Modification of Starch by Grafting Acetylsalicylic Acid: Synthesis, Characterization, and Application in Drug Release Domain

SABA AMEEN AL-ADEEMY, MOUNIRA ALSHEIKH, and TAIEB AOUAK

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A series of modified starches were prepared by grafting acetylsalicylic acid (AsA) into starch by an esterification reaction then coated with poly(vinylalcohol). The structure of Starch-graft-AsA was confirmed by FTIR, NMR, and DSC. The release of AsA occurred via a retroesterification reaction of this modified coated starch (SAC) during 76 h at different pHs and AsA contents. The diffusion coefficient of AsA in the SAC matrix followed a Fickian model. The effect of AsA amount grafted on starch revealed that the higher AsA amount released was reached with SAC containing 16.18 mol% of AsA at pH 7.

Keywords: Acetylsalicylic acid, characterization, release, retroesterification, starch-graft-acetylsalicylic acid, synthesis

1. Introduction

A starch called amylum is a natural polymer containing a large number of glucose units linked by glycosidic bonds. This polysaccharide contains two types of molecules, 20–25 wt% of helical amylose and 75–80 wt% of branched amylopectin, depending on the plant origin. The possibility of starch to form a film is principally due to the bridges that exist between the nonramified long chains of amylose. Unfortunately, the high fragility due to the amylopectin prevents its commercial application as simple starch films. Starch is soluble in heated water, as the granules swell and burst, the semi-crystalline structure is lost and the smaller amylose molecules start leaching out of the granules forming a network that holds water and increase the viscosity of mixture. Due to its fragility when used as a film alone and its rapid degradation into sugar constituents in presence of amylases during its intestinal transit, not much investigation was reported on the starch use as a support in the drug delivery domain. Among their advantages, controlled drug delivery systems allow the achievement of optimum concentrations, prolong times, reduce the side effects, and enhance the drugs activity. The natural polymers are preferred to the synthetic polymers, generally because they are nontoxic, low cost, biodegradable, and freely available, compared with the synthetic polymers [1,2]. Recently, a vegetable organogel polymer was encapsulated in alginate microparticles (MPs) by Sagiri et al. [3], in which the authors used mustard oil as control and metronidazole as drug model. It was found that although the MPs were hemocompatible in nature and have shown good mucoadhesive and swelling properties, the encapsulation of the vegetable organogel altered the release pattern of the drug. According to Bibby et al. [2] there are many forms of polymeric delivery systems, such as microspheres, nanospheres, and polymeric films, which have been developed in an attempt to achieve a modified drug release and to improve efficacy, sustain effect, or minimize toxicity.

Doraswamy et al. [4] have used different synthetic polymers as the differently sulfonated crosslinked poly(2-methylacryloxyacetophenone) as carriers for drug delivery. The fexofenadine hydrochloride used as drug loaded in the resin increased with increasing the degree of sulfonic groups and hence the drug binding sites in resin employed. It was also observed that the drug release was lower from the resins containing high degree of sulfonic groups.

Recently, Hosseinzadeh et al. [5] used ionic liquid functionalized polymers as poly(1-(4-vinylbenzyl)-3-methyl imidazoliumhexafluorophosphate) and poly(1-(4-vinylbenzyl)-4(dimethylimidazol)-pyridiniumhexafluorophosphate) in which naproxen (anti-inflammatory drug) was used as anionic drug. It was found that the amount of drug loading increased with increasing positive charge densities resulting from the increasing number of ionic liquid groups.

Acetylsalicylic acid, called aspirin, is widely used as nonsteroidal anti-inflammatory drugs (NSAID). It prolongs bleeding time and inhibits platelet aggregation. Aspirin has a direct irritant effect on the gastric mucosa due to the inhibition of prostaglandins and prostacyclins, thus it causes ulceration, epigastric distress, and/or hemorrhage [6].

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Sustained release of aspirin formulation would reduce the undesired side effects, reduce the frequency of administration and improve patient compliance [7]. Several investigations have been developed to obtain a system of drugs delivery in which encapsulation or microencapsulation techniques have been used extensively [8–14], where solvent evaporation was used with different polymeric matrix and different experimental conditions. Several polymers are used as pH sensitive for drug delivery. These polymeric materials have the characteristic of protecting the drug from the action of enzymes and gastric fluids, which are in fact very acidic [15–19]. Yang et al. [20] used a novel guar gum-graft-poly (acrylic acid)/attapulgite (GG-graft-PAA/APT) composite hydrogel as polymer support and dichlorofenac sodium (DS) as drug model. It was found that the burst release effect of DS drug was eliminated due to the incorporation of APT, and the DS cumulative decreased with increasing the APT content. Jenquin et al. [21] studied the factors influencing the release of salicylic acid from poly(methacrylate amonester) copolymer films using the differential scanning calorimetry analysis. This technique was performed on the polymeric films to study the solubility of the drug in the polymer. The results obtained were an increase in both of drug dry rate released with increasing temperature and adsorption of salicylic acid by the polymer. This finding was believed to influence the drug release profiles observed for different drug loadings, ionic strengths and the drug–polymer because of the interactions that occurred.

Gavhane et al. [22], have investigated the effect of pH of microenvironment within the polymer matrix on drug release and studied the interference of polymer and drug solubility. It was found that as the pH of microenvironment increased, the rate of the drug release increased in a linear relationship. Zhuang et al. [23] used poly(N-isopropylacrylamide-co-N-vinylpyrrolidone) and poly(N-isopropylacrylamide)/poly (N-vinylpyrrolidone) interpenetrating polymer network (INP) synthesized by radiation polymerization. AcSa was used as a model drug in this investigation. It was observed from the results obtained that these materials had a higher drug release in a physiological environment and showed that these hydrogels were promising materials for causing solubilization and developing a long-term controlled release system.

In our recent work [24] on the release of AcSa from AcSa/poly(vinylalcohol-co-ethylene) blend, it was revealed that the increase in the thickness of AcSa/PEVA film decreased the AcSa amount released and this material was able to release the greatest amount of aspirin directly in the intestines (neutral pH) and not in the stomach. Although all these previous studies and others were reported on the influence of several parameters on the release dynamic of drugs, none was reported on the effect of the film thickness.

In this present work, three starch-graft-Acetylsaliclyc acid materials containing different acetylsaliclyc (AsA) contents were synthesized by grafting of AsA on starch using an esterification reaction then coated by a crosslinked polyvinylalcohol (PVA). Different techniques such as FTIR, NMR, DSC, and SEM were used to characterize the structure, composition, and surface morphologies of these materials. The release dynamic of AsA from starch-graft-AsA films through a retroesterification reaction was also investigated at body temperature and different pHs during 76 h.

2. Experimental

2.1 Materials

Potato native starch containing 20 wt% of helical amylose, 80 wt% of branched amylpectin, and 16 wt% of moisture content was purchased from Aldrich. PVA (BDH Society) has an average molecular weight number of 115,000 g/mol. Acetylsaliclyc acid (98 wt% purity) was purchased from Fluka AG Society. Oxalic acid (Aldrich, purity 99%) was used as crosslinking agent. All chemicals were used without purification.

2.2 Preparation of Modified Uncoated Starch (SAUC)

Starch solution was prepared at a concentration of 10 wt% by dissolving dried starch in 10 ml of dimethylformamide (DMF) at 80°C under continuous stirring for 6 h. AsA solution was also prepared in a concentration of 10 wt% in DMF at room temperature. Both solutions were mixed together and stirred for a few minutes to obtain a homogeneous solution. The reaction of starch with AsA was carried out at 60°C in a flask equipped with a magnetic stirrer in the presence of a few drops (3–5 drops) of concentrated HCl according to the scheme A of Figure 1. Water produced during the esterification reaction was removed by evaporation under reduced pressure. In this case the equilibrated reaction would be forced to produce only the ester. A white precipitate of grafted polymer was obtained from this reaction; it was then washed vigorously with water to remove the free residual AsA (non-reacted). The product was dried at room temperature for 48 h. Three starch-graft-AsA materials, SAUC11, SAUC16, and SAUC21, containing different AsA contents, were prepared by the same method and their preparation conditions are given in Table 1.

2.3 Preparation of Modified Starch Coated (SAC)

SAC preparation was carried out according to scheme B of Figure 1. Small pellets of modified starch (SAUC) with dimensions between 10 and 100 μm were dipped for 15 min in an aqueous solution containing 2.0 g of PVA and 0.05 g of oxalic acid in 100 mL of water acidified with about 3–5 drops of concentrated solution of hydrochloric acid. They were then casted on Teflon plate and allowed to dry at room temperature for 24 h, and then heated at 60°C for 24 h under vacuum. A white, thin and flexible film insoluble in water and DMF was easily removed from the Teflon plate.

2.4 Equipment

The FTIR spectra of pure starch, AsA and modified starch uncoated (SAUC) were recorded using a Perkin Elmer 1000 spectrophotometer at room temperature. In all cases, at least 32 scans with an accuracy of 2 cm⁻¹ were signal-averaged. The film samples used in this analysis were
sufficiently thin to obey the Beer Lambert law. $^{1}$H NMR and $^{13}$C NMR spectra of pure starch, AsA, and starch-graft-AsA were recorded at room temperature on a JEOL FX 90 Q NMR apparatus at 500 MHz and 200 MHz in DMSO-d$_6$, respectively. The AsA amounts released were determined using a UV-visible Aultropec 2100 Pro (Amersham Biosciences) spectrophotometer at 274 nm in water using AsA calibration curve. The melting point of AsA ($T_m$) and the glass transition temperatures ($T_g$) of starch and modified starch before and after coating were measured using a DSC DSC60A instrument (Shimadzu), previously calibrated with indium. Samples weighing between 10 and 12 mg were packed in aluminum pans before placing in DSC cell. The samples were heated from $-60$ to $200^\circ$C at a heating rate of $20^\circ$C min$^{-1}$. For morphology analysis, scanning electron micrographs (SEM) of dried thin films of pure starch, AsA, and SAC with gold grid were recorded using a Hitachi S4700 instrument (Japan).

3. Results and Discussion

3.1 Characterization

3.1.1 Solubility Test

The solubility tests of pure starch, AsA, and modified starch revealed that the starch swelled in water then break down to form small pieces, while the pure AsA was completely soluble. However, the films produced from their esterification reaction had the same behaviour as that of the pure starch, whereas the films of SAC were insoluble in water but swelled and remained as one piece. Such behavior confirmed the character of the crosslinked poly(vinylalcohol) used as polymer coat in this investigation.

3.1.2 FT-IR Spectrometry

The FTIR spectra of Figure 2 confirmed the starch-graft-AsA structure through the attenuation of the transmittance band at 1690.14 cm$^{-1}$ assigned to C=O of the carboxylic acid group of the pure AsA. According to the literature

<table>
<thead>
<tr>
<th>Sample code</th>
<th>Dry starch (g)</th>
<th>AsA (g)</th>
<th>DMF (mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAUC21</td>
<td>1.0</td>
<td>1.00</td>
<td>10.0</td>
</tr>
<tr>
<td>SAUC16</td>
<td>1.0</td>
<td>0.50</td>
<td>10.0</td>
</tr>
<tr>
<td>SAUC11</td>
<td>1.0</td>
<td>0.25</td>
<td>10.0</td>
</tr>
</tbody>
</table>

![Fig. 1. Scheme of (A) SAUC preparation and (B) SAC preparation.](image1)

![Fig. 2. FTIR spectra of starch, AsA, and SAUC16.](image2)
[25], the signal at 1757.18 cm\(^{-1}\) was assigned to the carbonyl of AsA ester group. The peak observed at 1616–1622 cm\(^{-1}\) on the SAUC16 spectrum is absent in that of the pure AsA and is attributed to the carbonyl of the carboxylic ester group grafted on the starch.

3.1.3 NMR Spectrometry

\(^1\)H NMR spectra of pure starch, AsA and SAUC21 are shown in Figure 3. The comparison of these spectra revealed on the SAUC21 spectrum the total disappearance of the signals centered at 13.20 ppm assigned to the proton of the carboxylic acid group of pure AsA, thus confirming the grafting of AsA to starch previously revealed by FTIR analysis. \(^{13}\)C NMR spectra of pure AsA, starch, and SAUC21 are shown in Figure 4. From the spectrum of SAUC21, an attenuation of the intensity of the signal at 172.60 ppm was observed assigned to the carbonyl group of the carboxylic acid of AsA and an appearance of a new signal localized at 162.65 ppm attributed to the ester carbonyl grafted to starch; these results thus confirmed the structure of starch-graft-AsA. The AsA content in this material was determined using the following equation:

\[
\text{AsA (mol\%)} = \frac{\delta(-O-C=O) - \delta(f)}{\delta(f)} \times 100
\]

where \(\delta(-O-C=O)\) and \(\delta(f)\) are the carbon areas of the AsA carbonyl directly linked to the starch observed at 162.65 ppm and the methylene group (-CH\(_2\)-) at 60.62 ppm attributed to acetylsaliclyl and hydroxyethynyl groups in the starch-graft-AsA, respectively.

Fig. 3. \(^1\)H NMR spectra of starch, AsA, and SAUC21 obtained in DMSO-\(d_6\) at 500 MHz.

Fig. 4. \(^{13}\)C NMR spectra of starch, AsA, and SAUC21 obtained in DMSO-\(d_6\) at 200 MHz.

3.1.4 DSC Analysis

Figure 5 shows the DSC thermograms of starch, AsA, and SAC with different AsA contents. These curve profiles showed that an important shift in \(T_m\) value of starch toward the left from 109.0 to 92.0°C was observed as the AsA content decreased in the copolymer. This finding seemed to be essentially due to an ordered/disordered structure in the starch chains caused by a decrease of the hydrogen bond intensity due to the substitution of important hydrophilic (hydroxyl) groups by hydrophobic (carboxylate) groups favoring the chains sliding and led by this way to a decrease in the \(T_m\) value of the starch. It was also noted from the thermograms of modified starch a total disappearance of the melting point at 140°C observed on the thermogram of pure AsA indicating the absence of residual AsA in the SAC matrix. Concerning the glass transition temperature \((T_g)\), according to the literature [26–28], the \(T_g\) value depends on the amylose and moisture contents of the starch.

Table 2. Determination of AsA contents in starch-graft-AsA copolymers (SAUC) by \(^{13}\)C NMR

<table>
<thead>
<tr>
<th>Copolymer</th>
<th>ASA grafted (mol-%)</th>
<th>Starch (mol-%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAUC21</td>
<td>21.05</td>
<td>78.95</td>
</tr>
<tr>
<td>SAUC16</td>
<td>16.18</td>
<td>83.82</td>
</tr>
<tr>
<td>SAUC11</td>
<td>11.24</td>
<td>88.76</td>
</tr>
</tbody>
</table>
For example, it was observed from these studies that the $T_g$ value of starch was shifted from 47 to 27°C when the water content incorporated in the starch varied from 15.9 to 18.7 wt% [26]. On the other hand, this value was shifted from 67.1 to 63.9°C as the amylose content in the starch varied from 27.4 to 29.9 wt% [27]. Therefore, in this present study, the breaking point observed on the thermogram of starch at 33°C was probably attributed to the $T_g$ of starch, which decreased when the AsA amount grafted on the starch increased.

### 3.1.5 Surface Morphology of Modified Starch

The SEM micrography was considered as the most intuitive method to characterize the morphologies of surface features of SAC before and after the release process. Figure 6A shows the micrograph of pure AsA in which the particles have a typical crystalline pale in stick of wood form of different sizes gathered in aggregates of different sizes. Similar observation was reported by different authors [29,30]. The picture of Figure 6B referred to the typical granules of starch which showed large and small oval particles with similar shapes and diameters varied between 20 and 70 μm, which have been extensively described in the literature [31–33]. The surface of starch film as presented in this figure demonstrated no cracks, scratches or cavities. The micrograph of Figure 6C showed the particles of starch grafted with AsA gathered in aggregates form of different sizes comparable to those of the pure starch showed in Figure 5B, whereas, the SEM image of Figure 6D presented the same coated sample in which the same AsA aggregates were well wrapped up in crosslinked PVA. According to these SEM images obtained for SAC21 films before (Figure 6D) and after (Figure 7) the release process, it was possible to see the differences in their morphology. For example, the micrograph of SAC21 containing 21.05 mol% of AsA before the release process (Figure 6D) showed clearly the free AcSa encapsulated on the surface and grouped in aggregates of different forms. Their dimensions varied between 1 and 100 μm. After 76h of the release process at pH 1, the same sample showed through the micrograph of Figure 7 a total disappearance of the microcapsules leaving erosion characterized by the typical cavities and pores occupied initially by the free AsA.

![Fig. 5. DSC thermograms of starch, AsA, and SAC with different AsA contents.](image)

![Fig. 6. SEM photomicrographs of (A) AsA, starch; (B) AsA; (C) SAUC21; and (D) SAC21 before the release process.](image)
aggregates encapsulated during the coating operation and by the AsA grafted. On the other hand, the micrograph of the same sample, in which AsA was released at pH 7, presented a surface morphology consisting of residual AsA nanoparticles coated of a diameter size varied between 100 and 200 nm deposited uniformly on the surface, while some of them were gathered in aggregates dispersed randomly on the surface. This material has a capacity to release AsA again as long as possible.

3.2 In Vitro Acetylsalicylic Acid Released Study

The acetylsalicylic acid released from SAC films occurred at 37°C (body temperature) according to the retroesterification reaction shown in Scheme 1A. Figure 8 depicts the release profiles of AsA released at different pH from SAC11 (Figure 8A), SAC16 (Figure 8B), and SAC21 (Figure 8C) during 76 h. According to these data it was observed that the best performance was obtained with SAC16 in which a maximum of 58 wt% of AsA released was reached at pH 7 during 76 h. On the other hand, as shown in Figure 8A, the minimum amount of AsA was obtained with SAC21 (22.0 wt%) also at pH 7 during the same period. In the last case, the decrease of AsA amount released could be attributed to the reduction of the hydrophilicity of SAC21 in water, because this hydrogel initially contained relatively high ester groups grafted (21.05 mol%). At this AsA content, the SAC21 hydrogel began to shrink; starch-graft-AcSa film was in a contracted state and swelled slowly. The same phenomenon was also observed in our previous investigation [24,34] using poly(vinylalcohol-co-ethylene) as a polymer support. At pH 1, the profile of SAC16 containing 11.24 mol% of AsA (Figure 8B) showed an irregularity beyond 48 h of the release process characterized by a positive abrupt deviation from the linearity due to a probable dislocation of starch-graft-AsA film occurred in this pH media. Therefore, a huge amount of AsA could be released in these conditions.

3.2.1 Diffusion Behaviour of AsA Through SAC Films

According to Lin et al. [35], for a release less than 60 wt% of initial load, the release dynamics follows the Fickian model for the diffusion from a polymeric film. The value of the diffusion coefficient, \( D \), can be calculated according to the following Eq. 2 [36–38].

\[
D = \frac{0.196 \times l^2}{t} \left[ \frac{M_t}{M_o} \right]^2
\]
where $M_t/M_0$ and $l$ are the fraction of drug released during (t; hours) and the thickness of the film (the value taken in this work as an average thickness was 273 μm), respectively. $D$ value was determined when the permanent regime was reached and the AsA particles deposed on the material surface were totally washed. In these conditions the curve profiles of $D$ versus time were meaningful and reflected exactly the dynamics of AsA/media solution inside the material. For example Figure 9 shows the variation of $D$ of SAC versus the inverse of time calculated from the data of Figure 7C using Eq. 2. According to these experimental curve profiles, for all samples and at any pH, two distinct zones were observed in which the diffusion coefficient linearly increased with $1/t$. This observation perfectly confirmed the Fickian model for the diffusion of AsA from the SAC films and also proved that the release dynamics of AsA from these films was only due to the diffusion of AsA through the modified starch matrix. In this condition the permanent regime of the release process was reached. The presence of discontinuity in the straight lines revealed the presence of two types of AsA released. The first one is characterized by a greater AsA amount released during the first hour; it could be probably attributed to the release of the free AsA trapped in PVA coating films occurring during the coating operation. The second part released beyond this period was attributed to the AsA released directly from the SAC through a retroesterification reaction. According to these results, it was possible to build our investigation on the second zone of the release process in which the permanent regime was reached and the dynamics of the release was governed only by the diffusion phenomenon of AsA released only through the retroesterification reaction.

3.2.2 Effect of the Initial AsA Amount Grafted on Starch

The variation of AsA released versus the initial amount of AsA grafted on starch was followed at different pHs during 24h of the release process. For example, as showed in the curve profiles of Figure 10 at pH 3 and 7, the AsA released reached a slight maximum at 16.18 mol% of AsA grafted on starch, while at pH 1 and 5 the AsA released decreased as the initial AsA content increased in the SAC. The smallest amount of AsA released obtained with SAC containing 21.05 mol% of AsA could be explained by the hydrophilic-hydrophobic balance of material. Indeed, the solubility of starch modified decreased when the ester groups grafted on starch increased and consequently the swelling degree of SAC decreased and led to the decrease of AsA released.

3.2.3 Effect of pH Media on the Release Dynamic of AsA

The influence of pH on the release dynamic of AsA from SAC with different AsA contents occurred during 24h of the release process and the results obtained are illustrated in Figure 11. Practically the same behavior was observed from the curve profiles of the SAC containing 11.24 and 21.05 mol% of AsA in which the release dynamic of AsA reached a maximum at pH 5. In case of SAC21 a minimum was also observed at pH 3. The curve of AsA released from the SAC16 material versus the pH of media showed a different profile in which the AsA amount released increased when pH of media was inferior to 3, beyond this pH value a pseudostability was observed at about 41.6 wt% of AsA released. The same observation was also showed.

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Fig. 9. Variation of the diffusion coefficient ($D$) of AsA through the SAC21 films versus $1/t$ (h) at different pHs media.

Fig. 10. Influence of AsA content on the release dynamic of AsA from SAC films at different pHs media during 24h of the release process.
at 48 h of the release process. The lowest AsA amount released observed with SAC 11 and SAC 16 at pH 1 could be explained by the fact that the retroesterification reaction which generated the free AsA was disfavored at low pH, while the esterification reaction corresponding to the starch-graft-AsA formation would be favored; therefore, the dynamics of AsA released would be dramatically reduced. However, the variation of AsA released from SAC21 containing the higher AsA amount (21.05 mol%) presented a complex behavior. This complexity could be explained by a competition, which occurred between the swelling degree of SAC which decreased when the ester (hydrophobic) groups grafted on starch increased involving a reduction of AsA released and the solubility of AsA particles released inside the starch which increased when pH of media decreased involving an increase in the AsA released.

3.2.4 Kinetic Study of AsA Released from SAC Films

The instantaneous release rates of AsA from SAC films of different AsA contents were calculated from the slopes of the linear portions of the curves showing the variation of AsA released versus time of Figure 8; the results obtained are gathered in Table 3. From these data, the presence of two important stable zones of the release rate was observed in all samples. The first one was short (0–2 h) and characterized by a high release dynamics in which SAC16 showed a higher AsA amount released (37.60 ± 0.20 wt%) at pH 3. The second zone was relatively larger (36–72 h) and characterized, in general, by a relatively low release rate in which SAC16 showed also a higher performance, because this material was able to release uniformly a higher AsA amount (19.04 ± 1.36 wt%) at pH 7 with a constant rate of 0.28 ± 0.02 wt%/h during 68 h. At pH 1, this same material was capable to release uniformly 6.12 ± 0.72 wt% of AsA during 68 h with a rate of 0.17 ± 0.02 wt%/h. On the other hand, the material containing initially a higher AsA amount (21.05 mol%/SAC21) showed a lower performance because this material was capable to release a smaller AsA amount, notably at pH 7 (4.32 ± 1.44 wt%). Such results were also observed using acetylsalicylic acid as a drug grafted on poly(vinylacohol-co ethylene) [34].

4. Conclusions

Very interesting results were obtained from this investigation. A relatively high amount of acetylsalicylic acid could be grafted easily on starch by esterification reaction. The conversion rate in the starch grafted could be controlled by removing water produced during the reaction under reduced pressure. This method compared with those of encapsulation permitted to obtain a material characterized by a perfect distribution of acetylsalicylic acid into the starch. The starch-graft-AsA particles could be easily coated by impregnation with PVA then crosslinked through an esterification reaction using oxalic acid. The acetylsalicylic acid released from SAC in an aqueous media occurred by retroesterification reaction, notably at a neutral pH. The results obtained from the release of AsA at different pHs revealed that the maximum amount of AsA released (more than 58 wt%) was reached at pH 7 during a period of 68 h with SAC containing initially 16.18 mol% of AsA. The study...
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of the release rate indicated that the stability of the AsA release rate during the time depended on the initial amount of AsA incorporated in starch and the pH of media. The effect of the initial AsA amount grafted on starch revealed that the higher AsA amount released was reached with SAC16 when the pH of media was 7. These results were found to be satisfactory and could be applied in a wide range of drugs containing carboxylic groups. The results obtained seemed to be very important in the drug release domain, because the prepared material was able to release a greatest amount of aspirin directly into the intestines (at neutral pH) and only a small amount into the stomach during a long period.

Funding

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