

Research Article

Pectin-Coated Curcumin-Chitosan Microparticles Crosslinked with Mg^{2+} for Delayed Drug Release in the Digestive System

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Curcumin-loaded chitosan-pectin microparticles based on polymeric microencapsulation were prepared by two methods to delay the release of curcumin in the digestive system, employing Mg^{2+} as a pectin-crosslinking agent for the first time. Pectin-coated curcumin-chitosan microparticles (C-g-P_{Mg}) and curcumin-loaded chitosan-pectin composite microparticles ($\text{C-P}_{\text{Mg-g}}$) were formulated, and their release profiles at pH 1.2 and at pH 6.8 were tested. The former (C-g-P_{Mg}) showed slower curcumin release profiles than the latter ($\text{C-P}_{\text{Mg-g}}$) because the C-g-P_{Mg} are composed of two layers, a chitosan-glutaraldehyde layer and a pectin- Mg^{2+} layer, which together hold the curcumin for a longer duration. Of the pectin-coated microparticles, those crosslinked with Mg^{2+} showed a slower release rate than those crosslinked with Ca^{2+} , but the former showed a faster release rate at pH 6.8 in the presence of pectinase, acting as a promising drug delivery carrier for treating a colonic disease. The pectin layer and the pectin-crosslinking agent play a vital role in prolonging the release of curcumin until pectin is degraded by pectinase.

1. Introduction

Curcumin, 1,7-bis[4-hydroxy-3-methoxyphenyl]-1,6-heptadiene-3,5-dione, which has been used for centuries in traditional Indian medicines, spices, and food colorings, is a polyphenol with conjugated double bonds [1, 2]. Curcumin is safe and nontoxic, exhibiting a broad range of biological activities such as anti-inflammatory, antioxidant, antimicrobial, antitumor, anticoagulant, antiviral, and antiamyloid properties [2–4]. Preclinical studies on curcumin also found that it inhibits carcinogenesis in a variety of cell lines, including breast, colon, gastric, liver, leukemia, oral epithelial, ovarian, pancreatic, and prostate [1]. The medicinal benefits of curcumin are limited by its extremely low aqueous solubility, rapid metabolism, and instability in the gastric fluid [3–6]. However, curcumin is soluble in low polar solvents such as ethanol and acetone. Curcumin dissolved in low polar foods can be easily metabolized in the stomach.

Thus, relevant formulation strategies based on polymeric nano/microencapsulation have been employed to prevent the metabolism of curcumin at the upper part of the GIT (gastrointestinal tract) for medical use [5].

Encapsulation technologies using polymeric drug delivery systems to improve pharmacological response and to allow time- and distribution-controlled drug delivery have been studied in detail [7–13]. Various types of polymers have been used, such as nano- and microparticles, micelles, dendrimers, and capsosomes, where drugs can be encapsulated or conjugated in polymer matrices [13]. These drug carriers have been used in a wide range of treatments, including antineoplastic activity, bacterial infections, and inflammatory processes, and vaccines [13]. Polymers used in drug delivery systems play a vital role in providing controlled drug release in which constant dosing, cyclic dosing, and the tunable release of both hydrophilic and hydrophobic drugs can be accomplished over long periods [14]. Such

delivery systems retain the structural integrity of a drug, protecting the drug from degradation in the upper GIT [5, 6].

Of the biopolymers derived from natural sources, chitosan is particularly well-suited for mucosal delivery, being relatively nonimmunogenic and nontoxic, as well as having good biodegradability and biocompatibility. Chitosan-based particles have been studied for the effective delivery of many drugs, including anticancer agents, therapeutic proteins, genes, and antigens [15–18]. Chitosan is poorly soluble in water, but it easily dissolves in acidic environments such as the gastric fluid in the stomach. Upon protonation in an acidic environment, it stays positively charged and can interact with negatively charged molecules [19], which plays an important role in drug transport and in the reduction of enzymatic drug degradation in the GIT [16]. Moreover, chitosan crosslinked with a hardening agent can impede the degradation of drug molecules in the GIT [20].

A second biopolymer such as pectin which is a water-soluble and linear anionic polysaccharide in the primary cell walls of most plants has been used in conjunction with chitosan, which forms a stable polymer complex [1, 5]. Since chitosan and pectin are oppositely charged, they interact through intermolecular electrostatic attractions to form a polyelectrolyte complex structure. The complex remains stable until its pectin component is degraded by pectinase enzymes produced by the colonic microflora [5, 21]. The microorganisms that ferment pectin exist in the colon and are qualitatively consistent in composition across a diverse human population [22]. However, pectin alone is unsuitable for drug transport as it swells under alkaline conditions, potentially triggering premature release of the drug contents [5]. The complexation of pectin with chitosan or the crosslinking of pectin by divalent metal cations such as Ca^{2+} decreases the permeability, solubility, and disintegration extent of the polymer structure but increases the density and mechanical strength of the dosage form [23], thereby delaying the release of the drug. The physical crosslinking through electrostatic interactions between Ca^{2+} and the negatively charged carboxyl groups of pectin strengthens the rigidity of the polymer gel.

This study was designed to prolong and control the release of curcumin by encapsulating it with the biodegradable polymers, chitosan and pectin. Specifically, curcumin-loaded chitosan-pectin microparticles were prepared by two new methods, and their relative abilities to accomplish a delayed release of curcumin in the GIT were measured. A microparticle can encapsulate a higher amount of curcumin than a nanoparticle which may contain little or no curcumin due to its small size. In the first method, curcumin-loaded chitosan microparticles were fabricated using glutaraldehyde as a hardening agent and then coated by pectin which was complexed with Mg^{2+} cations (called C-g- P_{Mg} , referring to chitosan-glutaraldehyde, and pectin crosslinked by Mg^{2+}). Generally, Ca^{2+} has been used as a pectin-crosslinking agent. In this research, Mg^{2+} was used for the first time as a pectin-crosslinking agent because it is one of the important electrolytes in the human body. The release rate of curcumin resulting from Mg^{2+} was compared with that resulting from Ca^{2+}

cations. In the second method, pectin was added to a mixture of chitosan-curcumin solutions to formulate the composite particles which were hardened by glutaraldehyde (called C- P_{Mg} -g, referring to chitosan-pectin composite crosslinked by Mg^{2+} , and hardened by glutaraldehyde). The curcumin release profiles of the microparticles were observed to compare the effects of the formulation method, pectinase, and divalent cations on drug release. Thermal analysis on pectin- M^{2+} , where $\text{M}^{2+} = \text{Mg}^{2+}$ or Ca^{2+} gel, was conducted to identify the release rate of curcumin in relation to the network strength of pectin- M^{2+} .

2. Materials and Methods

2.1. Materials. Chitosan was obtained from Showa Chemical Industry Co. Ltd. (Tokyo, Japan). Curcumin (synthetic, >97.0%) and pectin (from citrus) were purchased from Tokyo Chemical Industry Co. Ltd. (Tokyo, Japan). Pectinase (from *Aspergillus aculeatus*), glutaraldehyde solution (50% in water), span 80, and $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$ were supplied by Sigma-Aldrich (St. Louis, MO, USA). $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$, tween 80, NaCl (>99%), HCl (>35%), and toluene (>99.5%) were purchased from Daejung Chemical Co. Ltd. (Shiheung City, South Korea). $\text{Na}_3\text{PO}_4 \cdot 12\text{H}_2\text{O}$ (G.R.) and liquid paraffin were supplied by Junsei Chemical Co. Ltd. (Tokyo, Japan).

2.2. Preparation of Microparticles. Before formulating the microparticles, the glutaraldehyde saturated toluene as a hardening agent for chitosan was prepared as follows.

A glutaraldehyde solution (25 ml, 50% in water) and toluene (25 ml) were placed in a beaker and stirred at 1000 rpm for two hours. Then, the mixture was poured into a separatory funnel and allowed to stabilize. After 15 hours, the upper toluene layer saturated with glutaraldehyde was decanted and used as the glutaraldehyde saturated toluene solution [24].

2.2.1. Method A: Pectin-Coated Curcumin-Chitosan Microparticles (C-g- P_{M} , where $\text{M} = \text{Mg}$ or Ca). Chitosan (0.35 g) was dissolved in 1% (v/v) aqueous acetic acid solution (15 ml). The solution was stirred at 700 rpm for 15 hours. Under continuous magnetic stirring, a solution of curcumin (3.5 mg) dissolved in ethanol (7 ml) was slowly added. The mixture was incorporated into liquid paraffin (100 ml) containing span 80 (1.5 ml) by dropwise addition, with further stirring at 1500 rpm for 30 minutes. It was homogenized at 5000 rpm for 40 minutes with a homomixer (T.K. Homomixer Mark II 2.5, Primix Co.). Next, glutaraldehyde saturated toluene solution (2 ml) was added dropwise, and the mixture was homogenized at 5000 rpm for one hour to facilitate external crosslinking, where aldehyde groups of a glutaraldehyde molecule crosslink with chitosan chains of the surface of a microparticle. For the internal crosslinking of the microparticles, glutaraldehyde solution (0.4 ml, 50% in water) was added dropwise. The mixture was homogenized at 5000 rpm for an additional hour and centrifuged (Hanil Sci. Ind. Co. MF80) at 4000 rpm for five minutes. Subsequently, the precipitate of curcumin-loaded chitosan particles (called C-g, referring to chitosan-glutaraldehyde)

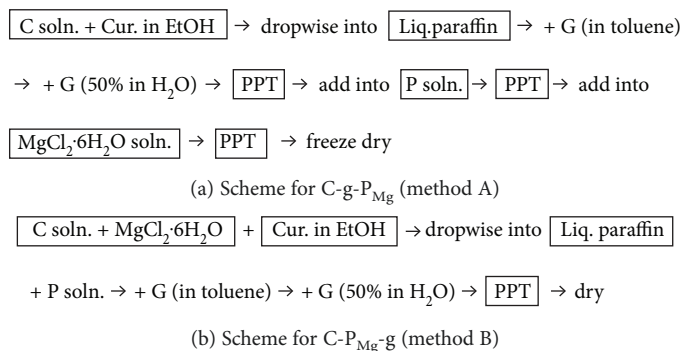


FIGURE 1: Fabrication schemes for (a) C-g-P_{Mg} and (b) C-P_{Mg}-g, where C is chitosan, Cur. is curcumin, G is glutaraldehyde, P is pectin, and PPT is precipitate.

was washed twice with n-hexane. After 0.5% (w/v) pectin solution (70 ml) containing tween 80 (0.7 ml) was homogenized, the dried C-g were poured into the solution, followed by continuous homogenization at 5000 rpm for 30 minutes and the entire mixture was centrifuged. The pectin-coated precipitate (called C-g-P, referring to chitosan-glutaraldehyde-pectin) was added to 5% (w/v) MgCl₂·6H₂O or CaCl₂·2H₂O solution (80 ml) to crosslink the pectin layer and was homogenized at 5000 rpm for one hour. The resulting mixture was centrifuged, washed twice with distilled water, and then freeze-dried.

2.2.2. Method B: Curcumin-Loaded Chitosan-Pectin Composite Microparticles (C-P_{Mg}-g). Chitosan (0.35 g) was dissolved in 1% (v/v) aqueous acetic acid solution (15 ml), followed by the addition of MgCl₂·6H₂O (0.2 g). This solution was stirred at 700 rpm for 15 hours. Under continuous magnetic stirring, a solution of curcumin (3.5 mg) dissolved in ethanol (7 ml) was added slowly. This solution was incorporated into liquid paraffin (100 ml) containing span 80 (1.5 ml) by dropwise addition, stirred at 1500 rpm for 30 minutes, and homogenized at 5000 rpm for 40 minutes. Then, 1% (w/v) pectin solution (2 ml) was dropped into the mixture, with further homogenization for 30 minutes. A saturated solution of glutaraldehyde in toluene (2 ml) was added dropwise into the solution for external crosslinking, and the mixture was homogenized continuously for one hour. Subsequently, glutaraldehyde solution (0.4 ml, 50% in water) was dropped into the mixture for the internal crosslinking of chitosan microparticles, with further homogenization for one hour. The entire solution was centrifuged, and the precipitate of chitosan-pectin composite microparticles was washed twice with n-hexane. Figure 1 describes the fabrication schemes for methods A and B. The morphology of the microparticles dried at room temperature was determined by SEM (Ultra Plus, Carl Zeiss). Figure 2 shows the schematic microparticles formulated by methods A and B.

2.3. Preparation of SGF (Simulated Gastric Fluid) and SI/CF (Simulated Intestinal/Colonic Fluid). Prior to the determination of the encapsulation efficiencies and the *in vitro* curcumin release test, SGF and SI/CF were prepared to mimic the natural dissolution conditions of a typical human GIT: SGF of pH 1.2 was produced by introducing sodium

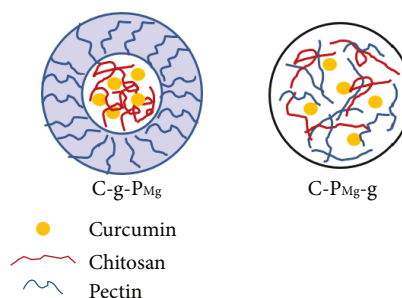


FIGURE 2: Schematic presentation of C-g-P_{Mg} and C-P_{Mg}-g formulated by methods A and B.

chloride (2.0 g) into 0.1 M HCl (1 L), and SI/CF of pH 6.8 was made from a mixture of 0.2 M Na₃PO₄·12H₂O (250 ml) and the SGF (750 ml) at a volume ratio of 1 to 3 [25].

2.4. EE (Encapsulation Efficiency). For the calibration of curcumin, the absorbance intensities of the standard curcumin solutions of pH 1.2 (SGF condition) and of pH 6.8 (SI/CF condition) containing 1% (v/v) tween 80 were measured at 427 nm by a UV-VIS spectrophotometer (Scinco Co., LTD S-3100) [1]. The experiment was carried out in triplicate. The microparticles obtained from methods A and B (about 15 mg) were ground for 30 minutes to break them down completely. Each ground sample was weighed and dissolved in SGF (20 ml) of pH 1.2 containing 1% (v/v) tween 80 at 37 ± 0.5 °C. The solution was stirred at 50 rpm for two hours and then centrifuged. The absorbance of the resulting supernatant was measured at 427 nm to estimate the amount of curcumin released in the SGF. Next, the precipitate sample was taken into SI/CF (20 ml) of pH 6.8 containing 1% (v/v) tween 80 at 37 ± 0.5 °C. The solution was stirred at 50 rpm for three hours, and 1% (v/v) pectinase enzyme (0.2 ml) was added. After stirring the resulting solution for 12 hours followed by centrifugation, the absorbance of the supernatant was measured again to determine the amount of curcumin released in the SI/CF. The encapsulation efficiency is as follows:

$$EE(\%) = \left(\frac{E}{T} \right) \times 100\%, \quad (1)$$

where T is the initial total amount of curcumin used and E is the loaded amount of curcumin in the sample, that is, E is the

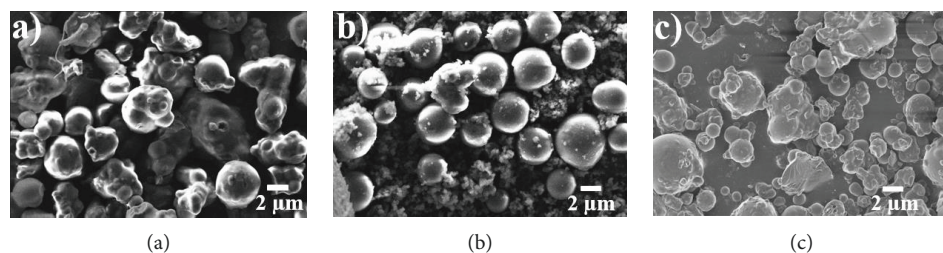


FIGURE 3: SEM images of (a) C-g-P_{Mg}, (b) C-P_{Mg}-g, and (c) C-g-P_{Ca}.

released amount of curcumin from the ground sample in the SGF for two hours and in the SI/CF for 15 hours. The experiments were performed three times.

2.5. Measurement of In Vitro Curcumin Release. *In vitro* curcumin release profiles were investigated by observing the release rates of the encapsulated curcumin, with slight modifications of the USP (United States Pharmacopeia) dissolution procedure [25]. SGF maintained at $37 \pm 0.5^\circ\text{C}$ (20 ml) was added to each sample (15 mg) with stirring at 50 rpm to measure the amount of curcumin released in SGF for two hours. After centrifugation of the SGF solution, 20 ml of SI/CF was transferred to the remaining precipitated sample for the release test until the 12th hour, which was also immersed in a water bath maintained at $37 \pm 0.5^\circ\text{C}$ with a rotation speed of 50 rpm. The detailed procedure for the measurement of the curcumin release is illustrated below.

From the beginning (0 hour) to the 2nd hr, the measurement was performed in the SGF as the gastric dissolution medium. During the 3rd to the 12th hr, the release test was carried out in the SI/CF as the intestinal/colonic dissolution medium. During the 6th to the 12th hr, the measurement was conducted in the absence or in the presence of 1% (v/v) pectinase to study the effects of the enzyme on Mg^{2+} - and Ca^{2+} -pectinates. For the experiment, pectinase was added to the SI/CF medium at the 5th hr to observe the release profile from the 6th hr. Throughout the release studies, 1% (v/v) tween 80 was added to the SGF and the SI/CF to prevent the possible sedimentation of curcumin released. 3 ml of the supernatant was periodically withdrawn from each dissolution medium at 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12th hr, followed by keeping the total volume of dissolution medium constant after each sampling. The absorbance of each sample was measured at 427 nm, and the curcumin released from the microparticles was estimated. The experiments were performed in triplicate.

2.6. Thermal Analysis. The strengths of crosslinks between pectin and the divalent metal cations in the surfaces of the microparticles were characterized by thermal analysis (Scinco Co., STA N-1000). Specifically, 5% (w/v) pectin solution (5 ml) was added to a 10% (w/v) solution of $\text{MgCl}_2 \cdot 6\text{H}_2\text{O}$ or $\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$ (5 ml) under slow stirring. After gelation, the samples were freeze-dried. Each sample (3–6 mg) was accurately weighed and placed into a platinum pan for thermal analysis from 100°C up to 600°C . The heating rate was kept at $15^\circ\text{C}/\text{min}$ under the atmospheric condition.

TABLE 1: Encapsulation efficiencies (%) of curcumin-loaded chitosan-pectin microparticles.

Sample	C-g-P _{Mg}	C-P _{Mg} -g	C-g-P _{Ca}	C-g-P	C-g
EE (%)	62.8	62.9	60.9	51.6	42.2

3. Results and Discussion

The SEM image of C-g-P_{Mg} is depicted in Figure 3(a). The microparticles prepared by method A have double-layered walls, wherein the pectin coats the surfaces of curcumin-loaded chitosan microparticles. The inner layer is formed by crosslinking the chitosan with glutaraldehyde, which builds the spherically shaped microparticles. The outer layer is formed by the pectin- Mg^{2+} structural network. Thus, two or more chitosan microparticles are often coated together by a pectin layer as seen in Figure 3(a). The C-g-P_{Mg} prepared by method A has a thick pectin layer, and the particle size is $6 \pm 2.5 \mu\text{m}$. In contrast, the C-P_{Mg}-g prepared by method B have a single-layered wall in the form of a chitosan-pectin composite with the particle size being $4 \pm 1.5 \mu\text{m}$ and exhibit more clearly shaped particles than those produced by method A as shown in Figure 3(b). The positively charged chitosan and Mg^{2+} ion interact with the negatively charged pectin in the composite that is hardened again with glutaraldehyde, building spherically shaped microparticles. Figure 3(c) depicts the SEM image of C-g-P_{Ca} microparticles prepared by method A. They also show double-layered walls, where the outer layer is formed by the pectin- Ca^{2+} structural network.

The EE (%) of the microparticles, C-g-P_{Mg}, C-P_{Mg}-g, C-g-P_{Ca}, C-g-P, and C-g, is listed in Table 1. The EE (%) value is relatively low for C-g prepared in the absence of pectin, indicating that the incomplete structural network of chitosan is not strong enough to encapsulate the curcumin.

Figure 4 reveals the cumulative curcumin release (%) at pH 1.2 and at pH 6.8 in the absence of pectinase and in the presence of pectinase for the two samples prepared by methods A (C-g-P_{Mg}) and B (C-P_{Mg}-g). The slope at each time in the figure reflects the release rate of curcumin. The microparticles synthesized by method B are enclosed with a single-layered wall and show a faster release rate than those produced by method A, holding the curcumin inside the microparticles less strongly than the C-g-P_{Mg}. In contrast, microparticles prepared by method A have double-layered surface membranes, due to chitosan-glutaraldehyde crosslinks and pectin- Mg^{2+} , holding curcumin for a longer duration, thereby prolonging the release of curcumin in a

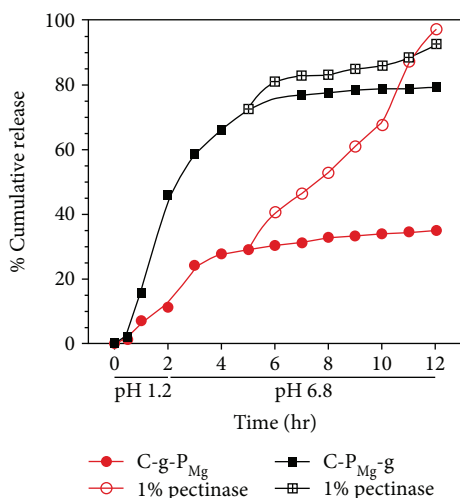


FIGURE 4: Curcumin release (%) profiles of C-g-P_{Mg} (filled circle) prepared by method A and C-P_{Mg}-g (filled square) prepared by method B in the absence of pectinase. The release profiles of C-g-P_{Mg} (open circle) and C-P_{Mg}-g (crossed square) in the presence of pectinase from the 6th hour.

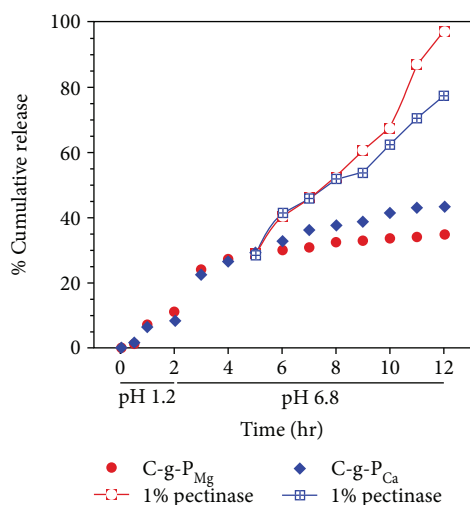


FIGURE 5: Curcumin release (%) for C-g-P_{Mg} (filled circle) and for C-g-P_{Ca} (filled rhombus) prepared by method A in the absence of pectinase. Curcumin release for C-g-P_{Mg} (circled square) and for C-g-P_{Ca} (crossed square) in the presence of pectinase from the 6th hr.

simulated digestive system. Specifically, the curcumin release is below 10% in SGF for the first two hours, which is about four times lower in value than the release from the C-P_{Mg}-g in SGF. However, the curcumin release from the C-g-P_{Mg} increases abruptly from the 6th hr in the presence of pectinase. This demonstrates that curcumin is readily released from the microparticles after the outer pectin-Mg²⁺ surfaces of C-g-P_{Mg} particles are degraded by pectinase. Degradation of the pectin layer on a C-g-P_{Mg} particle is accelerated by pectinase. Then, the inner layer which becomes exposed to the SI/CF begins to release curcumin more rapidly. Hence, C-g-P_{Mg} formulated by method A are very effective in treating a colonic disease because they prolong the release of curcumin

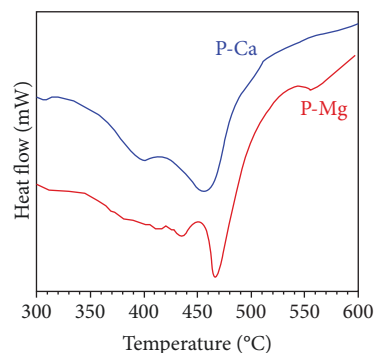


FIGURE 6: Thermal analysis of pectin-Mg²⁺ and pectin-Ca²⁺ gels.

over the longest period of time in the GIT but release it quickly in the colon where pectinase is present.

The plots for both C-g-P_{Mg} and C-g-P_{Ca} in the absence of pectinase and in the presence of pectinase are presented in Figure 5 to compare the effect of the pectin-crosslinking agent on the release of curcumin, where Mg²⁺ is newly employed in this study and Ca²⁺ has been generally used as a pectin-crosslinking agent. The C-g-P_{Mg} sustain the release of curcumin for a longer period of time than C-g-P_{Ca} in the absence of pectinase, but they release curcumin more quickly than C-g-P_{Ca} microparticles when pectinase is present, which reconfirms that C-g-P_{Mg} are highly effective in treating a colonic disease compared with C-g-P_{Ca} microparticles. This demonstrates that the drug release profile of pectin-based dosage forms strongly depends on the nature of the divalent cations used.

A study on the relative strength of the pectin-M²⁺ network through thermal analysis in the temperature range from 300 to 600 °C was performed (see Figure 6). The pectin component of the pectin-M²⁺ network does not decompose at temperatures below 320 °C, except for the dehydration processes such as $\text{MgCl}_2 \cdot 6\text{H}_2\text{O} \rightarrow \text{MgCl}_2 \cdot 4\text{H}_2\text{O} \rightarrow \text{MgCl}_2 \cdot 2\text{H}_2\text{O} \rightarrow \text{MgCl}_2 \cdot \text{H}_2\text{O}$ and $\text{CaCl}_2 \cdot 2\text{H}_2\text{O} \rightarrow \text{CaCl}_2 \cdot \text{H}_2\text{O} \rightarrow \text{CaCl}_2$ [26]. The degradation of the pectin component is mainly observed at temperatures above 350 °C. Of the crosslinked pectin-M²⁺, the decomposition temperature of calcium pectinate is lower than that of magnesium pectinate as observed in Figure 6, suggesting that magnesium pectinate forms a stronger network than that of calcium pectinate. In other words, the Mg²⁺ ion has a smaller size and a higher charge density, compared with the Ca²⁺ ion. Thus, the microparticles crosslinked with Mg²⁺ show a prolonged release rate due to the structurally stronger pectin-Mg²⁺ network in the absence of pectinase as described in Figure 5.

Figure 7 depicts the release of curcumin for curcumin-loaded chitosan microparticles (C-g), pectin-coated chitosan microparticles (C-g-P) in the absence of pectin-crosslinking agent, and pectin-coated curcumin-chitosan microparticles (C-g-P_{Mg}) crosslinked with Mg²⁺. From the cumulative release profiles of the three types of microparticles, it can be observed that the roles of the pectin layer and the pectin-crosslinking agent are crucial in delaying the release of curcumin in the digestive system. Thus, the delayed release of curcumin could be achieved in this study by encapsulating it

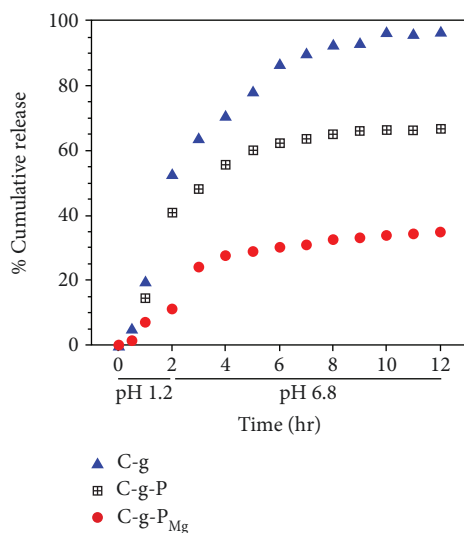


FIGURE 7: Cumulative release (%) of curcumin for C-g (filled triangle), C-g-P (crossed square), and C-g-P_{Mg} (filled circle) in the absence of pectinase.

with a pectin-coated chitosan layer, in which Mg²⁺ acts as a pectin-crosslinking agent.

4. Conclusions

In order to prolong the medicinal benefits of curcumin by delaying its release in a simulated digestive system, formulation strategies based on chitosan/pectin microencapsulation techniques were used. For this purpose, glutaraldehyde was employed as a hardening agent for chitosan and the newly selected Mg²⁺ was utilized as a pectin-crosslinking agent. Two new methods were applied to prepare spherically shaped curcumin-loaded chitosan-pectin microparticles in the W/O phase. In method A, the curcumin-loaded chitosan-glutaraldehyde microparticles were coated by pectin, followed by their complexation with Mg²⁺ (C-g-P_{Mg}). In method B, pectin was added to a mixture of Mg²⁺ chloride and curcumin-loaded chitosan solutions to form a composite, in which pectin and chitosan were crosslinked with Mg²⁺ and glutaraldehyde (C-P_{Mg}-g), respectively. The release profiles of curcumin were investigated to study the effect of its release in the simulated digestive system, that is, in the SGF medium of pH 1.2 for the first two hours and in the SI/CF medium of pH 6.8 from the 3rd to the 12th hr at 37 ± 0.5 °C. The release of curcumin was found to be more prolonged for the pectin-coated microparticles (C-g-P_{Mg}), because of their double layer effect, than for the chitosan-pectin composite (C-P_{Mg}-g) particles. The microparticles crosslinked with Mg²⁺ showed a slower release rate in the absence of pectinase, but they showed a faster release rate in the presence of pectinase compared with those crosslinked with Ca²⁺ which has been used as a conventional pectin-crosslinking agent. The pectin layer and the pectin-crosslinking agent played a very important role in delaying the release of curcumin. The experimental results show that the C-g-P_{Mg} are promising drug delivery carriers in treating the colon, where a large amount of curcumin is released.

Data Availability

The data (figures and a table) that support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Acknowledgments

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