexamethasone-Loaded Chitosan Beads Coated with a pH-Dependent Interpolymer Complex for Colon-Specific Drug Delivery

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Chitosan (CS) microparticles loaded with dexamethasone were prepared by spray drying, followed by coating with a pH-dependent interpolymer complex based on poly(acrylic acid)/poly(vinyl pyrrolidone) using an water-in-oil emulsion technique. The aim of this research was to evaluate the influence of PAA/PVP coating on the release of dexamethasone from loaded chitosan microparticles, in simulated gastric fluid (SGF, pH = 1.2) and simulated intestinal fluid (SIF, pH = 6.8). The release of dexamethasone from uncoated loaded CS microparticles was similar in both fluids, and almost complete release of the drug was achieved in 5 hours. In the coated loaded CS microparticles, the release of dexamethasone in SGF was reduced considerably, very close to zero, due to the interpolymer complex formation at low pH, demonstrating that this system applied as pH-dependent coating has a potential as a site-specific delivery system.

1. Introduction

Colon drug delivery has been an important research topic for many years, due to the recognized importance of this region of the gastrointestinal tract (GIT) not only for local therapy but also for systemic therapy. The colon offers several advantages such as (i) near neutral pH, (ii) very long transit time, (iii) reduced digestive enzymatic activity, and (iv) a great responsiveness to absorption enhancers [1–3]. In addition, the colonic region offers a potential site for the systemic absorption of several drugs for the treatment of noncolonic conditions, such as asthma, arthritis, or inflammations [4, 5].

Dexamethasone is a synthetic glucocorticoid that suppresses inflammation and normal immune response. It is widely used as a therapeutic agent in cerebral oedema, nausea, and vomiting specially that associated with high dose of anticancer agents, cerebral malaria, opportunistic mycobacterial infections, respiratory disorders, skin disorders, and rheumatism. However, when administered by oral route, it produces systemic side effects and gastric irritation. Consequently, selective delivery of drug to the colon may not only lower the required dose but also reduce the systemic side effects caused by high doses [6]. Different techniques have been used to deliver drugs to the colon. These had been based on the variation of the pH through the

GIT, enzymatic degradation by colonic bacteria, and even the relatively constant transit time into the small intestine. Enteric formulations using pH-sensitive polymers (enteric coating polymers) are most commonly used for colonic drug delivery and constitute the majority of commercially available preparations for colon targeting [7–9].

A promising approach for delivering drugs at the colon appears to be the use of formulations based on biopolymers that can be degraded by colon-specific enzymes [1, 2]. Promising choice polymers are natural polysaccharides whose glycosidic bonds are hydrolysed at the colon. Chitosan (CS) is considered a good candidate as it is biocompatible, widely available at low cost, completely digested by colonic bacteria, and toxicologically harmless [8, 10, 11]. However, as CS dissolves in acidic conditions, its successful use in colon-specific delivery requires the coating of the particles by an enteric polymer layer in order to endure the acidity of the stomach without dissolution [8, 12]. Eudragit copolymers (a family of methacrylic acid copolymers with different acrylates for drug delivery applications) have been the most commonly used pH-sensitive coatings for microparticles or tablets for colon drug delivery. These polymers are insoluble in acidic media, providing protection to the drug core in the stomach and to some extent in the small intestine. Furthermore, they dissolve at pH 6 or higher, allowing the release of drugs only in the colonic region [12].

For instance, Oshi et al. [13] coated dexamethasone microcrystals with multilayers of chitosan oligosaccharide, alginate, and finally Eudragit using a layer-by-layer coating technique for colon targeting of the drug. pH-dependent interpolymer complexes stabilized by hydrogen bonding have been proposed for the design of mucoadhesive dosage forms, hydrogels, and encapsulation technologies, among others [14]. For instance, poly(acrylic acid) (PAA) and poly(methacrylic acid) (PMAA) are H-bond donor polyelectrolytes, which can form interpolymer complexes with H-bond acceptor polymers such as poly(ethylene oxide) (PEO) and PVP [15, 16]. PAA complexes with hydroxypropylcellulose and dextran have been exploited for the preparation on nano- and microcapsules [17–19], and PAA-PVP complexes have also been used as pH-sensitive materials for the design of pH-controlled drug delivery systems [20].

In the present paper, we report on the application of hydrogen-bonded interpolymer complexes as pH-sensitive materials and as enteric coatings for dexamethasone-loaded chitosan microparticles. The stability constants or PAA-PEG and PAA-PVP complexes were determined, and the latter was selected for coating. The PAA-PVP interpolymer complex was characterized by FTIR spectroscopy and thermogravimetric analysis. Chitosan microparticles were coated with PAA-PVP complexes by a water-in-oil emulsion technique. The effects of PVP molecular weight on the coating properties and dexamethasone release profiles were studied.

2. Materials and Methods

2.1. Materials. Chitosan (79.0 ± 0.4% deacetylation degree) was obtained from Aldrich (Dorset, UK). Dexamethasone phosphate sodium salt (DMT) was supplied by Biomont Laboratories S.A. (Perú). Poly(acrylic acid) (PAA, MW 45 kDa) and poly(N-vinyl-2-pyrrolidone) (PVP-29, MW 29 kDa and PVP-360, MW 360 kDa) were obtained from Sigma (Germany).

2.2. Methods

2.2.1. Evaluation of the Stability Constant of Interpolymer Complexes. The study was performed through pH measurements of the aqueous solutions of the polyacid or the complex. These measurements were carried out at $30°C ± 0.5°C$ using a digital Crison Basic 20 pH meter (Crison Instruments, Alella, Spain) with a glass combination electrode with a precision of $±0.02$ pH unit. In all experiments, the temperature was thermostatically controlled. The pH was measured at a polymer concentration of $5 × 10^{-3}$ mol L^{-1}, and interpolymer complexes were prepared by mixing PAA with stoichiometric quantities of PEG and PVP (1 : 1 molar ratio) in pure aqueous medium. Complexes do not precipitate at this concentration.

2.2.2. Preparation of Dexamethasone-Loaded CS Microspheres by Spray Drying. Loaded CS microspheres were prepared as follows. First, dexamethasone phosphate sodium salt (30 wt.%, with respect to CS) and sodium tripolyphosphate (1 wt.%) were added to a CS solution (2 wt.% in 2 vol.% aqueous acetic acid) and stirred at 1000 rpm for 15 min with a magnetic stirrer (Bunsen MC-8, Spain). The solution was then dried in a Büchi Mini Spray Dryer B-191 (Büchi Labortechnik AG, Flawil, Switzerland). The inlet temperature, outlet temperature, and flow rate were set at 170°C, 115°C, and 5 mL min^{-1}, respectively. The obtained powder was collected and stored at room temperature for further investigation.

2.2.3. Determination of Encapsulation Efficiency and Yield. Dexamethasone-loaded CS microspheres (50 mg) were suspended in 50 mL of simulated gastric fluid (SGF) with agitation. Microparticles were completely dissolved after 5 h, and the concentration of dexamethasone in the solution was determined by UV-Vis at 242 nm using a GBC Cintra 10-UV-Visible Spectrophotometer (GBC Co., Australia). Encapsulation efficiency (EE %) was calculated from the real drug loading in the microspheres and the theoretical drug loading. All samples were analyzed in triplicate.

$$EE\% = \frac{Drug\ loading}{Theoretical\ drug\ loading} * 100. \quad (1)$$

The yield of microspheres ($Y\%$) obtained is reported as the ratio between the total weight of microparticles collected after the process and the weight of the initial mass of CS and dexamethasone used.

$$Y\% = \frac{W_{microparticles}}{W_{chitosan} + W_{dexamethasone}} * 100. \quad (2)$$

2.2.4. Coating of Dexamethasone-Loaded CS Microspheres with the PAA-PVP Complex. The coating of loaded microspheres was performed by a simple water-in-oil (W/O) emulsion solvent evaporation technique. Microparticles
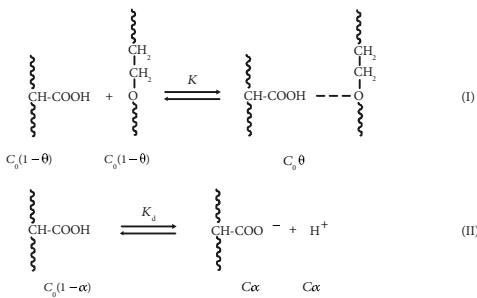
FIGURE 1: Scheme of the equilibrium reactions involved in the complexation reaction between PAA and PEG.
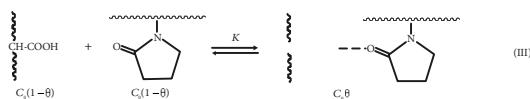
FIGURE 2: Scheme of the equilibrium reactions involved in the complexation reaction between PAA and PVP.

TABLE 1: Degree of linkage (θ) and stability constants (K) of PAA-PEG and PAA-PVP complexes at 30°C.

	$MW \times 10^3$	θ	$K \cdot 10^3$ (L mol^{-1})
PEG-1.2	1.2	0.34	0.155
PEG-2	2.0	0.43	0.256
PEG-4	4.0	0.47	0.345
PEG-6	6.0	0.54	0.520
PEG-35	35.0	0.62	0.858
PVP-29	29.0	0.97	233.500
PVP-360	360.0	0.98	492.400

(50 mg) were dispersed in 10 mL of PAA-PVP solution (aqueous solution mixture of 5 mL of PAA (2.5 wt.%) and 5 mL of PVP (3.5 wt.%)). This suspension was then dropped into 80 mL of corn oil containing 2 vol.% Span 80 as a surfactant under continuous stirring (500 rpm) to obtain the W/O emulsion. Afterwards, the solvent was evaporated by heating the emulsion at 60°C for 3 h. Finally, particles were filtered off and washed several times with acetone/water mixture (70 : 30), freeze-dried, and stored at room temperature.

2.2.5. Scanning Electron Microscopy. The morphology of coated and uncoated dexamethasone-loaded CS microspheres was assessed by scanning electron microscopy (SEM) using a JEOL JSM-6460LV (JEOL, Tokyo, Japan) electron microscope, after sputter coating with gold. The images were taken at an excitation voltage of 15 kV.

2.2.6. ATR-FTIR Analysis. Infrared analysis was performed at room temperature on a Thermo Scientific Nicolet 6700 FTIR spectrometer (Madison, WI, USA) equipped with an attenuated total internal reflectance (ATR) system. Spectra were collected from 64 scans at 2 cm^{-1} resolution. The analysis was performed to detect the presence of dexamethasone

in drug-loaded microparticles and also to confirm the complexation between PAA and PVP via hydrogen bonding. To observe the hydrogen bonding interaction, two different samples were prepared: (i) the physical blend, prepared by mixing both polymers at a pH where the complex did not form and by drying the mixture, and (ii) the interpolymer complex, prepared by mixing polymers at low pH to obtain the complex and then by drying.

2.2.7. Thermogravimetric Analysis (TGA). Thermal characterization of the homopolymer and complex was performed using Shimadzu TGA-50 (Shimadzu Co., Tokyo, Japan). Experiments were conducted from room temperature to 900°C at a heating rate of 10°C min^{-1} under a nitrogen atmosphere (20 mL/min).

2.2.8. In Vitro Drug Release Studies. Dexamethasone release from coated and uncoated CS microparticles was followed in two different dissolution media: (i) simulated gastric fluid (SGF) (pH 1.2 ± 0.1) and (ii) simulated intestinal fluid (SIF) (pH 6.8 ± 0.1). Release studies were carried out in 100 mL dissolution medium at 37 ± 0.1°C with agitation at 50 rpm. In the release study on coated loaded CS microparticles, 100 mL of SGF was used as dissolution medium during 2.5 h and then it was replaced by 100 mL of SIF for the rest of the experiment. An aliquot (1 mL) of the release medium was withdrawn at predetermined time intervals, and an equivalent amount of fresh medium was added to replace it. Drug content was determined spectrophotometrically at 242 nm. The in vitro release studies were performed in triplicate.

Release data were fitted to Ritger and Peppas's mathematical model [21]:

$$\frac{M_t}{M_\infty} = kt^n, \tag{3}$$

where M_t and M_∞ are the total amount of dexamethasone in the sphere after time t and after infinite time, respectively, k is a constant that incorporates structural and geometric characteristics of the device, and n is the diffusion exponent, which is indicative of the release mechanism. Ritger and Peppas have defined the exponent n as a function of the aspect ratio for 1-dimensional to 3-dimensional systems (discs, slabs, and cylinders). The aspect ratio is defined as the ratio of diameter to thickness. For a spherical sample, $n \leq 0.43$ indicates Fickian controlled drug release and $n = 0.85$ indicates a purely relaxation-controlled delivery (case II transport) [22]. Values of n between 0.43 and 0.85 can be regarded as indicators of the superimposition of both phenomena, commonly called anomalous transport [14, 21]. Fitting of release data to equation (3) was made with Statgraphics Plus version 5.1 (Rockville, MD, USA).

3. Results and Discussion

3.1. PAA-PEG and PAA-PVP Complexes by Hydrogen Bonding. The complex formation between PAA and polymers having H-bond acceptor groups such as PEG and
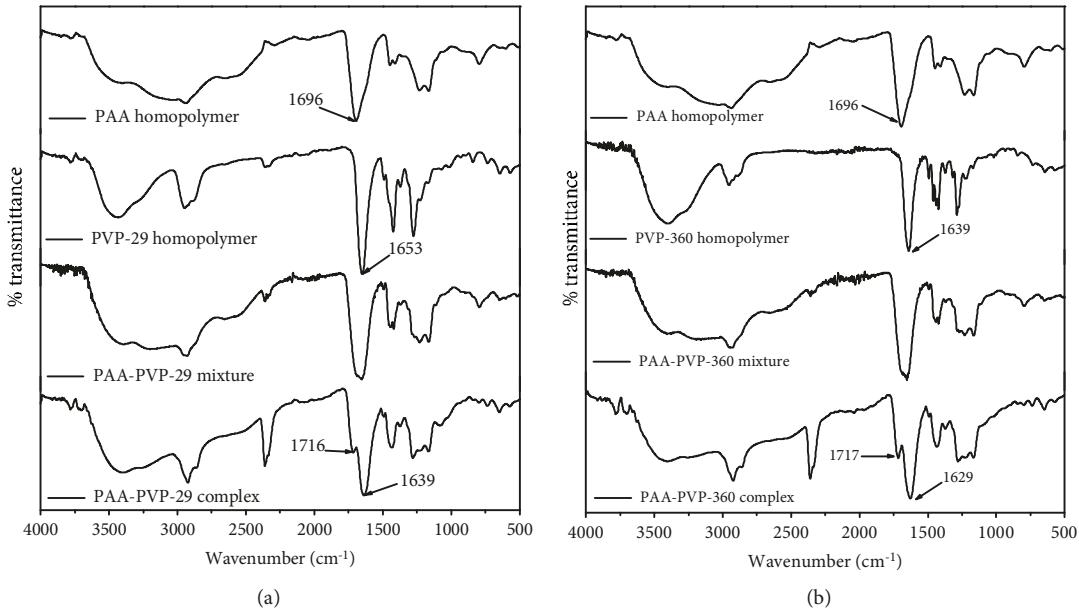
FIGURE 3: FTIR spectra of PAA, PVP, the physical mixture of PAA and PVP, and the PAA-PVP complexes: (a) PVP-29 and (b) PVP-360.
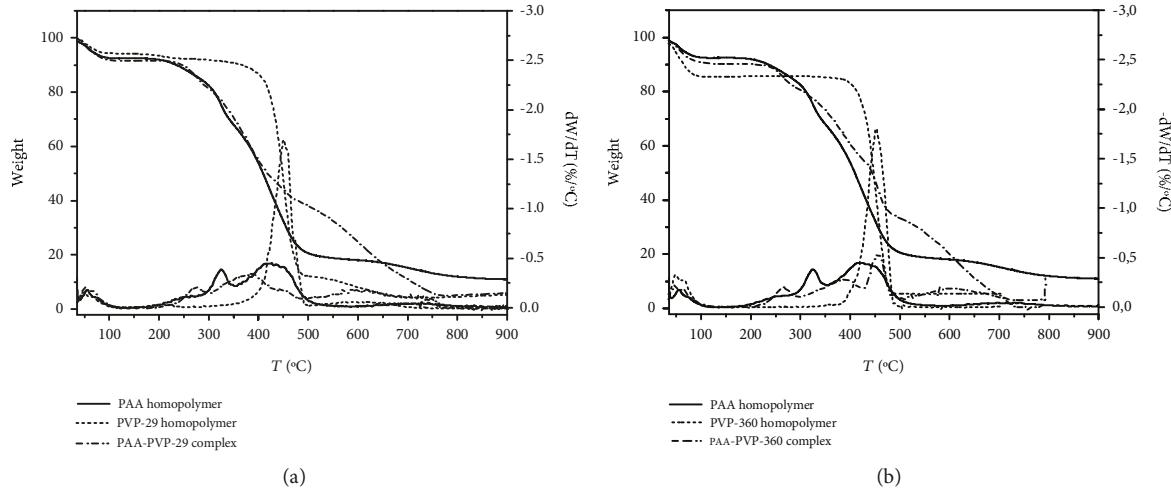

FIGURE 4: TGA thermograms of PAA, PVP, and the PAA-PVP complexes: (a) PVP-29 and (b) PVP-360.

PVP has been addressed by different authors [17–19, 23, 24]. The relevant equilibrium processes involved in the H-bonding interaction between PAA and PEG are the complexation reaction itself and the dissociation equilibrium of the polyacid, which can be represented as shown in Figures 1 and 2.

In equilibrium (I), C_0 is the initial concentration of PAA; θ is the degree of conversion, defined as the fraction of H-bonded carboxylic groups; and K is the stability constant of the complex. In equilibrium (II), C is the concentration of PAA, α is the dissociation degree of the polyacid, and K_d is its apparent dissociation constant.

A similar consideration can be made for the interaction between PAA and PVP. Figure 2 represents their interpolymeric reaction, where C_0, θ, and K have the same meaning as before.

It has been stated that if the dissociation degree of the polyacid does not change appreciably as a result of complexation, the degree of conversion θ can be evaluated as

$$\theta = 1 - \left(\frac{[\mathrm{H}^+]}{[\mathrm{H}^+]_0}\right)^2, \tag{4}$$

where $[\mathrm{H}^+]$ and $[\mathrm{H}^+]_0$ are the hydrogen ion concentrations of the PAA solution in the presence and absence of PVP, respectively [24]. The stability constant of the complex can then be calculated as

$$K = \frac{\theta}{C_0(1-\theta)^2}. \tag{5}$$

(a)

(b)
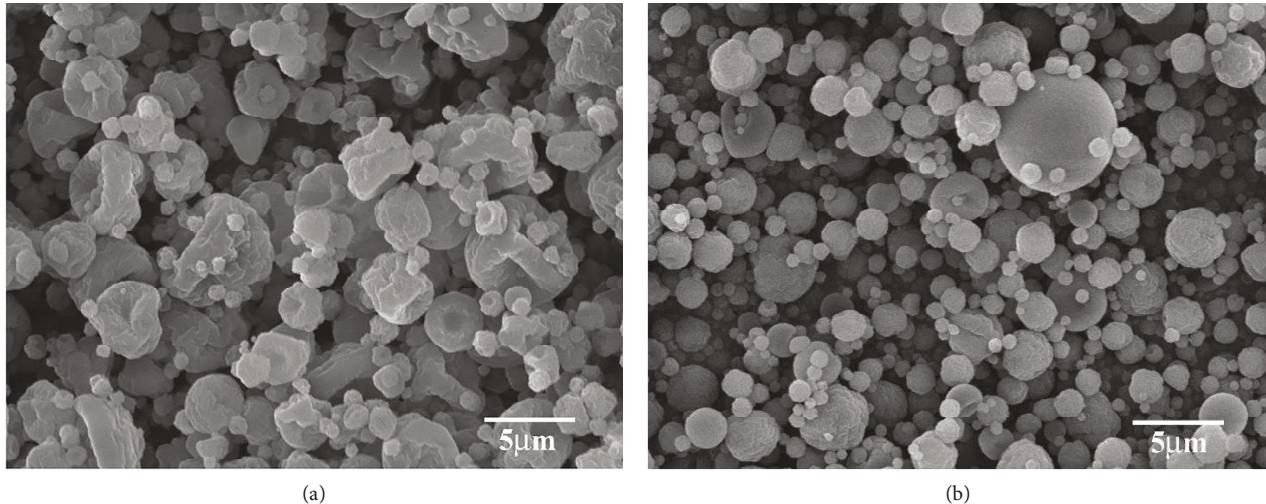
FIGURE 5: SEM image of the surface morphology of microparticles obtained by spray drying: (a) empty CS microspheres and (b) dexamethasone-loaded CS microspheres.
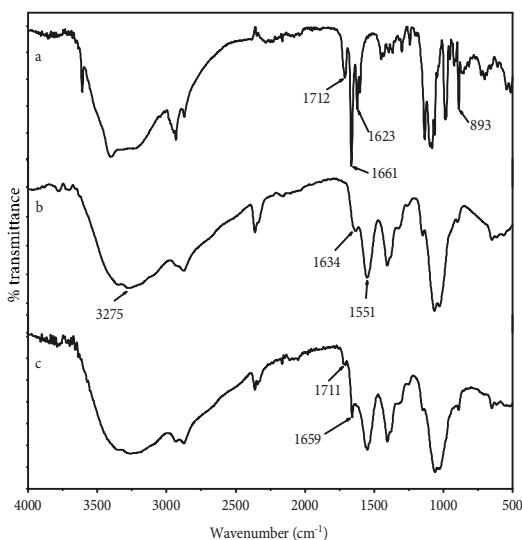

FIGURE 6: FTIR spectra of (a) dexamethasone, (b) CS microparticles, and (c) loaded CS microparticles.

The values of the conversion degree and the stability constant for the complexation reaction between PAA-PEG and PAA-PVP were determined by potentiometry for samples of PEG and PVP of different molecular weights. The results are shown in Table 1.

The increase in the degree of linkage and stability constant with the increase in the molecular weight of PEG and PVP reflects the cooperative nature of the interpolymer reaction [23–26]. In this connection, it is worth noting the influence of the nature of the proton-accepting polymer on the degree of conversion. For instance, PEG with a molecular weight as high as 35 kDa yields a complex with $\theta = 0.62$, whereas PVP with a slightly lower molecular weight (29 kDa) produces a complex with $\theta = 0.97$, indicating that the reaction proceeds almost to completion [24, 26].

It is worth pointing out that in a previous paper [23], it was observed that the increase in the values of θ and K in the temperature range from 30 to 40°C is relatively small for the PAA-PEG and PAA-PVP complexes. Therefore, the above outcome is also valid at 37°C.

In the light of these results, it is expected that the PAA-PVP hydrogen-bonded interpolymer complex should give rise to more compact and stronger films and membranes than the ones produced using the PAA-PEG system. Therefore, from now on, we will be devoted to the characterization of PAA-PVP complexes and their application as a pH-protective cover for a pharmaceutical formulation.

3.1.1. Characterization of PAA-PVP Complexes. FTIR spectra of PAA and the two PVP with different molecular weights previously employed (29 and 360 kDa), their 1 : 1 physical mixture, and their respective interpolymer complexes are shown in Figure 3. The polymer spectra show the characteristic C=O stretching signal at 1696 cm^{-1} for PAA and 1653 and 1639 cm^{-1} for PVP-29 and PVP-360, respectively. As expected in the infrared spectra of both physical mixtures, there is a wide absorption band in the C=O stretching region due to the overlapping of the corresponding C=O absorption bands of PAA and PVP. However, it can be seen that the position of the carbonyl absorption bands of PAA and PVP in the PAA-PVP complex spectra was changed. A shift of the carbonyl absorption band of PAA to a higher wavenumber (from 1696 to 1716 cm^{-1}) and the carbonyl absorption band of PVP to a lower wavenumber (from 1651 to 1638 cm^{-1} for PVP-29 and from 1639 to 1628 cm^{-1} for PVP-360) has been observed. These shifts in the FTIR spectrum indicate the PVP : PAA complex formation, since such carbonyl peak shifts are characteristic of strong hydrogen bonding [15, 27, 28].

The TGA thermograms for PAA, PVP-29, PVP-360, and their respective interpolymer complexes are shown in Figure 4. The PAA thermogram shows that decomposition occurs in three stages. The first stage ($T < 250$°C) is
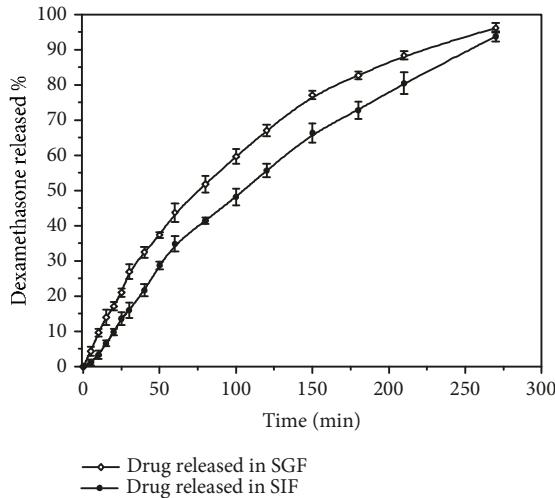
FIGURE 7: *In vitro* release profiles of dexamethasone from CS microparticles in different simulated fluids: simulated gastric fluid (SGF, pH 1.2) and simulated intestinal fluid (SIF, pH 6.8).

TABLE 2: Estimated values of n and k obtained from fitting the experimental data to the Ritger-Peppas model.

Medium/fluid	n	k (min^{-n})	R^2
SGF	0.61 ± 0.02	3.4 ± 0.4	0.9863
SIF	0.76 ± 0.03	1.4 ± 0.2	0.9892

attributed to the dehydration and decarboxylation of the polymer. The second one ($300°C < T < 350°C$, peaking at $325°C$) corresponds to the release of H_2O, CH_4, and the AA monomer. Finally, the third stage of PAA degradation above $350°C$, characterized by a 50% mass loss, is due to the release of AA moieties consisting of short-chain fragments from depolymerization [29–31]. The carbonaceous residue above $600°C$ is 15% of the initial mass. The thermal decomposition of PVP for both molecular weights occurs in a single step ranging from $250°C$ to $520°C$ with a mass loss of over 95% as a result of the cleavage of the pyrrolidone ring accompanied by the random scission of the polyenic sequences formed as a consequence of the volatilization of the pyrrolidone residue [32, 33].

It is observed that PAA has a lower thermal stability than PVP. However, the thermal analysis of the complexes formed with PVPs with different molecular weights shows an intermediate stability between both homopolymers; this suggests that hydrogen bonding between PAA and PVP stabilizes PAA increasing its thermal stability [20].

3.2. Characterization of the Drug-Loaded CS Microspheres. A simple and rapid method was employed to obtain chitosan microparticles for the controlled release of DMT. Dexamethasone-loaded CS microparticles (CS-DMT) were prepared by a spray drying technique. The yield of loaded CS microspheres obtained was 53.2%. This low value is generally obtained when this technique is used for preparing small samples, because the material lost in the walls

of the equipment becomes significant [34]. The mean drug content in microspheres was 20.2% w/w, giving an encapsulation efficiency of 87.4%. SEM images of empty CS microspheres and dexamethasone-loaded CS, prepared by spray drying, are shown in Figures 5(a) and 5(b).

The empty CS microspheres have a shrunken shape, as shown in Figure 5(a), due to the evaporation of the solvent contained inside them [35–37]. In contrast, dexamethasone-loaded CS microspheres present a spherical shape and a rough surface (Figure 5(b)). Comparing dexamethasone-loaded and dexamethasone-free microspheres, one could conclude that dexamethasone incorporation had influence on surface and morphological characteristics of the microspheres prepared.

3.2.1. ATR-FTIR Analysis. FTIR spectra of dexamethasone, the empty CS microparticles, and the drug-loaded microparticles are shown in Figure 6. In pure dexamethasone spectra (Figure 6(a)), the characteristic absorption bands at 1712, 1661, and $1623 \, cm^{-1}$ correspond to the stretching vibration of the $-C=O$ group of aliphatic ester and ketone and the double-bond framework conjugated to $C=O$ bonds, respectively. The band at $893 \, cm^{-1}$ corresponds to the axial deformation of the C-F group [38, 39]. In the spectrum of CS microparticles (Figure 6(b)), the characteristic CS absorption bands are present: two principal absorption bands, $1634 \, cm^{-1}$ and $1551 \, cm^{-1}$, were detected and they are attributed to the $C=O$ stretching (amide I) representing the structure of N-acetylglucosamine and the NH_2 stretching (amide II) associated with the glucosamine functional group, respectively [39, 40]. In Figure 6(c), the presence of the dexamethasone into CS cores was revealed by the peaks at 1711 and $1659 \, cm^{-1}$ (stretching vibration of $C=O$ and $C=C$ of dexamethasone) in the spectrum of drug-loaded microparticles [39, 41]. Other typical bands in the dexamethasone infrared spectrum (e.g., peaks at 1623 and $893 \, cm^{-1}$) overlapped with CS absorption bands.

3.2.2. Drug Release from CS Microparticles. Almost complete release of dexamethasone (>90%) from loaded CS microparticles was obtained in 4.5 hours (Figure 7) without displaying a burst effect. The observed release process suggests that the medium penetrates into the particles due to the hydrophilic nature of CS and dissolves the entrapped dexamethasone [34, 42].

According to our data, the amount of dexamethasone released from these CS microparticles was independent of pH (Figure 7). Although the release in SGF is greater than the release in SIF, this difference was not statistically significant ($p > 0.05$).

In order to investigate the release mechanism of dexamethasone from chitosan microparticles, the data were fitted to the Ritger-Peppas equation and are shown in Table 2. The results indicate that the drug is released at both pH values via case II mechanism which involves simultaneous contributions from diffusion, relaxation of the polymeric chain, and chitosan's swelling.

3.3. Loaded CS Microparticles Coated with the PAA-PVP Complexes. The last part of this work was focused on the coating of loaded CS microparticles with pH-dependent

(a)

(b)
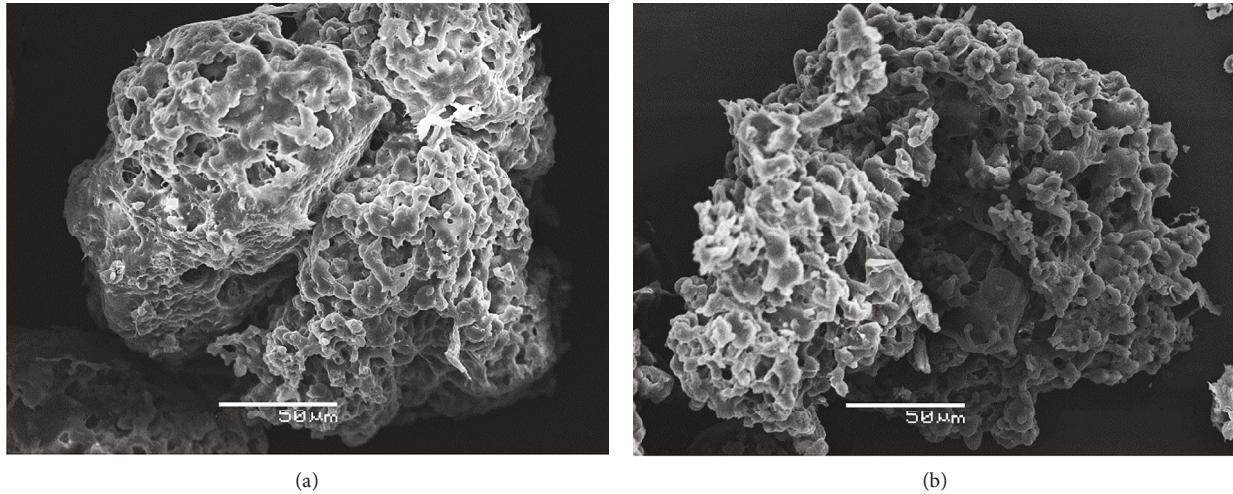
FIGURE 8: SEM image of the surface morphology of loaded CS microparticles encapsulated in PAA-PVP complexes: (a) PVP-29 and (b) PVP-360.
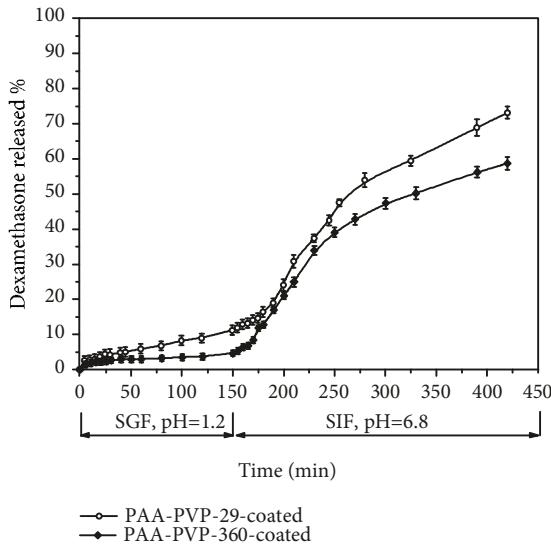

FIGURE 9: In vitro release profile of dexamethasone from coated loaded CS beads in different simulated fluids: simulated gastric fluid (SGF, pH 1.2) and simulated intestinal fluid (SIF, pH 6.8).

interpolymer complexes using the simple water-in-oil solvent evaporation technique. The effect of this coating on *in vitro* drug release in simulated fluids was studied.

3.3.1. Morphology of Particles Covered by the PAA-PVP Complexes. The loaded CS cores coated with the PAA-PVP complexes have an irregular form. As shown in Figure 8(a), the structure of the particles prepared with PVP-29 is slightly more compact than the particles obtained with PVP-360 (Figure 8(b)). The surface in both cases is highly rough, with large porosity. It was also observed that the PVP molecular weight does not have a notable influence on the morphology of the PAA-PVP-covered particles.

3.3.2. pH-Dependent Release Study. Uncoated loaded CS microparticles released almost 100% of the drug in the initial 4 to 5 h in both release fluids. Because the transit time through the GI tract is a critical point in colon drug delivery systems, this result is not viable for this purpose since the small intestinal transit time is generally accepted as 4 hours and the drug would be released before reaching the colon [43].

Hence, loaded CS microparticles were coated with pH-dependent interpolymer complexes PAA-PVP to avoid the release of the drug at pH values lower than 6.8. The initial release of dexamethasone from the coated loaded CS beads was low (Figure 9). After 2.5 h in the medium (SGF) (pH = 1.2), only 2.7% and 8.4% of the initial dexamethasone were released from CS microparticles coated with PAA/PVP-360 and PAA/PVP-29, respectively. After 4 h (including 1.5 h at pH 6.8), less than 40% had been released reducing almost 60% of the drug released with respect to the noncoated microparticles.

The release at pH 6.8 was very interesting. After medium change, a time lag occurs (30 min approximately). This lag could be produced by buffer exchange inside particles and dissolution of coating by disruption of linkage by H-bonds between PAA and PVP. Figure 8 shows that these particles had a large and rough coating. Consequently, buffer exchange and subsequent dissolution can take a significant time. After the time lag, a Fickian diffusion release occurs (the value of n for the Ritger-Peppas equation was 0.46 ± 0.03, $r^2 = 0.97$). This profile was somewhat different from that of the noncoated CS core (Figure 7). So, it is possible that interpolymer complex coating not only prevents release at acidic pH but also modifies the release profiles at higher pH.

The drug release behavior from loaded CS cores coated with PAA/PVP-29 and PAA/PVP-360 complexes was similar. Nevertheless, the release from the PAA/PVP-29 complex coating was higher, which could be due to a smaller number of linkages and consequently a decrease in the complex stability.

The protective effect of the PAA-PVP complex coating on the dexamethasone-loaded CS microparticles is similar to the effect of Eudragit on the multilayer CS/alginate

microparticles loaded with the drug prepared by Oshi et al. [13]. In their system, the release at pH 1.2 decreased to approximately 10% after 2 hours. After 2 hours at pH 6.4, the amount of the drug released was also near 20%. These results indicate that the PAA-PVP complex coating is also an efficient protective cover for colon-targeted drug release.

4. Conclusions

Release studies indicate that the CS beads coated with pH-dependent PAA-PVP interpolymer complexes offer a high degree of protection from drug release in SGF. A controlled release of the drug from the microparticles was observed, once the coating layer of the pH-dependent interpolymer complex starts to dissolve at a higher pH (pH 6.8). The influence of molecular weight of PVP on the rate and extent of drug release is evident, since increasing molecular weight reduces the dexamethasone released. It is concluded that the chitosan nanoparticles coated with PAA-PVP complexes can be used for effective controlled delivery of the dexamethasone drug directly to the colon. This site-specific delivery of dexamethasone could reduce side effects and loss of drug caused by its absorption from the upper part of the gastrointestinal tract. Thus, the results prove the potential application of this interpolymer complex in site-specific delivery systems in colonic drug release formulations.

Data Availability

The data used to support the findings of this study are available from the corresponding author upon request.

Disclosure

Conflicts of Interest

The authors declare that they have no conflicts of interest.
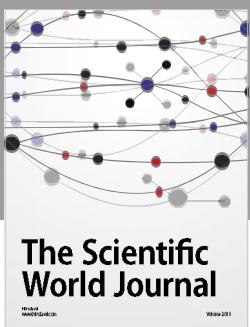
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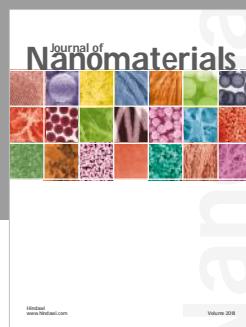
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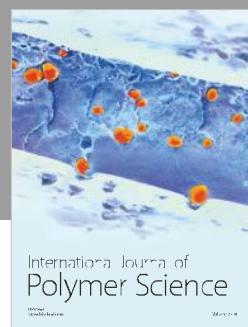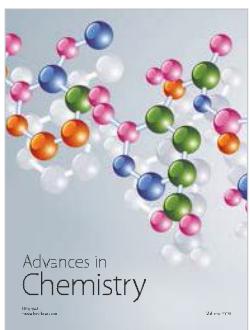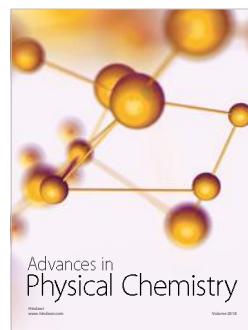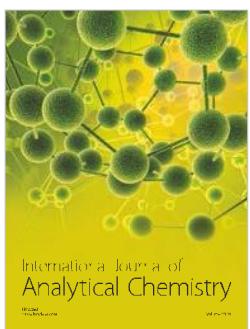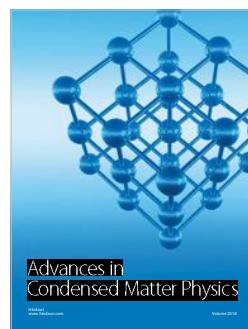
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