Acetylsalicylic Acid Loading and Release Studies of the PMMA-*g*-Polymeric Oils/Oily Acids Micro and Nanospheres

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ABSTRACT: Poly(methyl methacrylate) (PMMA) and PMMA copolymers derived from plant oils (Polylinseed oil-*g*-PMMA, Polysoybean oil-*g*-PMMA, Polylinoleic acid-*g*-PMMA (PLina-*g*-PMMA) and Polyhydroxy alkanoate-sy-*g*-Polylinoleic acid-*g*-PMMA (PHA-*g*-PLina-*g*-PMMA)) as hydrophobic polymers, a series of hydrophobic microsphere or nanosphere dispersions, were prepared by the emulsion/solvent evaporation method. The diameters of the nanospheres and microspheres were measured by dynamic light scattering with a zetasizer, optically and by scanning electron microscopy. The magnetic quality of the microspheres was determined by the electron spin resonance technique. Acetylsalicylic acid (aspirin, ASA) was used as a model drug and loaded into the microspheres during the preparation process. The effect of the stirring rate over the size and size distribution of the micro/nanospheres was evaluated, and the effects of copolymer types derived from plant oil/oily acids and the copolymer/drug ratios were evaluated. © 2010 Wiley Periodicals, Inc. J Appl Polym Sci 119: 1610–1618, 2011

Key words: drug release; magnetic polymer micro/nanospheres; polymeric oil/oily acids copolymers; PMMA; acetylsalicylic acid (Aspirin)

INTRODUCTION

The synthesis and characterization of biocompatible or biodegradable polymeric controlled release drug delivery systems have received considerable attention in the last years because of their potential applications, for example, to increase bio-availability, and to sustain, localize, or target drug action in the body.[1,2] Drug carriers such as polymer micro/nanoparticles have the ability to improve the pharmacokinetics and to increase the biodistribution of therapeutic agents to target organs, which will result in improved efficacy.[3–9] It was found that the presence of hydrophobic moieties in a polymer matrix can evidently retard drug (or solute) release. This is because the hydrophobic nanoparticles cannot become swollen by water, and thus, the diffusion and permeation of the drug in the polymer matrix may depend on the cavity size of the polymer and the mobility of the polymer chains themselves.[10]

Magnetic polymer particles from the nanometer to micrometer scale are being used widely in biomedicine and bioengineering.[11–13] Magnetic particles in a polymer matrix are preferable for some applications, such as the separation, purification, or detection of proteins, DNA, viruses, cells, or bacteria, and the magnetic guidance of particle systems for specific drug delivery processes.[14,15] In magnetic target delivery, drug-loaded magnetic micro/nanoparticles possessing ferromagnetic properties are administered intravenously and concentrated at a desired target body site using an external high-gradient magnetic field. The targeted systems improve the therapeutic index of drug molecules by minimizing the toxic side effects on healthy cells and tissues.[15–18] Chattopadhyay and Gupta[19] report the formation of magnetite encapsulated biodegradable polymer particles of controllable sizes for drug targeting.

Poly(methyl methacrylate) (PMMA) is an acrylic hydrophobic biostable polymer that is widely used in the biomedical field as bone cement in orthopedics and traumatology and as an implant carrier for sustained local delivery of anti-inflammatory or antibiotics drugs.[4] Acrylate-based polymers on magnetic

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particles are chosen as coating materials because of their biocompatibility and radiation stability in several areas of applications.[20–26]

The presence of oil/fatty acid chains in the polymer structure improves some physical properties of polymers, in terms of flexibility, adhesion, and resistance to water and chemicals. In biological applications, their biocompatibility and/or biodegradability play an important role.[27] Fatty acids are suitable candidates for the preparation of biodegradable polymers because they are natural body components, and they are considered safe and are hydrophobic; thus, they may retain an encapsulated drug for longer time periods when used as drug carriers.[28,29] Poly(ester-anhydrides) based on sebacic acid and ricinoleic acid and their use as a biodegradable carrier for paclitaxel have been reported.[30] The drug release rate from these fatty acid-containing polymers (copolymers of ricinoleic acid maleate (RAM) or ricinoleic acid succinate (RAS) with sebacic acid) was significantly slowed, and constant drug release for months was achieved.[31] The use of poly (3-hydroxy butyrate hexanoate) (PHBHx) was reported as drug carriers.[32]

Auto-oxidation of polyunsaturated oil is a versatile tool to obtain bio-based materials for medical applications. Auto-oxidized polymers contain peroxide moieties which are initiated free radical polymerization of vinyl monomers. We have recently reported the auto-oxidation of unsaturated edible aliphatic oils, such as linseed oil (LO), soybean oil (SB), and linoleic acid (Lina) to prepare polymeric peroxy initiators coded as PLO, PSB, and PLina, respectively, for free radical polymerization.[33–35] This polymerization system does not require any metal catalyst or solvent that may sometimes be harmful to the environment. Therefore, this polymerization system can also be considered suitable for green chemistry. Our latest research involved the synthesis of some new types of biodegradable polymer materials-graft copolymers containing PHA-soya (Polyhydroxy alkanoate-sy), polymeric oil/oily acid, and PMMA.[36] Similarly, unsaturated poly (3-hydroxy alkanoate)s (PHA)s can be auto-oxidized;[37–40] grafted with poly(ethylene glycol) (PEG)[41–43] and PMMA[44,45] to obtain bio-based materials for medical applications.

Acetylsalicylic acid (aspirin) is an important antiplatelet drug for preventing cardiovascular events, such as myocardial infarction and vascular occlusion in cerebral and peripheral circulation. It is also used in the prevention of thromboembolic disorders, reducing the incidence of colon cancer and delaying the onset of Alzheimer's disease. The administration of aspirin mainly relies on the oral dosage form and usually requires daily use for long periods of time. Clinical trials suggest that a controlled release of aspirin would enhance the therapeutic efficacy of the drug. Furthermore, aspirin has low solubility in water and is easily decomposed by hydrolysis, making it a relevant model drug to use in loading and release studies, while keeping costs low. The release of aspirin from the micro/nanospheres can be controlled by both drug diffusion and polymer degradation, and it was dependent on the composition of the block polymer and the release medium.[46–55]

In this study, based on the above considerations, our objective is to prepare hydrophobic micro/nanospheres of PMMA copolymers derived from plant oils dispersions to evaluate the feasibility of using them as possible carriers for drug release *in vitro* and to understand their structure-properties relationship. For this purpose, PMMA homopolymer and Polylinseed oil-*g*-PMMA (PLO-*g*-PMMA),[33] Polysoybean oil-*g*-PMMA (PSB-*g*-PMMA),[34] Polylinoleic acid-*g*-PMMA (PLina-*g*-PMMA),[35] and Polyhydroxy alkanoate-sy-*g*-Polylinoleic acid-*g*-PMMA (PHA-*g*-PLina-*g*-PMMA)[36] were produced as the hydrophobic units, and a series of microparticles and nanoparticles with different compositions were prepared. During this study, acetylsalicylic acid was used as the model drug molecule. In addition, magnetic forms of the microspheres were prepared and evaluated for targeted therapy. At the end of the study, drug loading and release mechanisms of the nonmagnetic and/or magnetic polymeric particles were investigated.

MATERIALS AND METHODS

Materials

The auto-oxidation of the unsaturated edible aliphatic oils—such as LO, soy bean oil (SB) and Lina—gave polymeric oil/oily acid peroxy initiators coded as PLO, PSB, and PLina, respectively, for the free radical polymerization of MMA. PMMA and a series of PMMA copolymers derived from polymeric oil/oily acids were produced in our research laboratories. These copolymers (PLO-*g*-PMMA,[33] PSB-*g*-PMMA,[34] PLina-*g*-PMMA,[35] and PHA-*g*-PLina-*g*-PMMA[36]) were used for the preparation of the drug-loaded/unloaded micro and nanospheres. Acetylsalicylic acid was purchased from Bayer (Leverkusen, Germany). Polyvinyl alcohol (PVA) (Fluka) was used as an emulsifier, chloroform (Fluka) as a solvent, and all the other chemicals received were of the highest purity and used without further purification.

Preparation of PMMA homo and copolymer micro/nanospheres

The spherical PMMA and PMMA copolymeric particles in the size range of 0.279 to 34 μm were

produced by the solvent evaporation method. In a typical procedure, 0.25 g of the polymer sample was dissolved into 5 mL of polymer solution in chloroform; then, this solution was added drop-wise to 50 mL of distilled water (i.e., the dispersion phase) containing 0.25 g of the emulsifier, as the precipitation medium was stirred with a mechanical stirrer at different stirring rates (2000, 10,000, and 24,000 rpm) at room temperature. The solvent was evaporated under these conditions for 20 min (except at 2000 rpm, it was for 2 h). The spherical particles were separated by centrifugation (18405 $\times$ g for 10 min) and washed twice with distilled water. In this group of experiments, the effects of the PMMA and PMMA copolymers, different stirring rates and drug concentration on the average particle size and size distribution were evaluated.

Synthesis of magnetic particles and preparation of ASA loaded magnetic microsphere

The magnetic particles (i.e., Fe_3O_4 particles, magnetite) were prepared by the conventional coprecipitation method.[15,56–58] In this method, 2.705 g of $FeCl_3$ $6H_2O$ and 1.857 g of $FeSO_4$ $7H_2O$ were dissolved in 150 mL of deionized water and heated to 30°C. Then, a sodium hydroxide aqueous solution (0.4 mol/L) was slowly added drop-wise into the solution with violent stirring until the pH of the solution increased to 11–12. After aging for 3 h at 50°C, a black powder was formed. This black powder was repeatedly washed with deionized water until neutrality was achieved. Finally, the magnetite particles were obtained by the magnetic separation process and dried at 60°C in a vacuum.

The spherical magnetic particles of PMMA and PMMA copolymers were produced by the solvent evaporation method described above. Here, in a typical procedure for the preparation of the PMMA homo and copolymer microspheres, 50 mg of the magnetic particles were added to 5 mL of chloroform using the same procedure delineated above.

Characterization

The size and morphological evaluations of PMMA and PMMA copolymers particles were observed with a scanning electron microscope (SEM) (JEOL JXA-840A Tokyo, Japan). The nano/microspheres were frozen under liquid nitrogen, then fractured, mounted, and coated with gold (about 300 Á) on an Edwards S 150 B sputter coater in a vacuum. The photographs were taken with an electron microscope at $\times$1000, $\times$5000, and $\times$6000 magnification levels. The particle size was determined by measuring photographs taken on an SEM system.

The size and size distribution of the PMMA homo and copolymeric microspheres were determined from the micrographs taken with an optical microscope (Nikon Eclipse E200). The particle diameters on the micrographs (each containing approximately 10–20 particles) were measured, and the average sizes with standard deviations were evaluated using an image analyzing software (Image-Pro). The size and size distribution of the PMMA copolymer nanoparticles were measured by dynamic light scattering (DLS) with a zetasizer.

Drug loading studies

Acetylsalicylic acid (ASA) was loaded by dispersing the drug into the polymer solution during the preparation of the PMMA homo and copolymeric microspheres. In this part of the study, the polymer and drug mixture in chloroform was kept in a water bath type of sonicator for 30 min initially, to form the homogen polymer-drug solution, and then it was added drop-wise into the dispersion medium, consisting of distilled water and polyvinyl alcohol as an emulsifier. During the study, the drug/polymer ratio was selected as an effective parameter over the release profile. The obtained drug-loaded microspheres were isolated from the dispersion medium by centrifugation and washed with distilled water twice; then, they were dried at room temperature for further *in vitro* release analysis.

Drug-loading ratio

The drug-loading ratio is one of the most important parameters in the preparation of drug delivery systems, resulting in different release profiles. Therefore, this amount was calculated by using the following equation:

$$\text{Drug Loading Ratio} = (\text{Mass of drug in microspheres}/\text{Mass of drug used in the formulation}) \times 100 \quad (1)$$

The mass of the drug in microspheres was calculated by subtracting the mass of the free drug in the dispersion medium and washing water from the total mass of the drug used in the formulation. The measurement of free ASA was done spectrophotometrically with a UV spectrophotometer (Unicam UV-vis spectrophotometer-UV-2, USA) at wavelength 297 nm, where the maximum absorbance was observed and not affected by other present components. The resulting amount of entrapped drug was correlated with the amount of total released drug in the *in vitro* release studies. The mass of ASA used in the formulation was 5 mg.

In vitro release studies

Release profiles of acetylsalicylic acid from different polymer particles (PMMA homo and copolymeric microspheres) were measured in a phosphate buffer solution at 25°C. The suspensions were agitated using the shaker at 50 rpm. At scheduled time intervals, 2 mL samples were taken for spectrophotometer measurements and refreshed with fresh medium. The measurements were repeated twice, and the absorbance measurements were performed at 297 nm. The particles were shaken for 24 h, and the concentration of drug released was measured.

Analysis of magnetism

The presence of iron oxide particles in the polymeric structure was confirmed by electron spin resonance (ESR) (EL 9, Variant). The intensity of the magnetite peak against the magnetic field (Gauss) is shown in Figure 4.

The application of an external magnetic field may generate an internal magnetic field in the sample, which will add to or subtract from the external field. The local magnetic field generated by the electronic magnetic moment will add vectorially to the external magnetic field (H_{ext}) to give an effective field (H_{eff}):

$$H_{eff} = H_{ext} + H_{local} \quad (2)$$

The g factor can be considered as a quantity characteristic of the molecules, in which the unpaired electrons are located, and it is calculated from the following equation:

$$h\nu = g_s \beta H_s \quad (3)$$

$$h\nu = g_r \beta H_r \quad (4)$$

In the above equations, g_s is the lande factor of standard; H_s is the magnetic field resonance of standard; h is the Planck constant (6.626×10^{-27} erg s); β is the universal constant (9.274×10^{-21} erg/Gs); and ν is the frequency (9.707×10^{9} Hz).

From eqs. (3) and (4) above, measurement of the g factor for an unknown signal can be obtained as indicated below.

$$g_r = \frac{H_s}{H_r} g_s \quad (5)$$

H_r is the resonance of the magnetic field (Gs).

RESULT AND DISCUSSION

In this study, hydrophobic PMMA homo and copolymer microparticles were prepared and investigated for the feasibility of using them as possible carriers for a hydrophilic drug (i.e., ASA). Furthermore, drug loading and release studies were done with magnetic and nonmagnetic forms of the microspheres. PMMA homopolymer, PLO-*g*-PMMA, PSB-*g*-PMMA, PLina-*g*-PMMA, and PHA-*g*-PLina-*g*-PMMA graft copolymers were used as the based matrices.

TABLE I
Effects of Comonomer Type and Drug (ASA) Loading on the Size and Size Distribution of the Microperes. In All Experiments, the Polymer and PVA Concentrations Were Kept at 50 and 5 mg/mL, respectively, and the Stirring Rate Was 2000 rpm

Comonomer type	Microsphere diameter (μm)
Effects of comonomer types	
PMMA homopolymer	19.0 ± 6.8
Linoleic acid (PLina-*g*-PMMA)	20.9 ± 3.5
Soybean oil (PSB-*g*-PMMA)	34.0 ± 8.0
Linseed oil (PLO-*g*-PMMA)	14.2 ± 3.7
Effects of drug molecules	
PMMA with drug	17.0 ± 9.8
Linoleic acid with drug (PLina-*g*-PMMA)	15.6 ± 5.1
Soybean oil with drug (PSB-*g*-PMMA)	21.8 ± 8.9

PMMA homo and copolymer microspheres

The spherical PMMA and PMMA copolymeric particles were produced by the solvent evaporation method. There are three important parameters for size and size distribution, which are: comonomer type, volume of solvent in the preparation of polymer spheres, and the stirring rate of the dispersion medium.

Copolymers used in this work were chosen from biocompatible copolymer samples, which have the lowest protein adsorption and bacterial adherence. These copolymers contained LO, SB, and Lina segments at approximately 8–10 wt %.[33–36] LO and SB compositions were largely oleic, linoleic, and linolenic acids. The amounts of Lina in LO and SB were found to be 15 and 53 wt %, respectively.

First, the size-size distributions of the microspheres were primarily affected by the comonomer type, especially in the cases of SB and LO, as seen in Table I. The microsphere diameters obtained from homo PMMA are 19.0 μm. The diameters of the PLin-*g*-PMMA microsphere obtained from LO were lower (14.2 μm), whereas diameters of the PSB-*g*-PMMA microsphere obtained from SB were higher (34.0 μm). Furthermore, the diameters of the PLina-*g*-PMMA microsphere obtained from Lina were 20.9 μm. This can be related to the nature of the comonomers, but the most important factors pertain to the morphology and characteristics of the drug-loaded forms of the microspheres. They can be altered by

TABLE II
Effects of Stirring Rate Over the Size and Size Distribution of the Microspheres

Comonomer type	Stirring rate (rpm)	Microsphere diameter (μm)
PLO-*g*-PMMA	2000	14.0 ± 3.7
	10,000	6.0 ± 3.2
PLina-*g*-PMMA	2000	15.6 ± 5.1
	24,000	0.587

In all experiments, PVA concentrations were kept at 50 and 5 mg/mL, respectively.

changing the comonomer types as required; this is discussed in greater detail in other subsections of the dissertation. On the other hand, the drug molecules do not change the size–size distribution trend of the plain microspheres significantly, as seen in Table I. This is important because of the small amount of drug molecules in the formulation of drug-loaded microspheres.

Second, in the study of stirring rate effects, PMMA microspheres were prepared with LO and Lina as a comonomer at different stirring rate (i.e., 2000, 10,000, and 24,000 rpm). The observed average diameters with standard deviations are presented in Table II. The diameter of the PLO-*g*-PMMA microsphere at 2000 rpm is 14 μm, whereas at 10,000 rpm, it is 6.0 μm. The average diameter of the PLina-*g*-PMMA sphere at 2000 rpm is 15.6 μm, and at 24,000 rpm, it is 0.587 μm. Herein, the stirring rate provides the required energy for the polymer solution to be dispersed as fine droplets in the suspension medium, and therefore, higher stirring rates create smaller microspheres. On the other hand, when the stirring rate increased dramatically to such rates as 24,000 rpm, the size of the microspheres decreased to the nanoscale (i.e., around 587 nm).

Third, the volume of solvent in the preparation of polymer spheres was also significant (Table III). For example, the size of the nanospheres of PLina-*g*-PMMA was 587 nm when 5 mL of solvent was used; however, it was 279 nm for PSB-*g*-PMMA and 282 nm for PLO-*g*-PMMA when 10 mL of solvent was used. However, further evaluation of different copolymers indicated that nanosphere diameters nearly decreased by 48% when the volume of solvent increased by 100%. The differences in nanosphere diameter could be explained by the rate of polymer amount/solvent volume, although the quantity of plant oil/oily acids remained the same (approximately 8–10%) for all copolymer structures.

It seems possible to prepare PMMA homo and copolymeric microspheres as nanospheres by using higher stirring rates. This offers some advantages when preparing drugs and magnetic particles loaded on PMMA copolymer micro/nanospheres for targeted therapy.

Morphological evaluation

The morphology of the PMMA homo and copolymer microparticles was investigated using SEM and an optical microscope. SEM micrographs of PMMA homopolymer and copolymer micro/nanoparticles are presented in Figure 1(A–C). As can be seen, PMMA homo and copolymer micro/nanospheres were well-shaped and spherical, with rather smooth surfaces. The sizes of the microspheres were found to be directly dependent on the stirring rate of the dispersion medium, and the size–size distribution were decreased by increasing the stirring rate, as seen in Figure 1(B) and explored in greater detail in the following subsections. The morphology of drug and magnetic particles loaded in the PMMA copolymer microspheres are presented in the SEM micrographs given in Figure 1(C). On the other hand, in the case of the magnetic form of the microspheres, Fe_3O_4 particle distribution within the microspheres was evaluated from optical micrographs. The unloaded, drug-loaded, drug and magnetic particles in the PMMA and PMMA copolymer microspheres are easily visible in the optical micrograph given in Figure 2(A,B). It is clear that a very homogenous distribution of drug and Fe_3O_4 particles was achieved in the microspheres.

Drug loading and release studies

In this part of the study, different types of comonomers (i.e., LO, SB, and Lina) were used to prepare drug-loaded, PMMA-based microspheres, as mentioned in the materials and methods section. The obtained results demonstrated that the nature of the comonomer was affected by the drug-loading ratio, as given in Table IV. The drug-loading ratio decreased in the order of PSB-*g*-PMMA (75%), PLina-*g*-PMMA (54%), PLO-*g*-PMMA (45%), and then graft copolymers. The drug-loading ratio is more lower (34%) for multigraft copolymers (PHA-

TABLE III
Acetylsalicylic Acid Loaded PMMA-*g*-Polymeric Oil/Oil Acid Nanospheres Size and Size Distribution. In All Experiments, the Stirring Rate was 24,000 rpm and PVA Concentrations Were Kept at 5 mg/mL (Polymer Solved in (a) 5 mL CHCl3, (b) 10 mL $CHCl_3$

Copolymer type	Nanosphere diameter (nm)	PDI*
PLina-*g*-PMMA	587[a]	0.44
PSB-*g*-PMMA	279[b]	0.60
PLO-*g*-PMMA	282[b]	0.32

* Poly dispersity index.

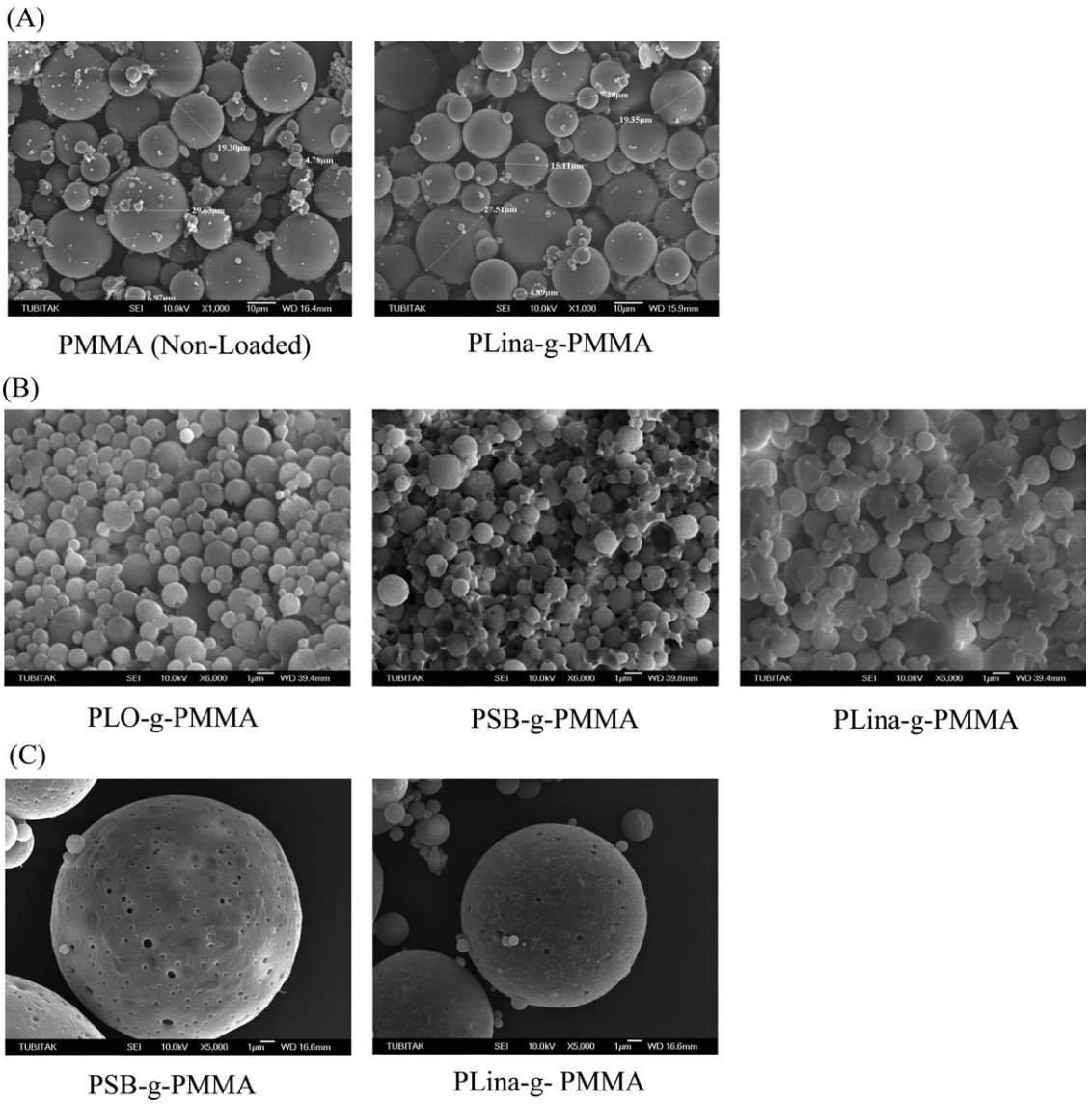

Figure 1 SEM micrographs of drug-loaded PMMA copolymeric microspheres; (A) Larger microspheres of PMMA non-loaded and PLina-*g*-PMMA (prepared with lower stirring rates) (magnification 1000×). (B) Smaller microspheres of PLO-*g*-PMMA, PSB-*g*-PMMA and PLina-*g*-PMMA (prepared with higher stirring rates) (magnification 6000×). (C) Drug-loaded and magnetic particles in the PSB-*g*-PMMA and PLina-*g*-PMMA microspheres (magnification 5000×).

g-PLina-*g*-PMMA). The type of polymeric oil in the copolymer affects the drug-loading ratio, as evident from above.

Similar characteristics were obtained for drug release values, meaning that the types of comonomers significantly affected the drug release profiles, as seen in Figure 3. This is also related to the nature of the comonomers. Furthermore, the slowest release profile was obtained with PLina-*g*-PMMA at Lina formulation, and the total drug was released after 24 h; the others completed the drug release process within the first 12 h.

Generally, solute or drug release from gels involves the process of diffusion and permeation from a polymer matrix. Carbonyl groups of ester bonds of polyacrylate may bind a small amount of water because of the hydrophobicity of polyacrylate.[10] In other words, the insides of particles cannot be markedly swollen by water. Therefore, the release kinetics of ASA may be related to particle cavities and the mobility of polymer chains. Obviously, increased cavity sizes are more conducive to the diffusion and permeation of ASA from a polymer matrix.

Magnetical properties of the magnetic PMMA-based microspheres

Magnetic forms of the PMMA-based homo and copolymeric microspheres were prepared. Initially,

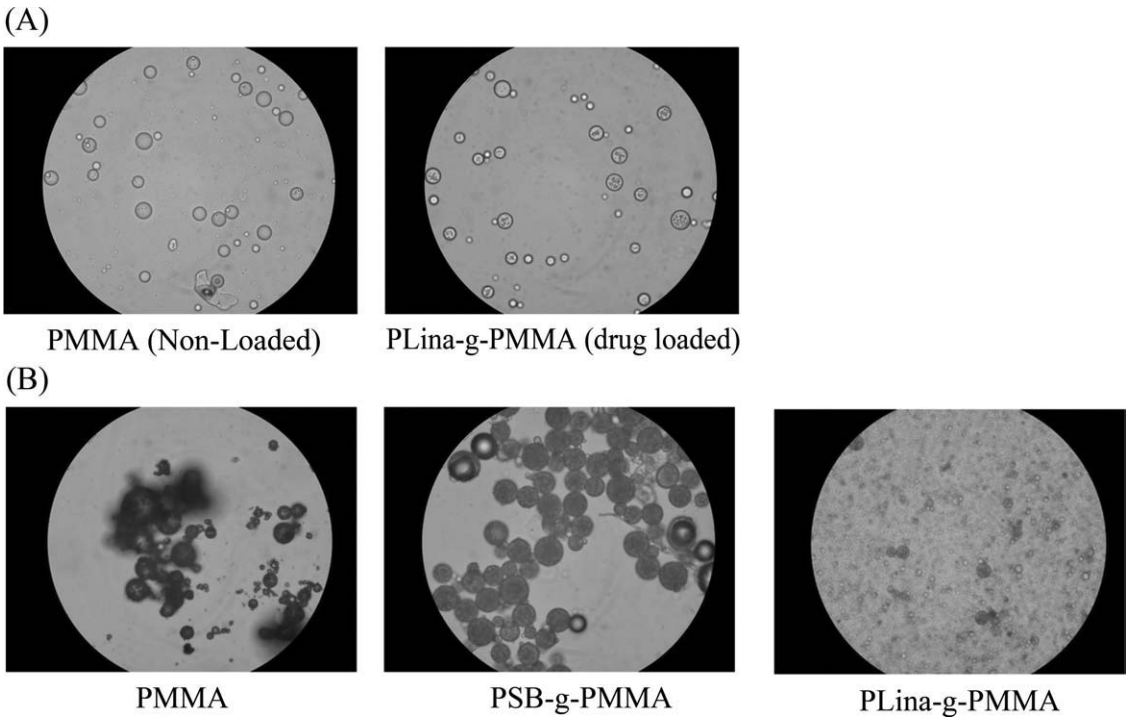

Figure 2 Optical micrographs of PMMA microspheres; (A) Plain (or non-magnetic form) microspheres of PMMA (non-loaded) and PLina-*g*-PMMA (drug-loaded); (B) magnetic form of the PMMA, PSB-*g*-PMMA and PLina-*g*-PMMA microspheres.

TABLE IV
Effects of Copolymer Type Over the ASA Loading Ratio. In all Experiments, MMA was Used as Comonomer

Copolymer type	Drug-loading ratio (%)
Soybean oil-*g*-PMMA	75
Linoleic acid-*g*-PMMA	54
Linseed oil-*g*-PMMA	45
PHA-linoleic acid-PMMA	34

In all experiments, the polymer and PVA concentrations were kept at 50 and 5 mg/mL, respectively.

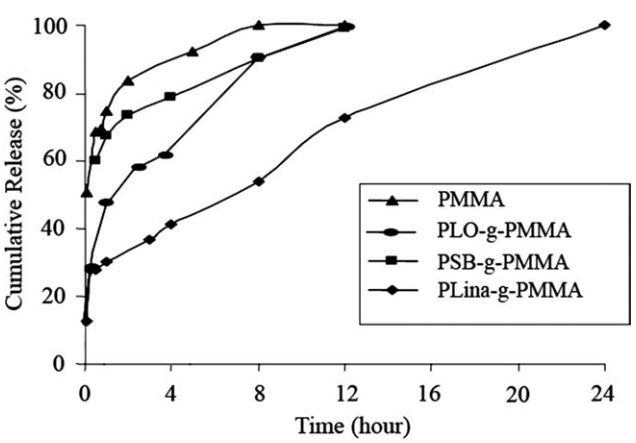

Figure 3 ASA release profiles based on the comonomer types.

the larger ones were produced as models, and the presence of magnetite nanopowder in the polymer structure was confirmed by the ESR technique. The intensity of the magnetite peak against the magnetic field (Gauss) is seen in Figure 4. The *g* factor can be considered as a quantity characteristic of the molecules in which the unpaired electrons are located. In this study, the *g* factor was obtained as 2.21 for magnetic particles used in the preparation of PMMA-

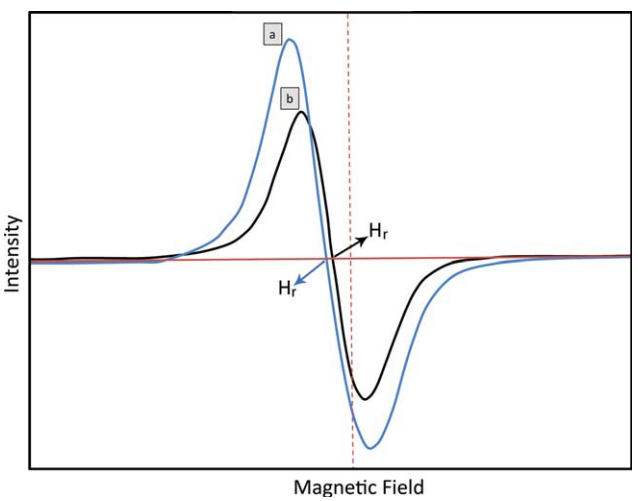

Figure 4 ESR spectrum (a) magnetite (b) PLina-*g*-PMMA copolymer. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

TABLE V
Magnetic Properties of ASA Loaded PMMA and PMMA-*g*-Polymeric Oil/Oil Acid Copolymer Microspheres

Sample name	g	H_r (gauss)
Magnetite	2.2088	4638
PMMA (drug+magnetite)	2.0958	4438
PSB-*g*-PMMA (drug+magnetite)	2.0799	4925
PLina-*g*-PMMA (drug+magnetite)	2.1012	4875

based microspheres, and 2.09, 2.08, and 2.10 for PMMA, soybean-*g*-PMMA, and linoleic acid-*g*-PMMA copolymeric microspheres, respectively (Table V). These values seem quite valid, according to previous literature,[15,56–58] in which the *g* factor of Fe^{+3} for the low-spin complex falls between 1.4 and 3.1, and it is between 2.0 and 9.7 for the high-spin complex. This quantity of the external magnetic field (H), in our calculation, was between 4.93 and 4.44 kG for the magnetic PMMA and PMMA copolymer microspheres (Table V). It can be said that the presence of the external magnetic field has greatly reduced axial mixing. As seen in Figure 4, copolymer spheres have a relative intensity of 400. This value shows that the polymeric structure has a local magnetic field because of the magnetite in its structure.

CONCLUSION

This work has demonstrated the feasibility of using PMMA-*g*-polymeric oils/oily acid graft copolymers as materials for loading and releasing a profile of aspirin in micro/nanoparticles. The release experiments indicate clearly that the plant oil/oily acid microspheres used in this work can retard ASA release more effectively than PMMA homopolymer microspheres. Increasing fatty acid content decreases the polymer degradation time. Accordingly, the drug release from these polymers was affected by the fatty acid content and hydrophobic character of polymeric oils/oily acid. In addition, the values of magnetic PMMA copolymeric microspheres show that the polymeric structure has a local magnetic field because of the magnetite in its structure, and copolymer beads require less magnetic intensity in a magnetically stabilized environment for various applications.

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