Starch–Acrylics Graft Copolymers and Blends: Synthesis, Characterization, and Applications as Matrix for Drug Delivery

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ABSTRACT: A series of acrylic monomers–starch graft copolymers were prepared by ceric ion initiation method by varying the amount of monomers. These graft copolymers were characterized by IR and ^{13}C-NMR spectroscopy. It was seen that as the concentration of monomer [acrylic acid (AA), methacrylic acid (MA), and methyl methacrylate (MMA)] increased the percent add-on increased in all the graft copolymers, whereas grafting efficiency increased initially but showed a slight decrease with further increase in the monomer concentration (except for MMA). The release rate of paracetamol as a model drug from graft copolymers as well as their blends was studied at two different pH, 1.2 and 7.4, spectrophotometrically. The release of paracetamol in phosphate buffer solution at pH 1.2 was insignificant in the first 3 h for St-*g*-PAA- and St-*g*-PMA-graft copolymers, which was attributed to the matrix compaction and stabilization through hydrogen bonding at lower pH. At pH 7.4, the release rate was seen to decrease with increase in add-on. The tablet containing poly(methyl methacrylate) (PMMA) did not disintegrate at the end of 30–32 h, which may be attributed to the hydrophobic nature of PMMA. These results indicate that the graft copolymers may be useful to overcome the harsh environment of the stomach and can be used as excipients in colon-targeting matrices. © 2009 Wiley Periodicals, Inc. J Appl Polym Sci 114: 2893–2900, 2009

Key words: starch; acrylic monomers; graft copolymer; redox initiator; drug delivery systems

INTRODUCTION

Colon-targeted drug delivery has gained increased importance in the field of drug delivery for the treatment of the local diseases associated with colon, such as ulcerative colitis, chron's disease, and bowel cancer, and also for the delivery of proteins and peptides.[1] To achieve a successful colonic delivery, a drug needs to be protected from the harsh environment of upper GI tract. This can be achieved by covalent linkage of a drug with a carrier, coating with pH sensitive polymers, and formulation of release system. For an effective colon drug delivery, a minimum of drug should be released in the environment of the stomach and small intestine, where the pH varies from 1 to 6.5. The transit time in the stomach is 2 h (which may vary) and small intestine it is 3 h. Colonic residence time is about 80% of total GI transit time and average of 20–30 h.[2] Thus, to be effective as colon drug delivery systems, the dosage forms have to pass through the stomach having an acidic pH and lower transit time and therefore should be stable at that pH.

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Natural polysaccharides have been used as tools to deliver the drug specifically to the colon. These polysaccharides remain intact in the physiological environment of stomach and intestine, but once the dosage forms enter into colon it is acted upon by the polysaccharidases, which degrade the polysaccharides and release the drug into the vicinity of bioenvironment of colon. However, polysaccharides show enormous swelling owing to their hydrophilic nature, which results in premature release of drug in the stomach/upper intestine, and therefore, they should be protected while gaining entry into stomach and small intestine. This can be achieved by the modification of polysaccharides. Polysaccharides, such as starch, cellulose, chitosan, and guar-gum, have been modified and used as a colon-targeting materials.[3–7] These modifications include crosslinking, addition of protective coating, or grafting using acrylic monomers. Other limitation to the use of polysaccharides is their lack of bioadhesion. Commercial poly(acrylic acid) (PAA)-based polymers, carbopol, have been known to possess good adhesion. Crosslinked PAA-based polymers have been reported to show better bioadhesion than polysaccharides and similar to that of carbopol. However, these PAA polymers alone cannot be used because they tend to be irritant. Therefore, research efforts

have been directed to combine the useful properties of PAA polymers, such as bioadhesion and stability in acidic environment with those of polysaccharides (starch), such as swelling characteristics and biodegradability. There are two approaches to achieve this: a direct and versatile approach is to prepare physical mixtures. Blends of PAA with polysaccharides, modified polysaccharides, such as starches, hydroxypropyl cellulose, carboxy methyl cellulose, and hydroxyl propyl methyl cellulose, have been reported as potential drug delivery systems.[8–12] Another approach is to synthesize polysaccharide–acrylic acid (AA) graft copolymers. Geresh et al.[13] have prepared starch–AA graft copolymers by irradiation technique for buccal application. There are few reports on the grafting of AA onto starch using chemical initiation,[14] but their use as a delivery system has not been investigated. In this investigation, we have grafted AA, methacrylic acid (MA), and methyl methacrylate (MMA) onto starch with varying the amount of monomers using ceric ammonium nitrate (CAN) as an initiator in aqueous medium. The use of CAN reduces the extent of homopolymerization.[14,15] These graft copolymers and blends of graft copolymers with their component homopolymers were used as matrix for the study of release rate of paracetamol as a model drug, at two different pH, 1.2 and 7.4.

EXPERIMENTAL

Materials

Potato starch (s.d. Fine chemicals, India) was used. Acrylic acid (Thomas Baker, India), methacrylic acid, and methyl methacrylate (Loba Chemie, India) were freshly distilled under reduced pressure before use. Ceric ammonium nitrate (Qualigens, Germany) was dried at 110°C for 1 h. Paracetamol (Gift sample from Vamsi Labs, India) and other chemicals were used as such.

Preparation of graft copolymers

Potato starch (2 g) was dispersed in 75 mL of double distilled water with constant stirring for 1 h at 70°C under nitrogen atmosphere. It was allowed to cool to room temperature and CAN was added over a period of 15 min, followed by addition of required amount of monomer (AA, MA, and MMA). The final volume of the reaction mixture was 100 mL. The concentration of CAN in the reaction mixture was kept at 0.005*M*. The polymerization reaction proceeded under N_2 atmosphere for 3 h at 37°C. After completion of the reaction, the product was washed two to three times with distilled water to remove homopolymers, if any, and filtered through sintered crucible. The starch-grafted poly(acrylic acid) (St-*g*-PAA) or starch-grafted poly(methacrylic acid) (St-*g*-PMA) was further Soxhlet extracted with ethanol to remove any homopolymer present, whereas the starch-grafted poly(methyl methacrylate) (St-*g*-PMMA) product was Soxhlet extracted with acetone to remove the homopolymer, if any. The final product was dried under vacuum until constant weight.

The percentage grafting efficiency (% GE) and percentage add-on (% add-on) were calculated as follows[14]:

$$\% \text{ GE} = \frac{W_2 - W_1}{W_3} \times 100$$

$$\% \text{ add-on} = \frac{W_2 - W_1}{W_2} \times 100$$

where W_1, W_2, and W_3 are the weights of pure starch, graft copolymer, and monomer charged, respectively.

Preparation of PAA, PMA, and PMMA

Polymerization of AA, MA, and MMA was carried out in nonaqueous and aqueous medium as described earlier in details.[16,17]

Preparation of blends

Blends of St-*g*-PMMA-10 and PAA (Blend 1); St-*g*-PMMA-10 and PMA (Blend 2) in the weight ratio 1 : 0.43; starch, PAA, and PMMA (Blend 3) and starch, PMA, and PMMA (Blend 4) in the weight ratio of 1 : 0.5 : 0.5 were prepared by mixing solid components physically until homogenous mixture was obtained.

Infrared spectral analysis

IR spectra of pure starch, graft copolymers were taken on Perkin Elmer FTIR spectrum BS spectrophotometer using KBr pellet technique.

^{13}C-NMR spectral analysis

^{13}C CP/MAS spectra were obtained on Bruker DRX-500 MHz NMR spectrometer with a 11.4 T magnet and the operating proton and carbon frequencies of 500 and 125 MHz, respectively. The samples were packed into a 4-mm Zirconia rotor and spun at a speed of 8–10 KHz.

Tablet preparation

Two hundred milligrams of graft copolymer and paracetamol (200 mg) were mixed until homogenous mixture was obtained and directly compressed in

TABLE I
Starch–Acrylic Graft copolymers[a]

Sr. no	Polymer	Monomer		% add-on[b]	% Grafting efficiency[b]	MW of grafted chain[c]	Grafting frequency
		Monomer	mmol $\times 10^{-1}$				
1	St-*g*-PAA-4	AA	5.8	31.03	21.40	–	–
2	St-*g*-PAA-6	AA	8.7	41.17	21.11	–	–
3	St-*g*-PAA-8	AA	11.6	43.82	18.55	–	–
4	St-*g*-PAA-10	AA	14.5	49.49	18.64	–	–
5	St-*g*-PMA-4	MA	4.7	30.84	21.97	–	–
6	St-*g*-PMA-6	MA	7.0	40.89	22.72	–	–
7	St-*g*-PMA-8	MA	9.4	46.75	21.62	–	–
8	St-*g*-PMA-10	MA	11.7	50.26	19.92	–	–
9	St-*g*-PMMA-4	MMA	3.7	43.19	40.62	3,44,826	2799
10	St-*g*-PMMA-6	MMA	5.6	57.19	57.78	3,64,754	1685
11	St-*g*-PMMA-8	MMA	7.4	72.09	65.42	4,24,785	1016
12	St-*g*-PMMA-10	MMA	9.3	77.42	73.29	4,56,142	821

AA, acrylic acid; MA, methacrylic acid; MMA, methyl methacrylate.
[a] Starch: 2 g, initiator: ceric ammonium nitrate (0.005*M* in 1*M* HNO_3), 10 mL; medium: water, total volume: 100 mL, temperature: 37°C, time: 3 h.
[b] By weight increase.
[c] Viscometrically.

hydraulic press using a 12-mm flat faced punch of a force of 90 kg/cm^2 to obtain tablets. Identical conditions were applied for making the tablets of pure starch, PAA, and PMA, Blend 1, Blend 2, Blend 3, and Blend 4 with the drug.

Swelling studies

The equilibrium swelling was measured according to the conventional "tea bag" method. The completely dried preweighed graft copolymer was placed in 200 mL of various buffer solutions at 37°C, respectively. The tea bag was taken out at regular time intervals, wiped superficially with filter paper to remove surface water, weighed, and then placed in the same bath. The mass measurements were continued until the equilibrium was attained. The percentage mass swelling was determined using the following expression[18,19]:

$$\% \text{ SM} = \frac{M_t - M_o}{M_o} \times 100$$

where M_o and M_t are the initial mass and mass at different time intervals, respectively.

In vitro drug release studies

To study the release of the drug from the tablets, the tablets were placed in 50 mL of phosphate buffer solution of pH 7.4 (USP XXIII) at 37°C under unstirred condition as well as in simulated gastric fluid pH 1.2 (2 g NaCl + 7 mL conc. HCl, diluted to 1 L by distilled water, USP XXIII). After predetermined time interval, the aliquot was removed and its absorbance was measured on Shimadzu UV–vis spectrophotometer at $\lambda_{max} = 299$ nm.

Statistical analysis

All the data are the means of results from three experiments ± SD. Statistical data analysis was performed using the one-way variance with $P < 0.05$ as the minimum level of significance.

RESULTS AND DISCUSSION

The graft copolymerization was carried out in aqueous medium using 2 g of potato starch and varying the amount of monomers (Table I). With the increase in the amount of the monomers, the percentage add-on and grafting efficiency were found to increase in the case of St-*g*-PMMA. In the case of St-*g*-PAA and St-*g*-PMA, grafting efficiency was found to decrease slightly with increase in the amount of monomer in the polymerization reaction, which is probably because of homopolymer formation. Because both the polymers are soluble in the reaction medium, the viscosity of the medium increases thereby hindering the rate of the diffusion of monomers molecules to the starch microradicals resulting in the decrease in the grafting efficiency.[14] St-*g*-PMMA was acid hydrolyzed to remove starch backbone, and the molecular weight of the grafted PMMA chains was determined viscometrically. Grafting frequency and molecular weight of the grafted chains for St-*g*-PMMA are recorded in Table I. These could not be obtained for St-*g*-PAA and St-*g*-PMA, because of the difficulty in isolating PAA and PMA after the acid hydrolysis of starch.

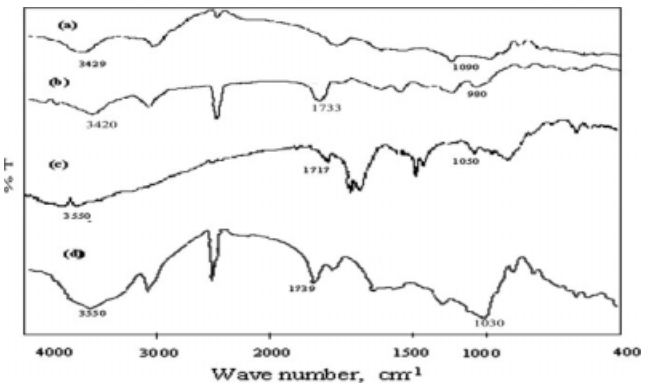

Figure 1 IR spectra of graft copolymers (a) ungrafted starch, (b) St-*g*-PMA, (c) St-*g*-PAA, and (d) St-*g*-PMMA.

IR spectra of starch, St-*g*-PAA, St-*g*-PMA, and St-*g*-PMMA are shown in Figure 1. The IR spectrum of starch showed absorption bands at 3429 (—OH stretching) and 1090 cm^{-1} (skeletal vibration of C—O—C). IR spectra of St-*g*-PAA, St-*g*-PMA, and St-*g*-PMMA show peaks at 3425 and 980–1050 cm^{-1}, which may be ascribed to the —OH stretching and skeletal (C—O—C) vibration of starch in addition to the bands at 1710–1739 cm^{-1} due to the carboxyl groups (>C=O stretching) of PAA, PMA, and PMMA, respectively, indicating that AA, MA, and MMA have been successfully grafted onto starch. This was further confirmed from the ^{13}C CP/MAS NMR spectra of St-*g*-PAA, St-*g*-PMA, and St-*g*-PMMA shown in Figure 2. The ^{13}C-NMR spectrum of St-*g*-PAA shows signals at δ = 175 ppm assigned to the carbonyl carbon (>C=O), δ = 35–42 ppm assigned to the α and β carbons of PAA, and δ = 101 ppm and at δ = 60–80 ppm assigned to C_1 and to C_2–C_6 of anhydroglucose repeat units of starch, respectively.[20] Similarly, the ^{13}C-NMR spectrum of St-*g*-PMA shows signals at δ = 176–179 ppm (carbonyl carbon of PMA), 17.4–20.3 ppm (—CH_2 and α-CH_3 of PMA), and at 100.3 (C_1 of starch) and 61–72 ppm (C_2–C_6 of starch). Similarly, the ^{13}C-NMR spectrum of St-*g*-PMMA shows signals at δ = 177 ppm (carbonyl carbon of PMMA), at 99 ppm (C_1 of starch), and 51–72 ppm (C_2–C_6 of starch). By comparing the intensity of signals at δ = 175–179 ppm (>C=O) with that of the signal at δ = 100–101 ppm (C_1 of starch) in St-*g*-PAA and St-*g*-PMA, it can be inferred that the amount of starch is higher than that of PAA and PMA in the respective graft copolymers.

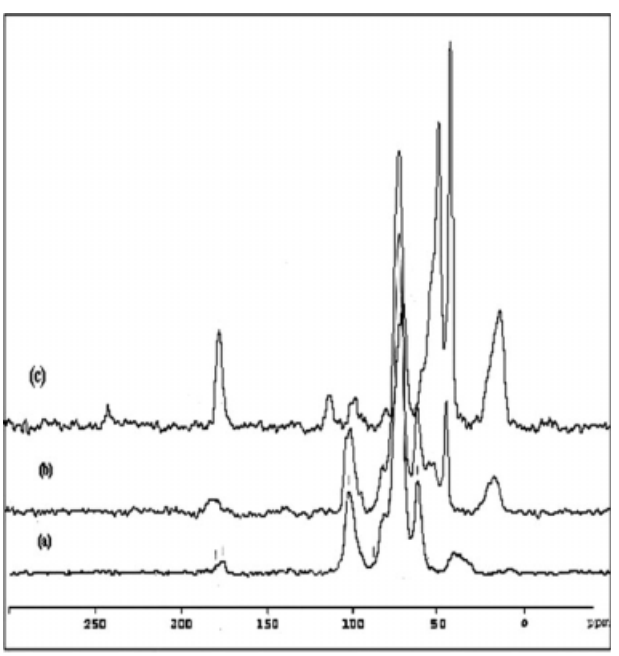

Figure 2 CP/MAS ^{13}C-NMR spectra of graft copolymers (a) St-*g*-PAA, (b) St-*g*-PMA, and (c) St-*g*-PMMA.

Swelling studies

One of the factors determining the drug release is the swelling of the matrix. Therefore, we studied the swelling behavior of the graft copolymers, St-*g*-PAA-4, St-*g*-PAA-10, St-*g*-PMA-4, St-*g*-PMA-10, St-*g*-PMMA-4, and St-*g*-PMMA-10 and the blends in medium of pH 1.2 and 7.4. Figure 3 shows the dynamic uptake of water by the graft copolymers at pH 1.2. The maximum swelling was about 10% in 3 h for St-*g*-PAA- and St-*g*-PMA-graft copolymer series, whereas it was about 29–125% in 6 h. The extent of swelling was found to be decrease with increasing % add-on. Thus, the swelling was seen to decrease from 59 to 29% in 6 h and 187–97% in 24 h, as the % add-on increased from 31.03 (St-*g*-PAA-4) to 49.49% (St-*g*-PAA-10). The swelling was found to be 125% in 6 h and 203% in 24 h for St-*g*-PMA-4 with 30.84% add-on, which decreased to 91% in 6 h and 158% in 24 h for St-*g*-PMA-10 with 51.26% add-on. Similarly, in case of St-*g*-PMMA-4 (43.19% add-on) and St-*g*-PMMA-10 (79.29% add-on), the swelling was decreased from 138 to 116% in 6 h and 415 to 384% in 24 h. Thus, from the results, it is seen that as the % add-on increases the swelling decreases. Figure 4

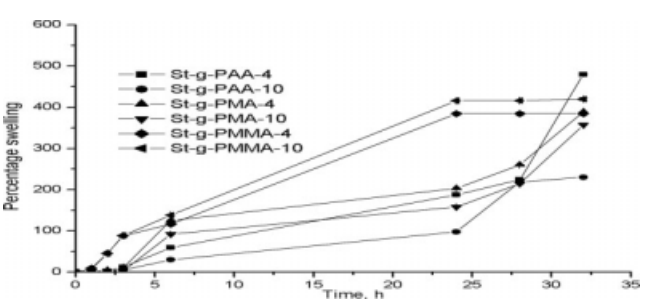

Figure 3 Dynamic uptake of water as a function of time for graft copolymers at pH 1.2. Values are mean ± SD of at least three experiments.

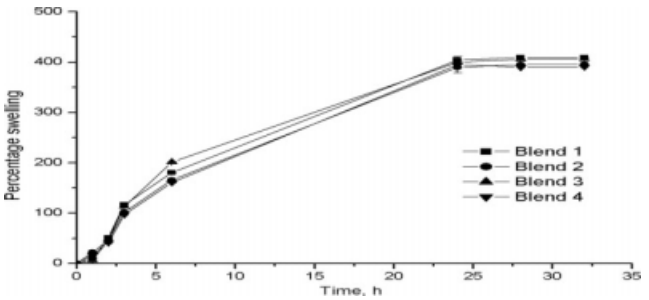

Figure 4 Dynamic uptake of water as a function of time for blends at pH 1.2. Values are mean ± SD of at least three experiments.

depicts the dynamic uptake of water by blends at pH 1.2. The swelling was found to be in the range of 160–200% in 6 h and from 380 to 400% in 24 h.

The dynamic uptake of water by the graft copolymers at pH 7.4 is shown in Figure 5. The swelling was found to range from 16 to 100% in 3 h for St-*g*-PAA series with the maximum swelling reaching about 650% in 24 h; from 120 to 200% in 3 h for St-*g*-PMA series with maximum swelling of about 400% in 24 h, and from 105 to 180% in 3 h in St-*g*-PMMA series with the maximum swelling of about 475% in 24 h. Figure 6 shows the dynamic uptake of water at pH 7.4, where the extent of swelling was seen to be 54, 48, 124, and 136% in 3 h, respectively, for Blend 1, Blend 2, Blend 3, and Blend 4. Similarly, in 6 h the swelling was 178, 295, 207, and 301% and the equilibrium swelling was 450, 352, 431, and 444% in 24 h.

In general, the results show that the swelling of the graft copolymers is lower in media of pH 1.2 and is higher in the media of pH 7.4. The swelling depends on the intermolecular interaction between the component polymers of the graft copolymers. At lower pH (pH = 1.2), the carboxyl group of the grafted acrylic chains is almost in nonionized state and is involved in extensive hydrogen bond formation with hydroxyl groups of starch. This strong intermolecular interaction renders the polymer segments rigid, thereby hindering the water uptake and lowering the extent of swelling. On the other hand, in the swelling medium of pH 7.4, the —COOH groups get ionized and polymer behave like a polyelectrolyte with an array of —COO^- group along the acrylic chains. The ionization of —COOH groups has threefold effect. It decreases the starch–acrylic interaction by decreasing H-bonding; the repulsion among similarly charged —COO^- group increases chain relaxation; and ionic nature of chains facilitates water uptake, with the overall result being increase in the extent of swelling in the medium of pH 7.4. The difference in the extent of swelling is less pronounced in case of the blends. Also, the swelling in case of copolymers of St-*g*-PMMA series, it is less sensitive to the pH of the swelling media, which is probably due to the ester groups in contrast to the carboxyl group in St-*g*-PAA and St-*g*-PMA series.

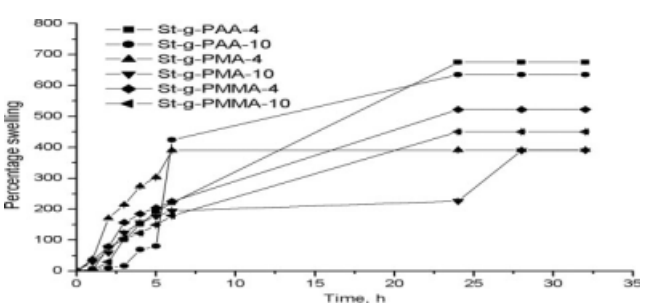

Figure 5 Dynamic uptake of water as a function of time for graft copolymers at pH 7.4. Values are mean ± SD of at least three experiments.

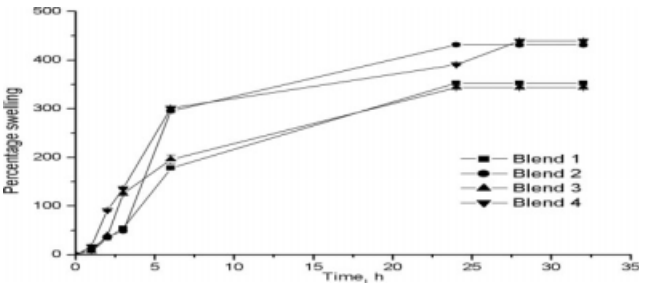

Figure 6 Dynamic uptake of water as a function of time for blends at pH 7.4. Values are mean ± SD of at least three experiments.

In vitro study of paracetamol release

In our earlier study, the graft copolymers prepared were evaluated for biodegradability using α-amylase, and it was found that the grafting of acrylic monomers onto starch delays the rate of enzymatic hydrolysis of starch, but did not affect its biodegradability as the starch present in the graft copolymers was completely hydrolyzed.[16,17] Similar results have been reported earlier.[21]

Figures 7–13(b) show the release profiles of paracetamol from the graft copolymers containing different amount of PAA, PMA, and PMMA and blends at two different pH (pH 1.2 and 7.4). The transit time in the stomach and small intestine is almost 2–3 h and the colonic residence time is about 20–30 h. Therefore, the fraction of drug released was determined at time intervals of 30 min initially and then 60 min upto a period of 6 h. The amount of drug released after 24 and 30 h was also determined. The results indicate that the ungrafted starch and the homopolymers, PAA, PMA, and PMMA, disintegrate within few minutes releasing almost all the

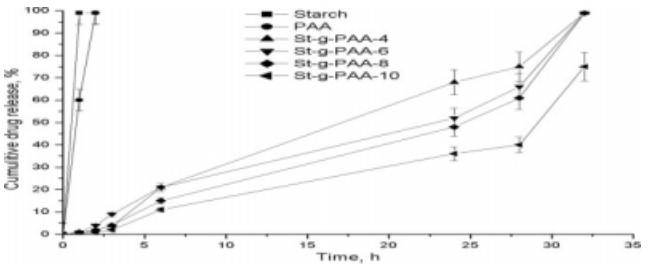

Figure 7 Release of paracetamol from St-*g*-PAA tablets as a function of time at pH 1.2. Values are mean ± SD of at least three experiments.

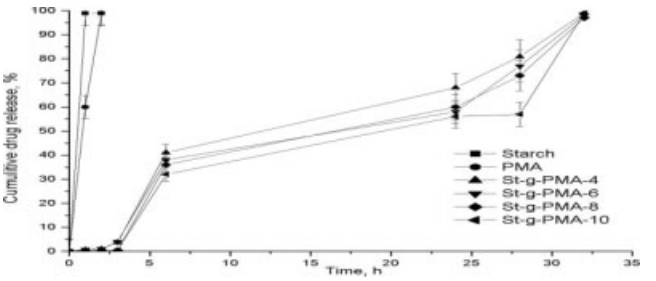

Figure 9 Release of paracetamol from St-*g*-PMA tablets as a function of time at pH 1.2. Values are mean ± SD of at least three experiments.

drug loaded at both the pH. What is more significant is that at pH 1.2 the amount of drug released within 3 h is less than 5% in St-*g*-PAA (Fig. 7) and St-*g*-PMA (Fig. 9) in contrast to the disintegration and complete release of drugs within few minutes from the matrix prepared from ungrafted starch, PAA or PMA. As discussed earlier, the extent of swelling at pH 1.2 in 3 h was found to be less than 10%. This observed "induction period" suggests that starch–PAA or starch–PMA form a more compact matrix than either of the polymers alone. At lower pH, the carbonyl groups are undissociated and involve in hydrogen bonding with hydroxyl groups of starch, which results in stabilization/compaction of the matrix.[22,23] It may be noted that the pH of gastrointestinal fluid in stomach is 1–3 and the residence time is 2–3 h, which means that all the graft copolymers would be useful as matrix to protect the drug from the harsh environment of stomach.

Figure 7 also shows that in the case of graft copolymers St-*g*-PAA at pH 1.2, the release of drug loaded decreases from 68 to 36% in 24 h as the % add-on increases from 31.03 (St-*g*-PAA-4) to 49.49% (St-*g*-PAA-10) and almost complete release was observed in 30 h for all matrices except St-*g*-PAA-10 where it was 75%. In case of St-*g*-PMA (Fig. 9), the release of drug loaded was seen to decrease from 68 to 56% in 24 h as the % add-on increases from 30.84 (St-*g*-PMA–4) to 50.26% (St-*g*-PMA–10) and complete release was observed in 30 h for all matrices. The decrease in the drug release with increasing add-on for the St-*g*-PAA and St-*g*-PMA series may probably be due to the increase in the number of —COOH groups with increasing add-on, which results in higher extent of hydrogen bonding and compaction of matrix. In case of St-*g*-PMMA (Fig. 11), the release of drug loaded decrease from 54 to 49% in 6 h as the % add-on increases from 43.19 (St-*g*-PMMA–4) to 77.42% (St-*g*-PMMA–10) and complete release was seen in 24 h. In case of Blend 1, Blend 2, Blend 3, and Blend 4 [Fig. 13(a)], the release was 61, 56, 50, and 55% in 6 h and a complete release in 24 h.

At pH 7.4, the drug release in 6 h was seen to decrease as the % add-on goes on increasing. For St-*g*-PAA (Fig. 8), the release of drug loaded was seen to decrease from 72% for St-*g*-PAA–4 (31.03% add-on) to 66% for St-*g*-PAA–6 (41.17% add-on) to 32% for St-*g*-PAA-8 (43.82% add-on) to 30% for St-*g*-PAA-10 (49.49 % add-on), and nearly complete drug release was observed in 24 h. In case of St-*g*-PMA-4, St-*g*-PMA-6, and St-*g*-PMA-8, about 96% of drug loaded was released in 6 h, whereas for St-*g*-PMA-10, it was 64% (Fig. 10) this may be attributed to the higher add-on (50.26 %) of the MA in the latter case. On the other hand, in case of St-*g*-PMMA-4, St-*g*-PMMA-6, and St-*g*-PMMA–8 about 71–76% of drug loaded was released in 6 h, whereas for St-*g*-PMMA-10, it was 56% (Fig. 12). This may be attributed to the higher add–on (79.29 %) of the MMA in the latter case. Similarly, in case of blends, the extent of

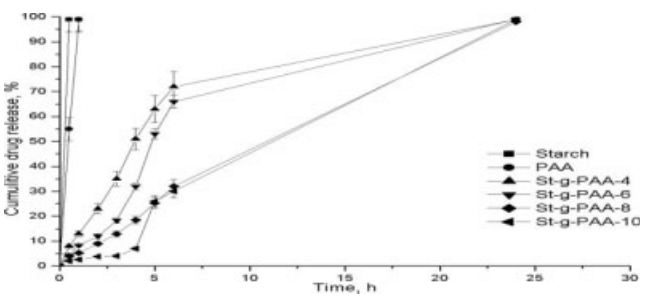

Figure 8 Release of paracetamol from St-*g*-PAA tablets as a function of time at pH 7.4. Values are mean ± SD of at least three experiments.

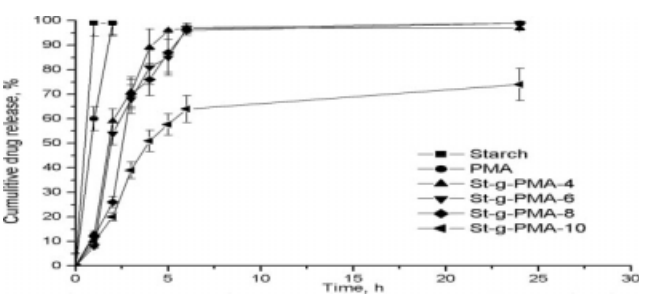

Figure 10 Release of paracetamol from St-*g*-PMA tablets as a function of time at pH 7.4. Values are mean ± SD of at least three experiments.

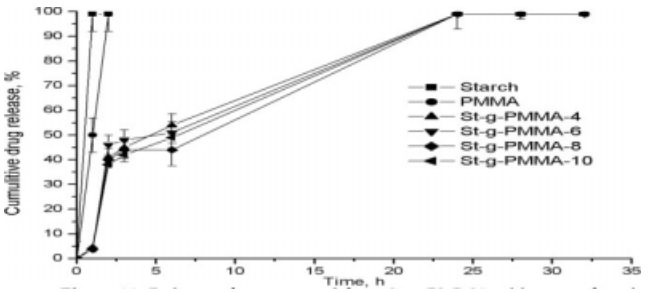

Figure 11 Release of paracetamol from St-*g*-PMMA tablets as a function of time at pH 1.2. Values are mean ± SD of at least three experiments.

release was 61, 72, 53, and 71% in 6 h [Fig. 13(b)] and complete release in 24 h. In the case of tablets prepared from St-*g*-PAA and St-*g*-PMA, complete disintegration of the tablet was observed within 30–32 h. However, when the tablets contained PMMA, either as St-*g*-PMMA or as free PMMA, the tablet did not disintegrate completely at any stage of release studies probably because of hydrophobic nature of PMMA. The release of drug was seen as the tablets swelled.

A comparison of the swelling of the copolymers, blends in the media of different pH with corresponding drug release show that the extent of swelling is much higher than the amount of drug released. This may be due to the fact that powdered sample was used for swelling studies, whereas tablets were used for drug release, so the extent of swelling would be higher in the former case owing to increased surface area. Furthermore, Dubey and Bajpai have reported that for poly(methacrylamide-*co*-acrylic acid) hydrogel intended for application in gastrointestinal drug delivery, the swelling was about 15% in 3 h in the medium of pH 1.2 and about 600% in next 9 h in medium of pH 6.8.[18]

As mentioned earlier, the St-*g*-PAA and St-*g*-PMA copolymer series reveal decrease in the drug release with increasing the % add-on. Geresh et al. have reported that the release rate of drug from the tablet prepared from starch–AA radiation grafted matrix

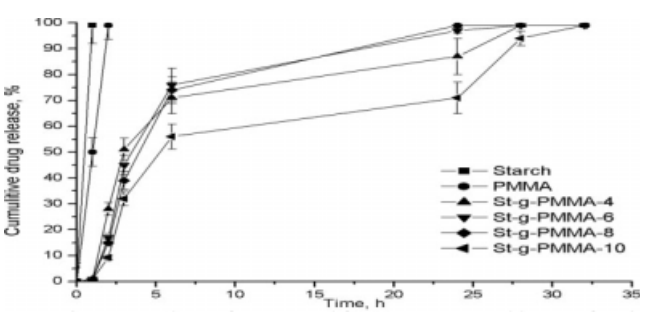

Figure 12 Release of paracetamol from St-*g*-PMMA tablets as a function of time at pH 7.4. Values are mean ± SD of at least three experiments.

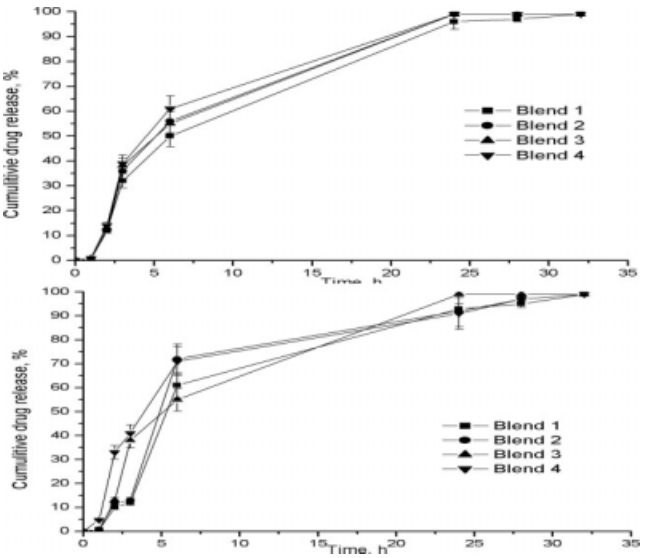

Figure 13 Release of paracetamol from tablets prepared from blends as a function of time at pH 1.2 and 7.4. Values are mean ± SD of at least three experiments.

decreased with increasing proportion of AA in the graft copolymer.[13] Also, it is seen that in both pH initial release of drug is very slow, that is, upto 1–3 h, which is also the transit time of stomach and small intestine. So, it can be inferred that the matrix can be designed in such a way that the major amount of the drug loaded can reach the colon, and also that in the presence of PMMA the tablet does not disintegrate completely, which may be due to the hydrophobic nature of the PMMA.

CONCLUSIONS

The graft copolymers, St-*g*-PAA, St-*g*-PMA, and St-*g*-PMMA provided a pH sensitive matrix system for site-specific drug delivery. *In vitro* release profiles of paracetamol showed that as the % add-on increases the drug release rate decreases, which may be attributed to the matrix stabilization due to the hydrogen bonding resulting in slower release of the loaded drug. Thus, it may be concluded that graft copolymers may be useful tool to overcome the harsh environment of the stomach and can possibly be used in future as excipient for the colon-targeted drug delivery.

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