Development of Antimicrobial Polypropylene Sutures by Graft Copolymerization. II. Evaluation of Physical Properties, Drug Release, and Antimicrobial Activity

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ABSTRACT: Polypropylene (PP) sutures are prepared by the simultaneous radiation grafting of 1-vinylimidazole (VIm) onto PP monofilament sutures. The tenacity slightly decreases whereas the elongation increases with the increase in the degree of grafting. Thermogravimetric analysis shows that the stability of the sutures is enhanced by the grafting process. The grafted sutures have reasonably good water uptake. They are subsequently immobilized with an antimicrobial drug, ciprofloxacin. The modified suture releases the drug over a period of 4–5 days. The antimicrobial activity of the modified suture is determined against *Escherichia coli* by the zone of inhibition technique. A clear zone of inhibition is observed around the drug-containing suture. © 2006 Wiley Periodicals, Inc. J Appl Polym Sci 103: 3534–3538, 2007

Key words: polypropylene; radiation grafting; 1-vinylimidazole; suture; antimicrobial

INTRODUCTION

Polymeric biomaterials have become increasingly interesting in medical science over the past few years. Some of the critical applications of biomaterials are in sutures, implants, wound dressings, and tissue engineering.[1–4] With the increasing demands for a biomaterial with better acceptability and functionality to the biosystem, stress has been focused on the development of newer materials. The recent developments in sutures have been directed toward making them knot secure and with improved biocompatibility. However, microbial infection has been an adverse observation at the site of the stitch. The microorganisms associated with wound infection include both Gram positive and Gram negative bacteria. At present, commercially available sutures do not possess antimicrobial activity; this is where biocidal materials and antibacterial finishing of materials have been investigated by many authors.[5–7] However, the development of a suture requires achieving chemical modification in such a way that it not only retains its inherent properties but also exerts antimicrobial activity.

Several studies have been carried out to develop polymeric materials with antibacterial activity by the incorporation of antimicrobial agents onto the surface of polymeric materials.[8–11] Although blending has been an effective way to produce antimicrobial sutures, it leads to severe problems in material processing and the stability of the antimicrobial agent. Radiation grafting has been an effective approach to impart desirable properties into a polymeric material without any consideration of the shape of the material.[12–14] The attractive feature of radiation grafting is that the size of the grafted component can be easily controlled by proper selection of the irradiation conditions. Recently, we carried out the grafting of acrylonitrile onto polypropylene (PP) sutures.[15] These grafted sutures were subsequently hydrolyzed to attain carboxyl groups for antimicrobial drug immobilization.[16] This process involves two steps (grafting and hydrolysis), which leads to significant loss in the mechanical strength of the suture. We therefore extended the suture development by a single step process, which is simultaneous radiation grafting of vinylimidazole (VIm) into PP sutures so that drugs may be immobilized onto the imidazole unit.[17–20] VIm is a water-soluble monomer and polymerizes to give hydrogels.[21] The monomer may be polymerized by radiation and subsequently crosslinked to the water-insoluble structure.[22,23] We previously reported the modification of PP sutures by radiation grafting of VIm monomer using the simultaneous radiation method.[24] In this work, the physical properties of the grafted sutures, immobilization of drug, and release behavior of the drug were investigated. Ciprofloxacin was chosen as an antimicrobial drug

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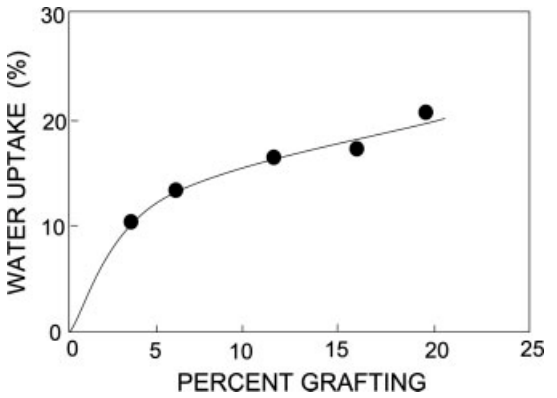

Figure 1 The variation of the water uptake with the percentage of grafting in PP-*g*-PVIm sutures.

for the study. The antimicrobial activity of the sutures was evaluated using *Escherichia coli* by the zone of inhibition method.

EXPERIMENTAL

Materials

Commercial grade, isotactic PP with a melt flow index of 20 was supplied by Reliance Industries. 1-VIm was supplied by Fluka. The irradiation of the samples was conducted with a ^{60}Co γ-radiation unit (900 Curies) supplied by Bhabha Atomic Research Centre. The irradiation dose rate was 0.2 kGy/h.

Grafting method

PP monofilament sutures were produced by spinning the PP on a BETOL spinning machine followed by two-stage sequential drawing as reported earlier. The grafting was carried out by irradiation of the tube containing the suture and the monomer solution in an ampoule under a nitrogen atmosphere. The poly(VIm) (PVIm) homopolymer adhering on the filament was removed by extraction with acetone, and the suture was dried in an air oven. The degree of grafting into the filament was calculated according to the following equation:

$$\text{degree of grafting} = [(W_g - W_0)/W_0] \times 100$$

where W_0 and W_g are the weights of the ungrafted and grafted sutures, respectively.

Mechanical properties measurements

The mechanical properties of various PP suture samples were investigated on a STATIMAT tensile tester using a gauge length of 5 cm and a crosshead speed of 75 cm/min. Five measurements were made for each sample.

Thermogravimetric analysis (TGA)

The TGA of the samples was carried out on PerkinElmer TGA-7 in a temperature range of 50–600°C under a nitrogen atmosphere. The scan rate was 10°C/min. Samples were dried under a vacuum overnight prior to the analysis.

Water uptake measurements

To measure the water uptake, clean and dried grafted sutures of known weight were immersed in distilled water at 30°C overnight (24 h). The sutures were removed, blotted with absorbent paper to remove the liquid attached to their surfaces, and weighed. The water uptake was calculated using the following formula:

$$\text{water uptake } (\%) = [(W_f - W_i)/W_i] \times 100$$

where W_f and W_i are the wet and dry weights of the sutures, respectively.

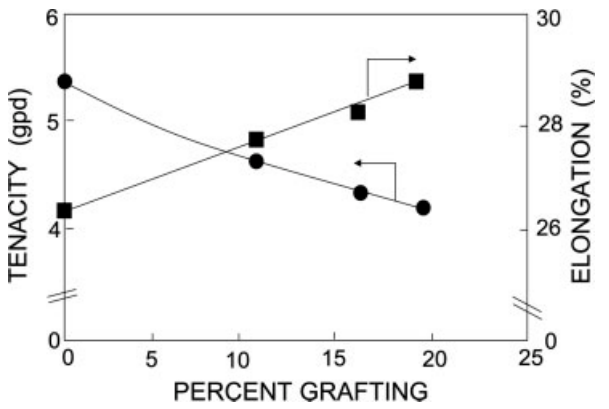

Figure 2 The variation of the tenacity and elongation with the percentage of grafting in PP-*g*-PVIm sutures.

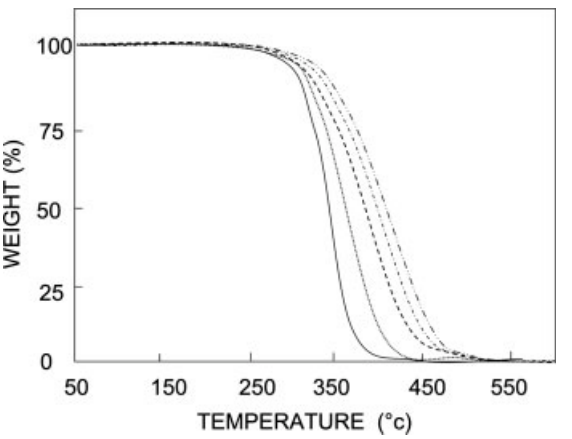

Figure 3 TGA thermograms of (—) virgin PP; and PP-*g*-PVIm sutures with (– – –) 4.7% grafting; (· · · ·) 9.7% grafting; (– · – · –) 16.7% grafting; (– · · – · ·) 20% grafting.

TABLE I
Variation of IDT and T50 with Percentage of Grafting

Grafting (%)	IDT (°C)	T_{50} (°C)
0	290	342
4.7	310	380
9.7	319	392
16.7	345	406
20	356	416

Immobilization of ciprofloxacin

A floroquinoline drug (ciprofloxacin) was immobilized on PP sutures by immersing it in a 15% aqueous solution of ciprofloxacin hydrochloride. This drug was chosen because of its broad antimicrobial spectrum and its ability to bind with the nitrogen atom of the modified suture in its protonated form. The samples were taken out at regular intervals in order to optimize the time required for maximum add-on. The samples were removed, washed thoroughly with distilled water, and dried under a vacuum at 40°C for 2 h. The percentage add-on of the drug was calculated by the following expression:

$$\text{add on } (\%) = [(W_d - W_i)/W_i] \times 100$$

where W_d is the weight of the drug-immobilized sample and W_i is the weight of the sample before immobilization.

Drug release studies

Release of the ciprofloxacin from drug-loaded modified PP sutures was studied on a UV spectrophotometer (Specord S 100). One gram of suture was immersed in a pH 7.4 phosphate buffer solution and the supernatant was replaced every day by fresh buffer solution. The amount of drug released in the supernatant was determined using a calibration curve plotted as the intensity versus the concentration using the UV spectrophotometer. The amount of drug released was reported as milligrams per gram of suture.

Antimicrobial studies

The antimicrobial properties of the sutures were assessed against *E. coli*. The bacteria was first inoculated in peptone solution with the help of a platinum loop in an incubator at 37°C. Nutrient agar plates were prepared and a layer of bacteria was placed on the plate with a cotton swab. A weighed amount of drug-immobilized suture was placed on the agar plate with sterilized forceps. An unmodified suture was also placed on each plate as a control. The plates were then incubated at 37°C for 24 h, and the clear zones thus formed on the plate around the drug-loaded sutures were measured.

RESULTS AND DISCUSSION

The grafting of VIm onto PP sutures leads to a copolymer structure in which grafted side chains contain imidazole units. These sites offer interaction with the drug to produce an antimicrobial suture. The water uptake results of various grafted sutures are presented in Figure 1. Reasonably good swelling of the suture in water is observed, which tends to increase as the graft levels in the suture increase. These results are the outcome of the hydrophilic nature of the imidazole unit. As a result, the hydrophilicity of the suture increases and is reflected in an increase in the water uptake with the degree of grafting.

The tensile results of the sutures are presented in Figure 2. In the present system, an increase in the graft level diminished the tenacity. However, the elongation showed an increasing trend. This can be explained on the basis that the grafting in polymers

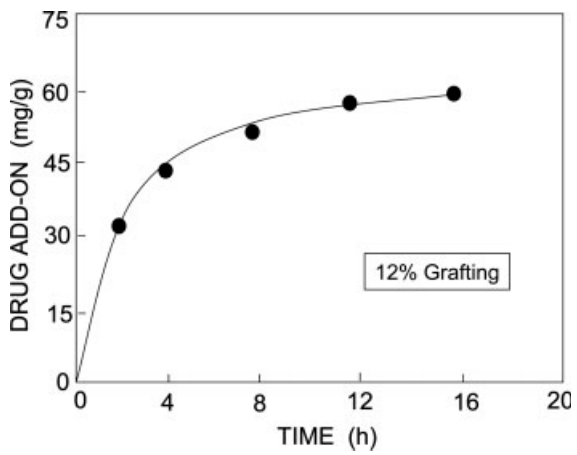

Figure 4 The variation of drug loading as a function of time in PP-*g*-PVIm sutures.

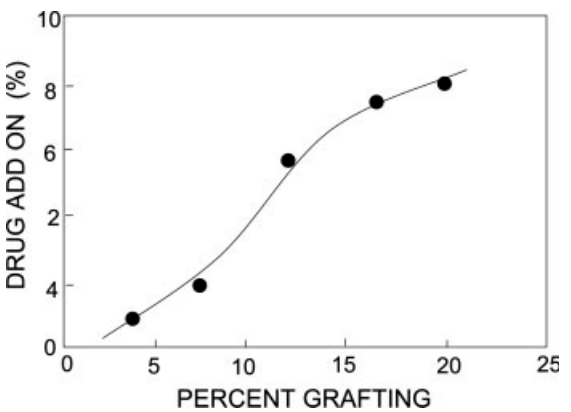

Figure 5 The variation of drug loading with grafting percentage in PP-*g*-PVIm sutures.

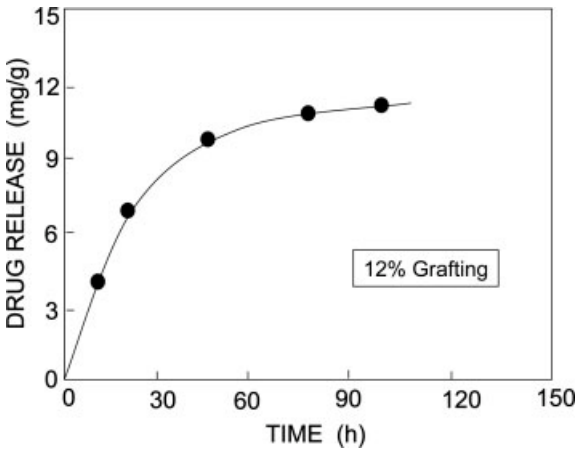

Figure 6 The variation of drug release with the time in PP-*g*-PVIm sutures.

is usually accompanied by incompatibility of the grafted component with the base matrix. As the grafting increases, the compactness of the PP chains is affected because of the pushing apart of the molecular chains in the amorphous region, which in turn increases the brittleness of the polymer backbone. As a result, the polymer fails to withstand tensile load in the grafted samples and a deterioration in the mechanical strength is observed.

Primary thermograms of virgin PP sutures and PP-*g*-PVIm sutures are presented in Figure 3. All samples show smooth degradation patterns, but the thermal stability tends to improve significantly with the increasing degree of grafting. An improvement in the initial decomposition temperature (IDT) and T_{50} of modified sutures as compared to the virgin suture was observed (Table I). The thermogram showed an increase in the IDT values from 290°C for the virgin suture to 356°C for the sample with 20% grafting. This increase in the thermal stability of PP fibers may be attributed to the incorporation of PVIm in the polymeric backbone, which has higher thermal stability than PP. An enhancement in the thermal stability of PP was also reported by Nagib et al.[17] However, in their study, the weight loss started at the beginning of the thermogram. It is possible that the samples undergo dehydration because of the presence of moisture in these films. Moreover, the carboxyl groups may also be involved in the cyclization reaction, leading to the anhydride structures and water molecules.

The immobilization of ciprofloxacin was carried out on a 20% grafted PP suture. The variation of the drug linked to the suture with the time is presented in Figure 4. The drug add-on increases with the time and almost reaches saturation within 12 h. We therefore kept 12 h as the immobilization time for our

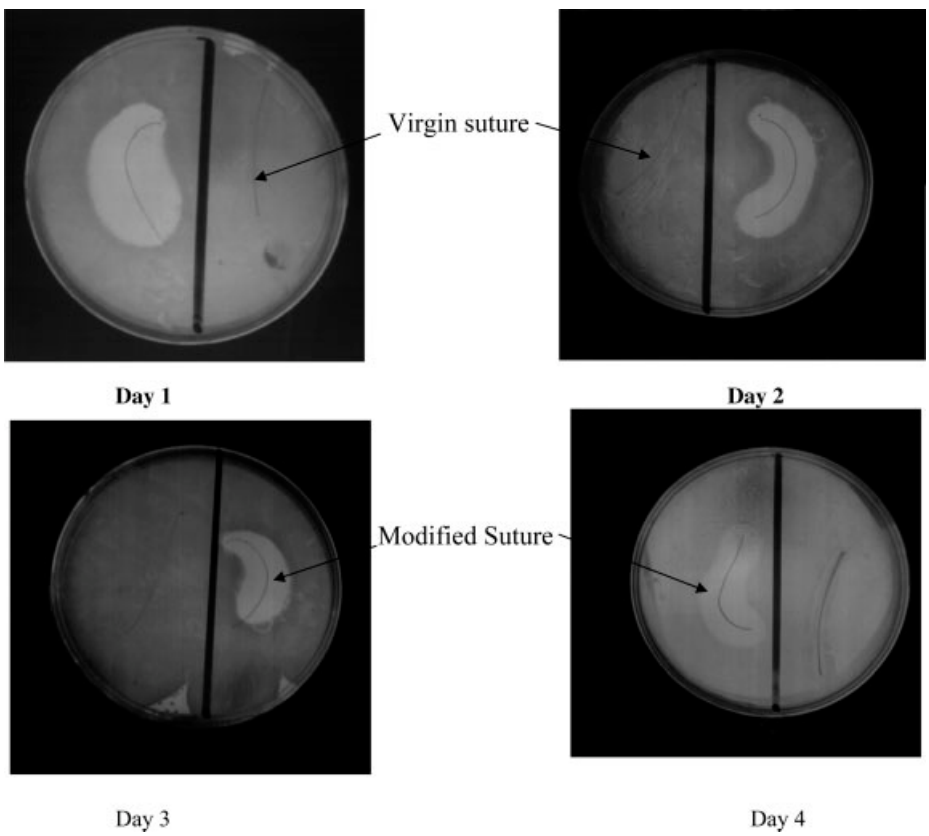

Figure 7 The antimicrobial activity of virgin PP and PP-*g*-PVIm sutures with 12% grafting.

subsequent studies. The variation of drug loading on the suture as a function of the degree of grafting is presented in Figure 5. No immobilization of drug is observed for unmodified PP suture. This is due to the lack of any polar group for interaction with the drug. However, modified sutures show good drug add-on, which increases as the degree of grafting increases.

The release pattern of the drug is demonstrated in Figure 6. The drug is released quickly for the initial periods and then tends to slow down. The drug release was observed for a period of 4–5 days. Note that the complete release of drug did not take place and a significant amount of drug remained embedded within the suture matrix. The drug release was around 20% of the total immobilized drug. However, the release pattern in our studies offers the required behavior as the suture is removed from the site within this period.

The *in vitro* antimicrobial activities of drug-loaded sutures are quite evident as shown in Figure 7. There is no inhibited zone around the unmodified suture (control) and it is completely surrounded by the colonies of bacteria. A clear zone of inhibition was observed around the drug-loaded suture on the agar plate inoculated by *E. coli*. This confirmed the antimicrobial nature of drug-loaded sutures because the microbes initially placed on the plate were killed and could not proliferate to produce a lawn surrounding them. The results demonstrated that the drug-loaded sutures showed continuous inhibition throughout the 4-day investigations.

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