 doi:10.20944/preprints202111.0543.v1

Article

Polypropylene graft poly(methyl methacrylate) graft poly(*N*-vinylimidazole) as a smart material for pH-controlled drug delivery

Felipe López-Saucedo*, Jesús Eduardo López-Barriguete, Guadalupe Gabriel Flores-Rojas, Sharemy Gómez-Dorantes and Emilio Bucio*

Departamento de Química de Radiaciones y Radioquímica, Instituto de Ciencias Nucleares, Universidad Nacional Autónoma de México, Circuito Exterior, Ciudad Universitaria, CDMX 04510, México

* Correspondence: felipelopezsaucedo@gmail.com (FLS) and ebucio@nucleares.unam.mx (EB)

Abstract: Surface modification of polypropylene (PP) films is achieved using gamma-irradiation-induced grafting to proffer with antimicrobial activity. The copolymer was obtained through a versatile two-step route; pristine PP is exposed to gamma rays and grafted using methyl methacrylate (MMA), then *N*-vinylimidazole (NVI) is grafted onto the copolymer PP-*g*-MMA by simultaneous irradiation. The characterization included Fourier-Transform Infrared Spectroscopy (FTIR), Scanning Electron Microscope (SEM), Thermogravimetric Analysis (TGA), X-ray Photoelectron Spectroscopy (XPS), and physicochemical analysis of swelling and contact angle. The copolymer (PP-*g*-MMA)-*g*-NVI was loaded with vancomycin, and the drug released was quantified by UV-vis spectrophotometry at different pH. The surface of (PP-*g*-MMA)-*g*-NVI exhibited pH-responsiveness and moderate hydrophilicity, suitable properties for controlled drug release.

Keywords: grafting; polypropylene; gamma rays; methyl methacrylate; *N*-vinylimidazole; pH-responsiveness; vancomycin; release

1. Introduction

It is well known the difficulty to modify polypropylene [1] using conventional chemical techniques. Such difficulty is attributed to the thermal stability and lack of reactivity from alkyl chains in the polymer. Nonetheless, the modification of polymer materials is often a task with prolific rewards because the addition of functional groups, whether in bulk or just in a specific part [2], is a standardized strategy to provide new characteristics to materials and boost their functionality [3].

Grafting polymerization has been demonstrated as an excellent option to modify PP [4], where different methods [5] have been tried to graft vinyl monomers such as *N*-vinylimidazole (NVI) [6], methyl methacrylate (MMA) [7], *N*-vinylcaprolactam (NVCL) [8], or glycidyl methacrylate (GMA) [9]. But there are issues related to the low reactivity of PP, which produces non-uniform grafting, low yields, waste, and residues [10].

Currently, alternative energy sources are becoming more relevant to carry out grafting polymerization, such as gamma rays [11], plasma [12], UV-light, and electron-beam [13]. Among these energy sources, high energy gamma rays of 1.17 and 1.33 MeV from ^{60}Co [14] are suitable to promote the homolytic rupture of stable C-H and C-C bonds such as the PP polymeric chains. Exposure to gamma rays produces free radicals (unstable), which are stabilized as peroxides and hydroperoxides under an oxidizing atmosphere [15]. Said process is named "pre-irradiation oxidative method" and is used to induce grafting polymerization onto PP surfaces with vinyl monomers [2]. The grafting degree of vinyl monomers depends on different factors, for example, solvent, time, or reaction

 doi:10.20944/preprints202111.0543.v1

temperature. In general terms, a well-understanding of reactants ensures the gathering of materials with the desired properties.

The current times demand that the new materials must satisfy multifunction or multipurpose needs [3]. MMA is a methacrylic monomer used for multiple purposes with an aliphatic (non-polar) side and a carbonyl group (polar) [16]. Also, NVI is a vinyl molecule with an N heteroatom ring used for diverse objectives [17,18]. Both carbonyl and imidazole groups can be employed in drug delivery systems, thanks to electrostatic interactions drug-polymer. Therefore, these polymers PP, PMMA, and PNVI may be implemented in the architecture of biomedical devices considering their biocompatibility [12,19,20].

In summary, this work presents grafting polymerization of MMA and NVI onto PP with the subsequent vancomycin loading [21], where the pH-responsiveness of NVI chains [22] was studied as well as other physicochemical properties such as swelling, contact angle, and vancomycin release.

2. Results

The materials were modified successfully with MMA by grafting polymerization using the pre-irradiation oxidative method. The grafting degree showed a dependence on the absorbed dose, temperature, monomer concentration, and reaction time, offering an excellent control on the yield and leading to the possibility of obtaining tailored grafted PP films. In the case of the grafting degree of NVI, this was carried out by direct method and did not show a considerable grafting yield if compared to MMA graft, which was more quantitative.

2.1. Grafting

During the grafting process on PP films, it is possible to observe certain tendencies regarding the acrylate grafted. Grafting of MMA exhibited a linear slope in the absorbed dose experiment (5 to 25 kGy) and in the time reaction experiment (5 to 26 h) reached a maximum grafting of 49.5% (25 kGy) and 31% (26 h), respectively (Figure 1a and b). However, the absorbed dose of 25 kGy could cause the detriment or deterioration on the PP matrix caused by polymer chain rupture, cross-linking, and increment of oxygenated groups [23]; for this reason, 5 kGy is the absorbed dose preferred.

Graft by varying temperature and monomer concentration completed the grating study. Regarding the effect of monomer concentration, there had a maximum grafting of 77.5% with a linear tendency (Figure 1c), but at the lower monomer concentration (20%), the graft is adequate to incorporate a superficial modification. Finally, the results indicated that the minimum activation temperature for this system is about 50 °C, which is congruent with the temperature to activate peroxides. The grafting degree increased progressively up to 80 °C, but at 90 °C the graft slightly decreased, indicating that when the reaction took place at 90 °C, the homopolymerization rate was also increased, so the graft is affected (Figure 1d). Therefore, the results suggest a possible control on the grafting rate either by reaction time or reaction temperature, offering a reasonable percentage of functionalization using a low absorbed dose of 5 kGy and low monomer concentration, thus, ensuring lesser damage in the properties of the matrix.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 29 November 2021 doi:10.20944/preprints202111.0543.v1

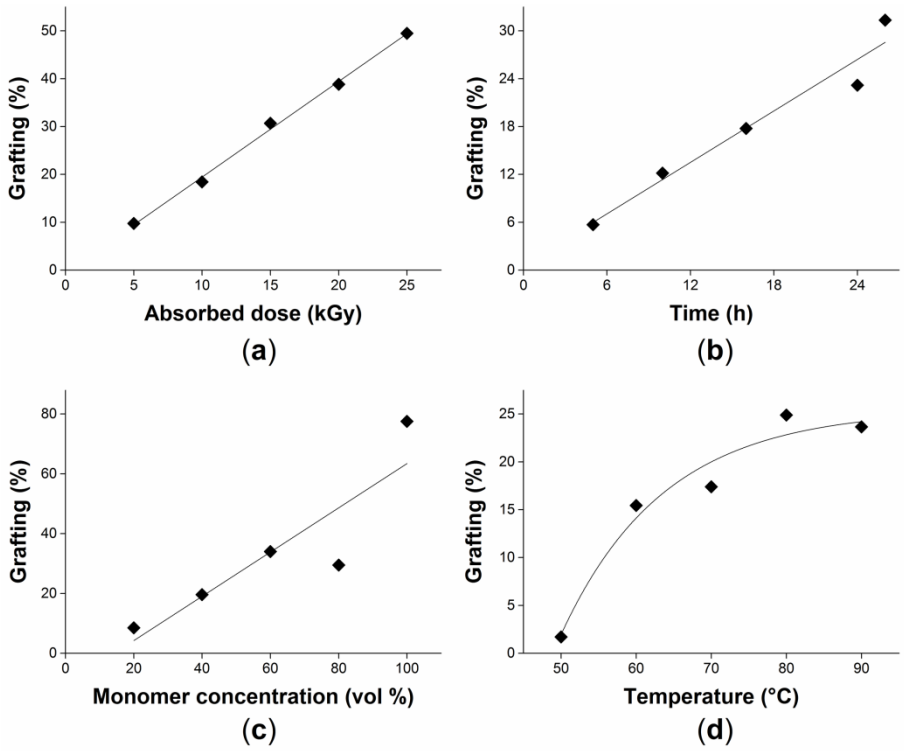


Figure 1. Grafting of MMA onto pristine PP: (**a**) effect of absorbed dose (16 h, 65 °C, MMA 20 vol%); (**b**) reaction time (5 kGy, 65 °C, MMA 30 vol%); (**c**) monomer concentration (15 kGy, 16 h, 70 °C); and (**d**) reaction temperature (5 kGy, 16 h, MMA 30 vol%).

The grafting of NVI was carried out on PP-*g*-MMA with different grafting degrees from 8.5 to 77.5%. The NVI grafting degree was lower compared to the results obtained in the MMA grafting indicating lower monomer reactivity. Since regardless of the MMA grafting degree of PP-*g*-MMA was higher, the grafting yield of NVI did not increase proportionally, obtaining yields ranging in 4-6.5%. Hence, it is understood that a slight modification with MMA is enough to promote the graft of NVI in a second step (Figure 2).

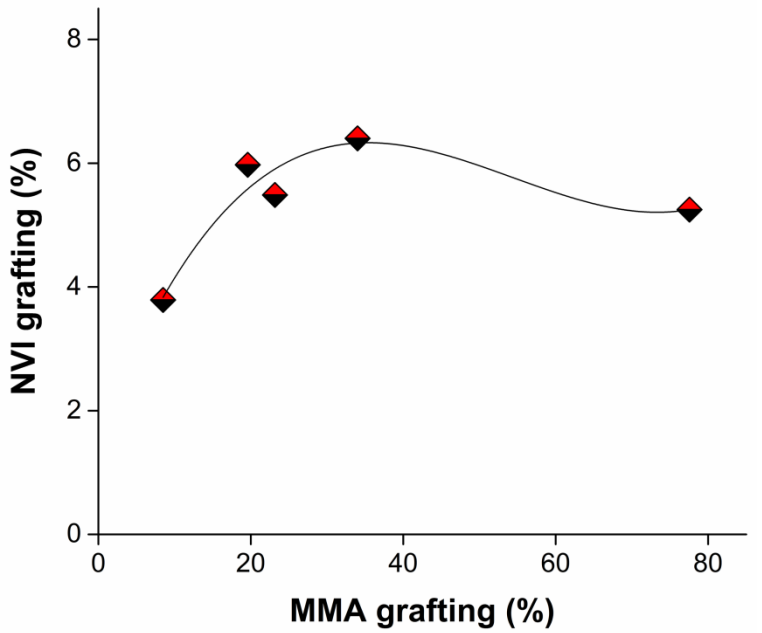


Figure 2. Results of NVI grafted on PP-*g*-MMA (50%); reaction conditions, absorbed dose 15 kGy, and room temperature (around 25 °C).

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 29 November 2021 doi:10.20944/preprints202111.0543.v1

SEM microscopy was performed to analyze the surface morphology of PP-*g*-MMA (17%) and (PP-*g*-MMA)-*g*-NVI (19.5/6%) (Figure 3). Morphological changes due to the polymerizations were observed, clearly indicating that the copolymerization brought to the surface an amorphous appearance, which is suitable for the adsorption of solids, as in this case was found.

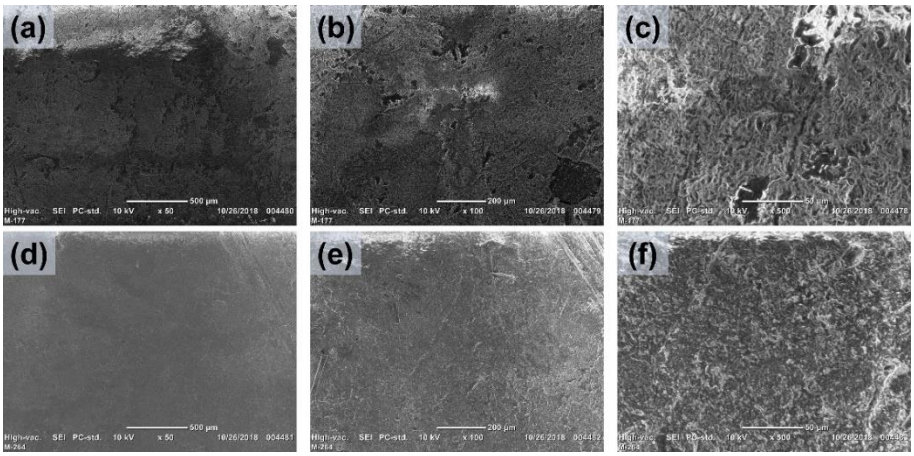


Figure 3. SEM images of (**a-c**) PP-*g*-MMA (17%) and (**d-f**) (PP-*g*-MMA)-*g*-NVI (19.5/6%), augmented from left to right x50, x100, and x500.

2.2. Infrared spectroscopy

Pristine PP, as a linear polymer constituted just of propylene units, displays in the infrared strong bands corresponding to different modes of C-H vibration, these are stretching in the region of 2949-2838 cm^{-1} and bending of methyl ($-CH_3$) and methylene ($-CH_2$) groups at 1456 and 1375 cm^{-1} respectively (Figure 4). Once achieved the first copolymer, the spectrum of PP-*g*-MMA, besides the aliphatic bands, shows the characteristic carbonyl band around 1724 cm^{-1}, which appears as a strong signal accompanied by the C-O stretching in 1145 and 1063 cm^{-1}. After the second graft with NVI, in addition the mentioned bands, there is an aromatic C-H stretching band in 3112 cm^{-1} and the characteristic bands of aromatic compounds in the fingerprint region between 900 and 650cm^{-1} [24].

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 29 November 2021 doi:10.20944/preprints202111.0543.v1

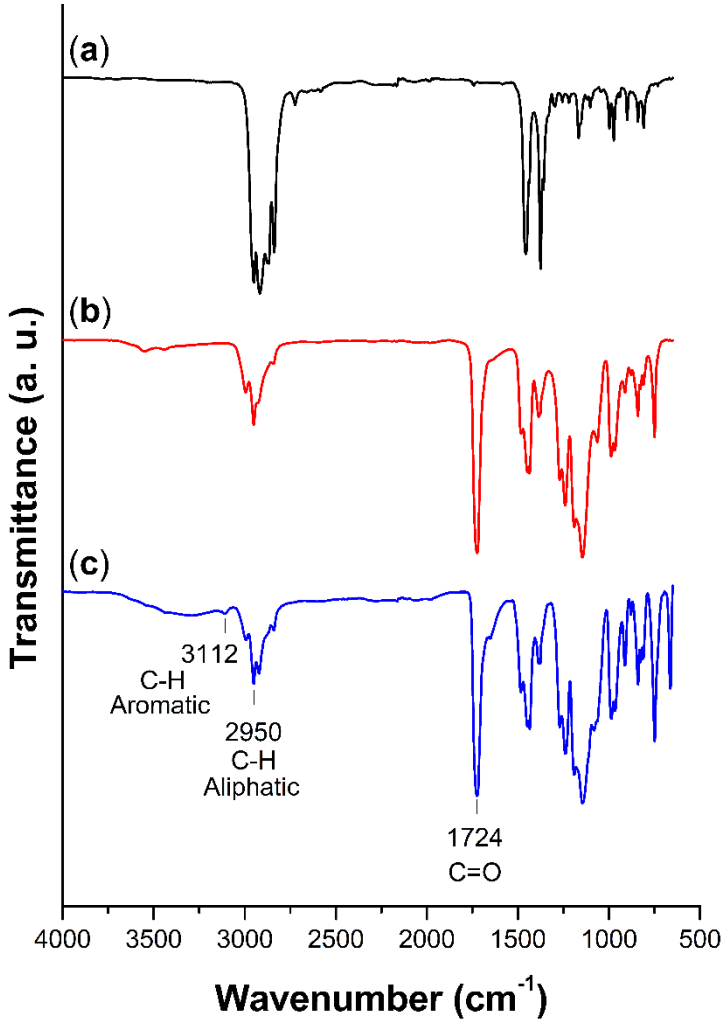


Figure 4. FTIR spectra: (**a**) non-irradiated PP, (**b**) PP-*g*-MMA (10%), and (**c**) (PP-*g*-MMA)-*g*-NVI (77.5/5%).

2.3. XPS spectroscopy

XPS study determined the surface atomic compositions of pristine PP [25] and grafted films, confirming the existence of MMA and NVI in the surface, as shown in Figure 5. The characteristic peaks of carbon (C 1s at 285.0 eV), oxygen (O 1s at 531.0 eV), and nitrogen (N 1s at 399.4 eV) were detected in the scanning, and the atomic level relationship was obtained from the core level peak areas of C 1s, O 1s, and N 1s, and multiplied by the corresponding sensitivity factors giving the results in Table 1.

Table 1. XPS results of pristine PP, PP-*g*-MMA (17%), and (PP-*g*-MMA)-*g*-NVI (77.5/5%): elemental composition used atomic sensitivity factor of C 1s: 0.314, O 1s: 0.733 and N 1s: 0.499.

Film	**Atomic (%)**		
	C	O	N
PP	100	-	-
PP-*g*-MMA (17%)	75.28	24.51	-
(PP-*g*-MMA)-*g*-NVI (77.5/5%)	72.59	22.90	3.76

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 29 November 2021 doi:10.20944/preprints202111.0543.v1

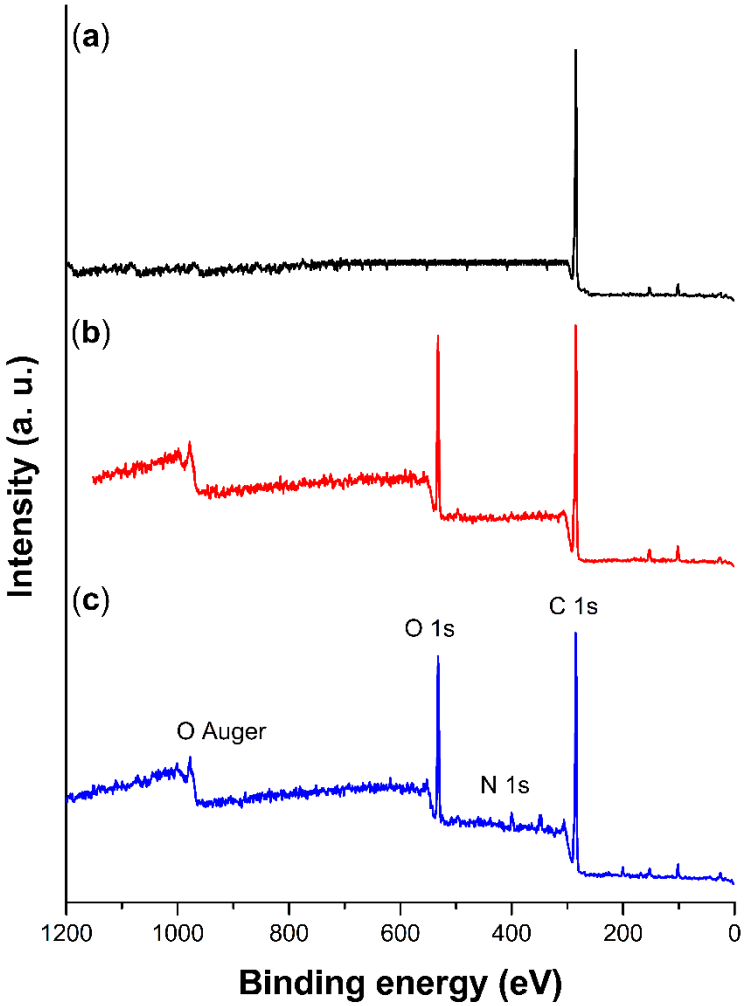


Figure 5. XPS scan of: (**a**) non-irradiated PP, (**b**) PP-*g*-MMA (17%), and (**c**) (PP-*g*-MMA)-*g*-NVI (77.5/5%).

2.4. Thermal gravimetry analysis

Thermograms of grafted films displayed a faster weight loss comparing the TGA curve observed in the non-irradiated PP film, as the 10% weight loss indicates (Figure 6). Decomposition temperature (Td) of pristine PP was higher than in the PP-*g*-MMA (25%) and (PP-*g*-MMA)-*g*-NVI (19.5/6%). The grafted films exhibited a multi-step decomposition; as is shown in the thermogram of PP-*g*-MMA (25%), there are two decomposition stages, while in the (PP-*g*-MMA)-*g*-NVI (19.5/6%), there are three decomposition stages (Table 2). In conclusion, the study showed that pristine PP had better thermal stability in comparison to grafted films, but this difference is merely informative because grafted films worked well at load and release temperatures.

Table 2. Results of TGA (weight loss, decomposition temperature, residue) analyses of non-irradiated PP film and films after single and binary graft.

Film	10 wt% loss (°C)	Td (°C)	Residue 800 °C (%)
PP	411.66	458.47	8.30
PP-*g*-MMA (25%)	358.52	370.28, 453.63	4.11
(PP-*g*-MMA)-*g*-NVI (19.5/6%)	303.43	291.32, 406.89, 455.90	2.33

Multiple decomposition stages in the grafted films suggest a localized polymer composition forming a multilayer material. These zones are core, internal layer, and surface;

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 29 November 2021 doi:10.20944/preprints202111.0543.v1

nonetheless, the PP zone is in the nucleus and preserves its inherent thermal properties. This characteristic is found in a surface-grafting polymer [26].

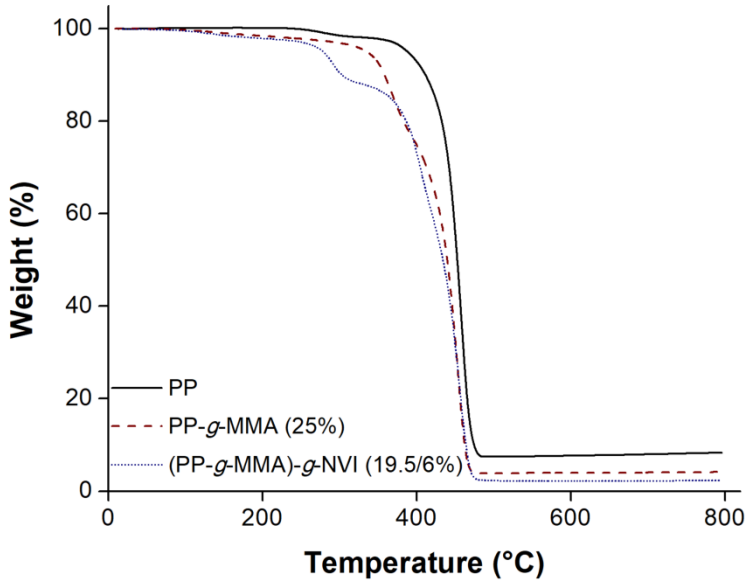


Figure 6. Thermogram runs under nitrogen atmosphere at 800 °C and heating rate 10 °C min^{-1}.

2.5. Swelling and critical pH

The unmodified and grafted PP films were put to swelling tests by immersion in different solvents for 24 h to determine their behavior and swelling in liquid mediums. Solvents were chosen according to their dielectric constant (ε), in order of polarity: water (78.5), dimethyl formaldehyde (DMF) (38.25), methanol (32.6), n-propanol (20.1), toluene (2.38), and n-hexane (1.89). The non-polar solvents n-hexane and toluene swelled the films more than the other solvents. One parameter to choose a suitable solvent to graft NVI was its capability to swell the film PP-*g*-MMA and as was expected, the highest swellings were achieved in toluene because both PP-*g*-MMA and (PP-*g*-MMA)-*g*-NVI have non-polar groups in their chains. These preliminary tests also helped to determine the viability of water for the load/release assays (Figure 7), despite water, as well as the other polar solvents, i. e., DMF, methanol, and n-propanol led the lowest percentages.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 29 November 2021 doi:10.20944/preprints202111.0543.v1

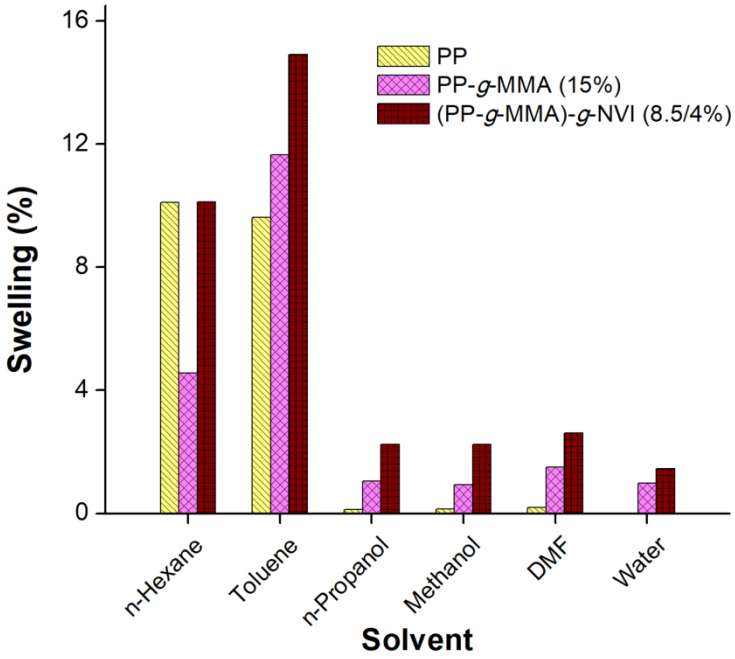


Figure 7. Swelling of the films in different solvents.

One of the characteristics of NVI-containing polymers is their pH response. This property is conferred by grafted PNVI, an electron donor polyelectrolyte (i.e., a Lewis base) that shrinks or expands by varying pH, as was verified with the study of swelling in pH range of 3-11. In this case, two films of (PP-*g*-MMA)-*g*-NVI with different compositions were analyzed, as shown in Figure 8. The behavior was similar in both films since they are hydrophilic at acid pH and hydrophobic at alkaline pH, with inflection points at pH 6.9 for (PP-*g*-MMA)-*g*-NVI (20/6%) and pH 7.3 for (PP-*g*-MMA)-*g*-NVI (34/6.5%), respectively. The most significant difference is the higher swelling in the film with more PMMA grafted, so it is inferred that this polyacrylate conferred a more hydrophilic behavior to the film. Although swelling between 1-4% would seem low, the thickness of the films is 18 mm, and samples were above 250 mg, so even small weight changes such as 0.1 mg are detected. Furthermore, swelling percentage was enough to load and release the vancomycin quantitatively (see section 2.7). Thus, it is concluded that the surface of the grafted films is moderately hydrophilic and pH-responsive able to uptake water and molecules between their chains.

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 29 November 2021 doi:10.20944/preprints202111.0543.v1

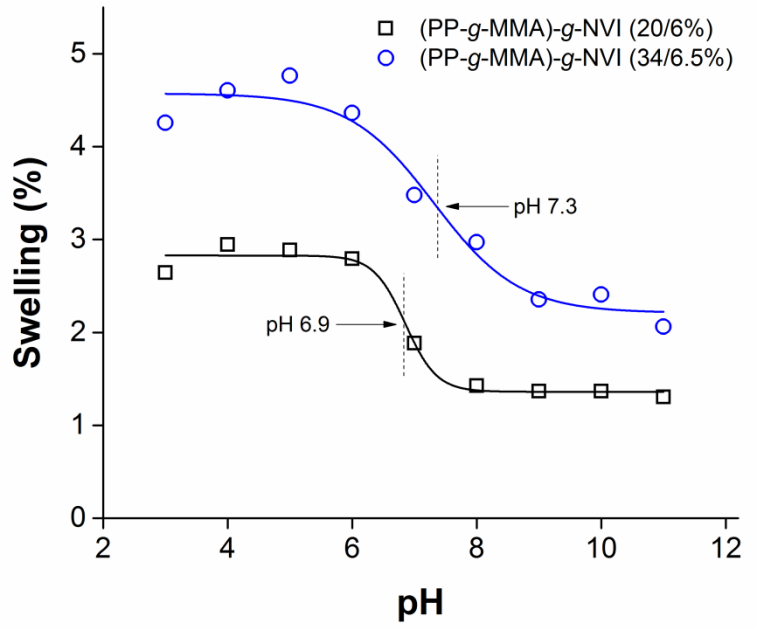
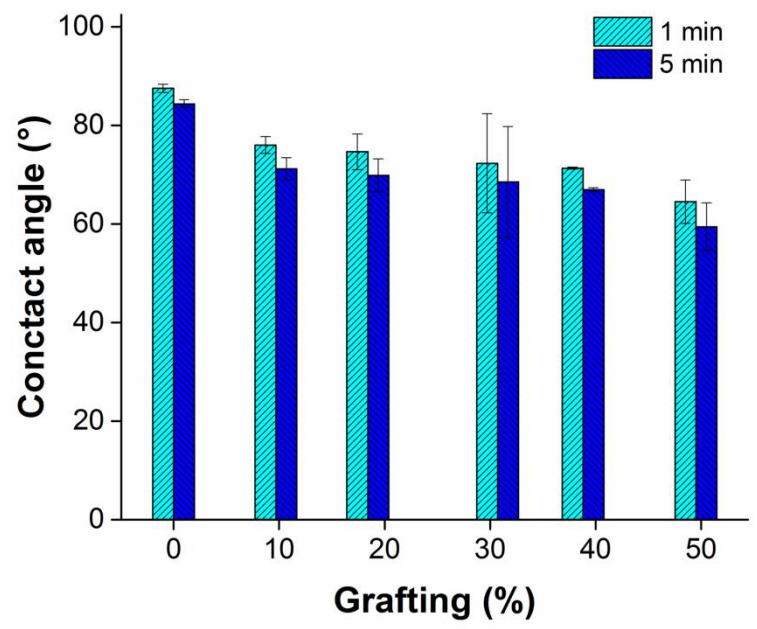


Figure 8. Critical pH, swelling in phosphate buffers.

2.6. Contact Angle

Wettability is an important parameter once MMA is grafted onto the surface because the acrylic chains are moderately hydrophilic, as swelling experiments showed (see section 2.5). Thereby, the contact angle before and after graft can be interpreted in terms of surface energy, increasing in this case, which means that grafted films are more hydrophilic than the pristine PP films, even when the grafted chains have a hydrophobic part, the amorphous acrylic chains increase the wettability (Figure 9). The contact angles determined by the drop of water on the pristine PP film were 87.5° at 1 min and 84.4° at 5 min, the highest compared with the grafted films, in which case the contact angle decreased as the MMA graft percentage increased. The change from hydrophobic to hydrophilic occurred since the first sample with the lowest graft that is PP-*g*-MMA (10%), with angles of 76° at 1 min and 71.2° at 5 min, and decreasing consecutively up to the last sample, PP-*g*-MMA (50%), exhibiting a contact angle of 64.5° at 1 min and 59.4° at 5 min, being the lowest angle and therefore the most hydrophilic.



Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 29 November 2021 doi:10.20944/preprints202111.0543.v1

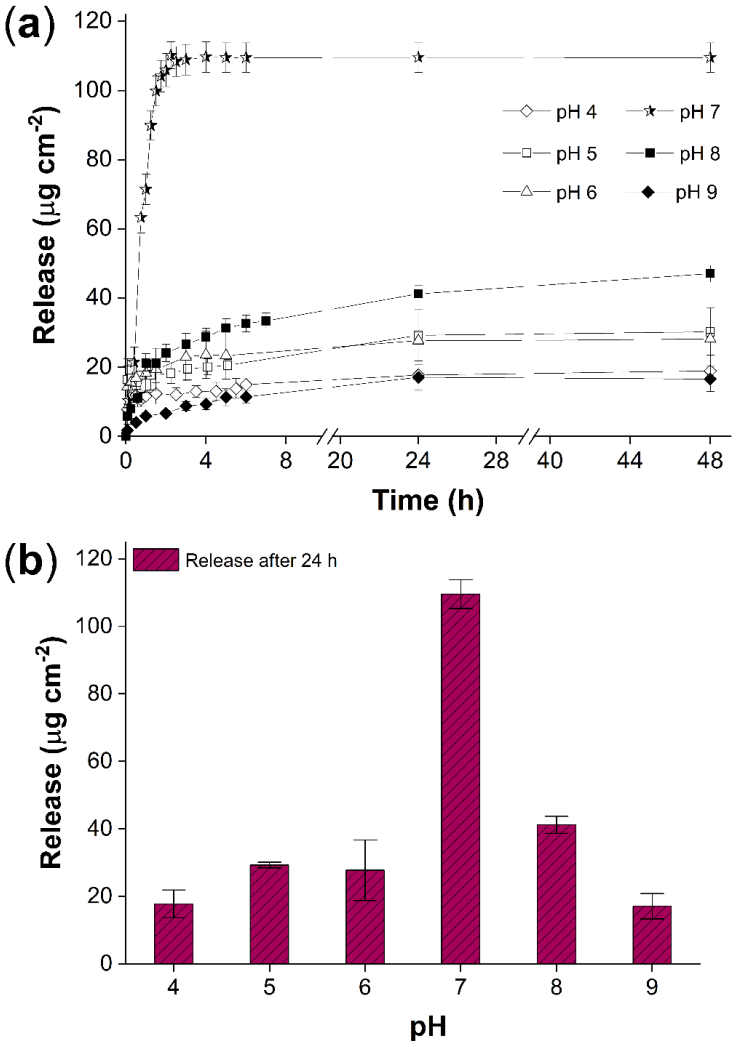
Figure 9. Contact angle of PP-*g*-MMA films, showed a change from hydrophobic to hydrophilic.

2.7. Load and release of vancomycin

Drug loading was performed using the sample (PP-*g*-MMA)-*g*-NVI (23/5.5%) in an aqueous solution of vancomycin hydrochloride [2 mg mL^{-1}]. The main reasons to choose water as solvent were its capability to dissolve the drug and its innocuousness. These properties are by far more relevant than the limited capability to swell the film [27].

Once the vancomycin was loaded, the release was in a controlled pH [28], in both acid (pH 4-6) and alkaline (pH 8-9) buffer medium to determine the release rate in simulated physiological conditions, considering the pH-responsiveness of PNVI grafted [29], particularly at a pH close to that of the skin [30,31].

At neutral pH, the release rate was the highest and the maximum reached within the first 2 h, that is 109.5 ± 4.25 μg cm^{-2} (Figure 10a), which is around 83% of total vancomycin loaded. While in alkaline and acid pH, the release rate and the amount of vancomycin released decreased considerably (Figure 10b). It was found that even after 48 h, the release value at pH 8 was only 47.1 ± 2.46 μg cm^{-2}. In all buffers, unlike neutral pH, release rates were slower, and the maximum concentration was not reached at 48 h. Checking that the kinetics follow a different path than at neutral pH given that under neutral conditions the release rate was around three times and in a fraction of the time (2 h). Therefore, there is an expedited diffusion at pH 7 and a prolonged release at pH 4, 5, 8, and 9.



 doi:10.20944/preprints202111.0543.v1

Figure 10. (PP-*g*-MMA)-*g*-NVI (23/5.5%): (**a**) release of vancomycin in phosphate buffers 0.1 M at different pH and (**b**) release reached at 24 h.

3. Discussion

The difficulty of grafting NVI directly onto pristine PP was overcome by the easiness to graft MMA. The difference between the reactivity of MMA and NVI is attributed to electronic effects, solvent, stability of intermediates (during chain reaction), and homopolymerization rate (reaction in competition during the copolymerization). The surface of PP grafted films exhibited changes in their hydrophilic/hydrophobic behavior and becoming them able to load and release vancomycin in different pH conditions. These grafted materials are not limited to the vancomycin evaluated since the drug loading by swelling is a general method for delivery with many bioactive principles [32].

SEM analysis suggested that the graft of both copolymers takes place onto the surface of PP-*g*-MMA and (PP-*g*-MMA)-*g*-NVI films, which is supported by observing amorphous layers and by the fact, there was no significant change in the film´s size. This information is consistent with infrared, where it was possible to observe the corresponding bands of the acrylic chains on the surface. While in XPS, elemental analysis detected the presence of O and N from the graft. Finally, in TGA it was confirmed that grafted PP is thermally stable [33], even when the amorphous grafted binary and single copolymers decomposed earlier than pristine PP.

Regarding the swelling properties, grafted films showed a slight swelling on the polar solvents, which is a significant difference with pristine PP because the polar solvent absorbs between the alkyl backbones. Although, the water drop contact angle showed that the surface of the PP-*g*-MMA was wet consistently as the contact angle decreased while the grafting degree increased. Overall, the swelling and contact angle results suggest an increase in the surface energy of the grafted films, being that suitable to use in drug release systems [34].

The release rate of vancomycin on (PP-*g*-MMA)-*g*-NVI (23/5.5%) was studied, finding that this molecule, with several amines and one carboxylic group, at an acid or alkaline pH formed strong H interactions with the grafted chains, prolonging the release and decreasing the release rate [35]. At these conditions, the release could be conducted by a simultaneous equilibrium, with an interchange of ions from the system and medium [36]. Opposite, the critical pH is reached at neutral conditions, where there is no excess of H^+ or OH^- ions, which eased the release due to the strong interaction among medium and grafted chains [37,38], yielding 83% of the total drug released in the first hours.

4. Materials and Methods

4.1. Materials

High-density polypropylene films (0.18 cm thickness) were from Goodfellow. Vancomycin hydrochloride, MMA (99%), and NVI (99%) were purchased from Aldrich Chemical Co. (St. Louis MO, USA), and monomers were purified by vacuum distillation. Boric acid, citric acid, trisodium orthophosphate, and solvents (including double distilled water) were acquired from Baker (Mexico City, Mexico).

4.2. Grafting method

MMA was grafted by oxidative pre-irradiation method, and NVI was grafted by direct method [39], in both cases using a gamma-rays source of ^{60}Co Gammabeam 651-PT (UNAM, Mexico) at a dose rate of 8.4 kGy h^{-1}, the methods are described in detail in the next sections 4.2.1 and 4.2.2.

4.2.1. Grafting polymerization of MMA using the oxidative pre-irradiation method

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 29 November 2021 doi:10.20944/preprints202111.0543.v1

PP films of 3x2x0.18 cm (wide, length, and thickness) were weighed (around 250 mg) and placed into open glass ampoules and exposed to gamma irradiation in the presence of air. Afterward, the solutions of MMA were prepared in methanol as the solvent in different concentrations (Table 3) and then added (5 mL) into the glass ampoules with the pre-irradiated PP film. The ampoules were degassed by freezing and thawing cycles with liquid nitrogen followed by a purged in the vacuum line; subsequently, the ampoules were sealed at vacuum. Finally, the polymerization was initiated by heating in a water bath at different times and temperatures. Once completed the reaction time, the ampoules were open, and the films were rinsed in a water/ethanol mixture 50/50 vol% under constant stirring for 24 h. Finally, the samples were dried in a vacuum oven at 60 °C for 24 h. The grafting percentage was calculated according to Equation (1), using the weight of pristine (W_0) and grafted (W_g) film.

$$Grafting\ (\%) = 100[(W_g - W_0)/W_0] \quad (1)$$

Table 3. Reaction conditions of grafting polymerization of MMA by pre-irradiation oxidative and grafting degree.

Experiment	Dose (kGy)	Time (h)	Temperature (°C)	Concentration (vol%)	Grafting (%)
Dose	5	16	65	20	10
Dose	10	16	65	20	18
Dose	15	16	65	20	31
Dose	20	16	65	20	39
Dose	25	16	65	20	49.5
Time	5	5	65	30	6
Time	5	10	65	30	12
Time	5	16	65	30	18
Time	5	24	65	30	23
Time	5	26	65	30	31
Concentration	15	16	70	20	8.5
Concentration	15	16	70	40	19.5
Concentration	15	16	70	60	34
Concentration	15	16	70	80	29.5
Concentration	15	16	70	100	77.5
Temperature	5	16	60	30	15.5
Temperature	5	16	70	30	17.5
Temperature	5	16	80	30	25
Temperature	5	16	90	30	23.5

4.2.2 Grafting of NVI on PP-*g*-MMA by direct method

PP-*g*-MMA films with a different MMA grafting degree (Table 4) were weighed and placed into glass ampoules containing 6 mL of NVI in toluene (50 vol%). Then, oxygen was removed from the ampoules with freezing and thawing cycles (see section 4.2.1), then the ampoules were sealed with a blowtorch and irradiated with an absorbed dose of 15 kGy at room temperature. Finally, the ampoules were open, and the grafted films were rinsed with methanol and dried into a vacuum oven at 60 °C for 24 h. The weight of films was recorded to calculate the grafting degree according to Equation (1).

Table 4. (PP-*g*-MMA)-*g*-NVI, reaction conditions of NVI grafting by direct method.

MMA grafting (%)	Dose (kGy)	Concentration (vol%)	Total grafting MMA/NVI (%)
8.5	15	50	8.5/4

Preprints (www.preprints.org) | NOT PEER-REVIEWED | Posted: 29 November 2021 doi:10.20944/preprints202111.0543.v1

19.5	15	50	19.5/6
23	15	50	23/5.5
34	15	50	34/6.5
77.5	15	50	77.5/5

4.3. *Swelling experiments*

The samples were placed in different solvents until they reached the limit swelling (maximum 24 h) at room temperature (around 25 °C). Excess solvent was removed with an absorbent paper. The solvents used for swelling were water, methanol, n-propanol, DMF, and n-hexane. The swelling percentage (%) was calculated according to Equation (2):

$$Swelling\ (\%) = 100[(W_s - W_d)/W_d] \quad (2)$$

where W_s and W_d are the weights of swollen and dried films, respectively.

The film (PP-*g*-MMA)-*g*-NVI (23/5.5%) was employed to determine the critical pH. The sample was put inside different phosphate buffers (pH 4-9) for 24 h to record the weight. After each measurement, the sample was rinsed with double distilled water and submerged in the next buffer. Equation (2) was also applied to calculate the swelling at different pH.

4.4. *Load and release of vancomycin*

Vancomycin was loaded in the film (PP-*g*-MMA)-*g*-NVI (23/5.5%). A fresh dissolution of vancomycin hydrochloride [2 mg mL^{-1}] was prepared with double distilled water and poured into a vial containing the grafted film. The vial was stored in refrigeration at 4 °C for 48 h; then, the film was extracted, dried, and stored at room temperature (around 25 °C). The amount of vancomycin loaded was calculated by measuring the vancomycin released under sonication and replacing the solvent (double distilled water) until reaching absorbances close to 0, these absorbances represent the total vancomycin concentration, which was 132.2±0.76 μg cm^{-2}.

Release experiments were performed using the same film that is (PP-*g*-MMA)-*g*-NVI (23/5.5%) in 4 mL of sodium phosphate buffer (pH 4-9), 0.1 M, and at 37 °C. The releasing was monitored at different times, recording absorbances by spectrophotometry at 280 nm [40].

4.5. *Instrumental*

Infrared spectroscopy attenuated total reflection (FTIR-ATR) spectra of dry pristine and modified films were analyzed using a Perkin-Elmer Spectrum 100 spectrometer (Perkin Elmer Cetus Instruments, Norwalk, CT) with 16 scans.

X-ray photoelectron spectroscopy was performed in an ultra-high vacuum (UHV) system Scanning XPS microprobe PHI 5000 Versa Probe II, with excitation source of Al Kα monochromatic, energy 1486.6 eV, 100 μm beam diameter, and with a Multi-Channel Detector (MCD). The XPS spectra were obtained at 45° to the normal surface in pass energy mode (CAE) E0 = 117.40 and 11.75 eV. Peak positions were calibrated to Ag 3d5/2 photopeak at 368.20 eV, having a full width at half maximum of 0.56 eV, and the energy scale corrected using the C 1s peak brought to 285.0 eV.

Kruss DSA 100 drop shape analyzer (Matthews NC, USA) was employed to measure water droplet contact angle at 1 and 5 min in triplicates.

Scanning electron microscope (SEM) images were acquired in the Zeiss Evo LS15 instrument. Small pieces (1cm length) of grafted samples were cut and directly analyzed under a high vacuum without using any coating.

Thermogravimetric analysis (TGA) data of weight loss and decomposition of pristine and modified films (around 10 mg) were analyzed under a heating rate of 10 °C min^{-1} and run from 20 to 800 °C in a TGA instrument Q50 TA Instruments (New Castle, DE).

Ultraviolet-visible (UV-vis) spectrophotometer model Agilent 8453 (Germany) was utilized to analyze the release of vancomycin at 280 nm, using quartz cuvettes (1 cm length).

5. Conclusions

Radiation-grafting was a convenient method to modify the surface of PP films. In the first step the PP-*g*-MMA was obtained by the pre-irradiation oxidative method, and in the second step, the final material (PP-*g*-MMA)-*g*-NVI was achieved by simultaneous irradiation. The grafting of NVI endowed the surface with pH-responsiveness and the chains were able to load vancomycin hydrochloride in a concentrate aqueous dissolution [2 mg mL^{-1}]. The release of vancomycin was dependent at the pH medium being higher the rate at pH 7 and more controlled release at non-neutral pH; the maximum amount of drug released at buffer pH 7 was [109.5 ± 4.25 μg cm^{-2}] after 48 h. These findings suggest an active interaction in the equilibrium of NVI chains-vancomycin-release medium. This kind of superficial modification onto a non-reactive thermoplastic, such as the PP, provides a route to upgrade materials to get more sophisticated devices.

Author Contributions: Conceptualization, FLS and EB; methodology, FLS; software, FLS and JELB; validation, JELB; formal analysis, GGFR and SGD; investigation, FLS; resources, EB; data curation, SGD; writing—original draft preparation, FLS; writing—review and editing, JELB, GGFR, and SGD; visualization, GGFR and SGD; supervision, EB; project administration, EB; funding acquisition, EB. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by DGAPA-UNAM, grant number IN202320 (Mexico).

Acknowledgments: FLS CVU 409872 thanks CONACyT. Authors would like to thank B. Leal from ICN-UNAM for his technical assistance in the irradiation experiments, to C. Flores from IIM-UNAM for his technical assistance in SEM, and to L. Huerta-Arcos from IIM-UNAM for his technical assistance in XPS.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Maddah, H.A. Polypropylene as a promising plastic : a review. *Am. J. Polym. Sci.* **2016**, *6*, 1–11, doi:10.5923/j.ajps.20160601.01.
2. Minko, S. Grafting on solid surfaces: "grafting to" and "grafting from" methods. In *Polymer Surfaces and Interfaces: Characterization, Modification and Applications*; Stamm, M., Ed.; Springer: Berlin, Heidelberg, 2008; pp. 215–234 ISBN 978-3-540-73865-7.
3. Zhang, S.; Yu, P.; Zhang, Y.; Ma, Z.; Teng, K.; Hu, X.; Lu, L.; Zhang, Y.; Zhao, Y.; An, Q. Remarkably boosted molecular delivery triggered by combined thermal and flexoelectrical field dual stimuli. *ChemistrySelect* **2020**, *5*, 6715–6722, doi:10.1002/slct.202000423.
4. Contreras-García, A.; Bucio, E.; Concheiro, A.; Alvarez-Lorenzo, C. Polypropylene grafted with NIPAAm and APMA for creating hemocompatible surfaces that load/elute nalidixic acid. *React. Funct. Polym.* **2010**, *70*, 836–842, doi:10.1016/j.reactfunctpolym.2010.07.019.
5. Flores-Rojas, G.G.; López-Saucedo, F.; Bucio, E.; Isoshima, T. Covalent immobilization of lysozyme in silicone rubber modified by easy chemical grafting. *MRS Commun.* **2017**, *7*, 904–912, doi:10.1557/mrc.2017.115.
6. Naguib, H.F.; Aly, R.O.; Sabaa, M.W.; Mokhtar, S.M. Gamma radiation induced graft copolymerization of vinylimidazole-acrylic acid onto polypropylene films. *Polym. Test.* **2003**, *22*, 825–830, doi:10.1016/S0142-9418(03)00018-7.
7. Chung, T.C.; Rhubright, D.; Jiang, G.J. Synthesis of polypropylene-graft-poly(methyl methacrylate) copolymers by the

borane approach. *Macromolecules* **1993**, *26*, 3467–3471, doi:10.1021/ma00066a001.

8. Kudryavtsev, V.N.; Kabanov, V.Y.; Yanul', N.A.; Kedik, S.A. Polypropylene modification by the radiation graft polymerization of N-vinylcaprolactam. *High Energy Chem.* **2003**, *37*, 382–388, doi:10.1023/B:HIEC.0000003396.56980.1d.
9. Xu, X.; Zhang, L.; Zhou, J.; Wang, J.; Yin, J.; Qiao, J. Thermal behavior of polypropylene-g-glycidyl methacrylate prepared by melt grafting. *J. Macromol. Sci. Part B* **2015**, *54*, 32–44, doi:10.1080/00222348.2014.983856.
10. Anastas, P.T.; Kirchhoff, M.M. Origins, current status, and future challenges of green chemistry. *Acc. Chem. Res.* **2002**, *35*, 686–694, doi:10.1021/ar010065m.
11. Bucio, E.; Burillo, G. Radiation-induced grafting of sensitive polymers. *J. Radioanal. Nucl. Chem.* **2009**, *280*, 239–243, doi:10.1007/s10967-009-0505-9.
12. Saxena, S.; Ray, A.R.; Kapil, A.; Pavon-Djavid, G.; Letourneur, D.; Gupta, B.; Meddahi-Pellé, A. Development of a new polypropylene-based suture: Plasma grafting, surface treatment, characterization, and biocompatibility studies. *Macromol. Biosci.* **2011**, *11*, 373–382, doi:10.1002/mabi.201000298.
13. Kumari, M.; Gupta, B.; Ikram, S. Characterization of N-isopropyl acrylamide/acrylic acid grafted polypropylene nonwoven fabric developed by radiation-induced graft polymerization. *Radiat. Phys. Chem.* **2012**, *81*, 1729–1735, doi:10.1016/j.radphyschem.2012.05.018.
14. Strohmaier, S.; Zwierzchowski, G. Comparison of (60)Co and (192)Ir sources in HDR brachytherapy. *J. Contemp. Brachytherapy* **2011**, *3*, 199–208, doi:10.5114/jcb.2011.26471.
15. Clark, D.E. Peroxides and peroxide-forming compounds. *Chem. Heal. Saf.* **2001**, *8*, 12–22, doi:10.1016/S1074-9098(01)00247-7.
16. Wypych, G. PMMA polymethylmethacrylate. In *Handbook of Polymers*; Wypych, G.B.T.-H. of P. (Second E., Ed.; ChemTec Publishing: Toronto, 2016; pp. 467–471 ISBN 978-1-895198-92-8.
17. Fink, J.K. Poly(vinylimidazole). In *Handbook of Engineering and Specialty Thermoplastics*; Fink, J.K., Ed.; John Wiley & Sons: Hoboken, NJ, USA, 2011; pp. 251–291.
18. Camacho-Cruz, L.A.; Velazco-Medel, M.A.; Parra-Delgado, H.; Bucio, E. Functionalization of cotton gauzes with poly(N-vinylimidazole) and quaternized poly(N-vinylimidazole) with gamma radiation to produce medical devices with pH-buffering and antimicrobial properties. *Cellulose* **2021**, *28*, 3279–3294, doi:10.1007/s10570-021-03725-w.
19. de Magalhães Pereira, M.; Lambert Oréfice, R.; Sander Mansur, H.; Paz Lopes, M.T.; de Marco Turchetti-Maia, R.M.; Vasconcelos, A.C. Preparation and biocompatibility of poly (methyl methacrylate) reinforced with bioactive particles. *Mater. Res.* **2003**, *6*, 311–315, doi:10.1590/S1516-14392003000300002.
20. Wang, B.; Liu, H.-J.; Chen, Y. A biocompatible poly(N-vinylimidazole)-dot with both strong luminescence and good catalytic activity. *RSC Adv.* **2016**, *6*, 2141–2148, doi:10.1039/C5RA20640E.
21. Szász, M.; Hajdú, M.; Pesti, N.; Domahidy, M.; Kristóf, K.; Zahár, ákos; Nagy, K.; Szabó, D. In vitro efficiency of vancomycin containing experimental drug delivery systems. *Acta Microbiol. Immunol. Hung.* **2013**, *60*, 461–468, doi:10.1556/AMicr.60.2013.4.7.
22. Zavala-Lagunes, E.; Ruiz, J.C.; Varca, G.H.C.; Bucio, E. Synthesis and characterization of stimuli-responsive polypropylene containing N-vinylcaprolactam and N-vinylimidazole obtained by ionizing radiation. *Mater. Sci. Eng. C* **2016**, *67*, 353–361, doi:10.1016/j.msec.2016.05.044.
23. Kawamura, Y. Effects of gamma irradiation on polyethylene, polypropylene, and polystyrene. In *Irradiation of food and packaging*; Komolprasert, V., Morehouse, K.M., Eds.; ACS Symposium Series; American Chemical Society: Washington DC, 2004; Vol. 875, pp. 262–276 ISBN 0-8412-3869-3.
24. Ramasamy, R. Vibrational spectroscopic studies of imidazole. *Armen. J. Phys.* **2015**, *8*, 51–55.
25. Lannon, J.M.; Meng, Q. Analysis of a poly(propylene)(PP) Homopolymer by XPS. *Surf. Sci. Spectra* **1999**, *6*, 79–82, doi:10.1116/1.1247902.
26. Abudonia, K.S.; Saad, G.R.; Naguib, H.F.; Eweis, M.; Zahran, D.; Elsabee, M.Z. Surface modification of polypropylene film

by grafting with vinyl monomers for the attachment of chitosan. *J. Polym. Res.* **2018**, *25*, 125, doi:10.1007/s10965-018-1517-3.

27. Alvarez-Lorenzo, C.; Bucio, E.; Burillo, G.; Concheiro, A. Medical devices modified at the surface by γ-ray grafting for drug loading and delivery. *Expert Opin. Drug Deliv.* **2010**, *7*, 173–185, doi:10.1517/17425240903483174.
28. Johnson, J.L.H.; Yalkowsky, S.H. Reformulation of a new vancomycin analog: an example of the importance of buffer species and strength. *AAPS PharmSciTech* **2006**, *7*, E33–E37, doi:10.1208/pt070105.
29. Obando-Mora, Á.; Acevedo-Gutiérrez, C.; Pérez-Cinencio, J.; Sánchez-Garzón, F.; Bucio, E. Synthesis of a pH- and thermo-responsive binary copolymer poly(N-vinylimidazole-co-N-vinylcaprolactam) grafted onto silicone films. *Coatings* **2015**, *5*, 758–770, doi:10.3390/coatings5040758.
30. Wagner, H. pH profiles in human skin: influence of two in vitro test systems for drug delivery testing. *Eur. J. Pharm. Biopharm.* **2003**, *55*, 57–65, doi:10.1016/S0939-6411(02)00125-X.
31. Hendi, A.; Umair Hassan, M.; Elsherif, M.; Alqattan, B.; Park, S.; Yetisen, A.K.; Butt, H. Healthcare applications of pH-sensitive hydrogel-based devices: a review. *Int. J. Nanomedicine* **2020**, *Volume 15*, 3887–3901, doi:10.2147/IJN.S245743.
32. Siepmann, J.; Siepmann, F. Swelling controlled drug delivery systems. In *Fundamentals and Applications of Controlled Release Drug Delivery*; Siepmann, J., Siegel, R., Rathbone, M., Eds.; Springer US: Boston, MA, 2012; pp. 153–170.
33. Quinelato, R.R.; Albitres, G.A.; Mariano, D.M.; Freitas, D.F.; Mendes, L.C.; Rodrigues, D.C.; Filho, M.F. Influence of polycaprolactone and titanium phosphate in the composites based upon recycled polypropylene. *J. Thermoplast. Compos. Mater.* **2020**, 1–21, doi:10.1177/0892705720963159.
34. Nasef, M.M.; Gupta, B.; Shameli, K.; Verma, C.; Ali, R.R.; Ting, T.M. Engineered bioactive polymeric surfaces by radiation induced graft copolymerization: strategies and applications. *Polymers (Basel).* **2021**, *13*, 3102, doi:10.3390/polym13183102.
35. Ahmad Nor, Y.; Zhang, H.; Purwajanti, S.; Song, H.; Meka, A.K.; Wang, Y.; Mitter, N.; Mahony, D.; Yu, C. Hollow mesoporous carbon nanocarriers for vancomycin delivery: understanding the structure–release relationship for prolonged antibacterial performance. *J. Mater. Chem. B* **2016**, *4*, 7014–7021, doi:10.1039/C6TB01778A.
36. Zhuo, S.; Zhang, F.; Yu, J.; Zhang, X.; Yang, G.; Liu, X. pH-Sensitive biomaterials for drug delivery. *Molecules* **2020**, *25*, 5649, doi:10.3390/molecules25235649.
37. Shan, S. -o.; Herschlag, D. The change in hydrogen bond strength accompanying charge rearrangement: Implications for enzymatic catalysis. *Proc. Natl. Acad. Sci.* **1996**, *93*, 14474–14479, doi:10.1073/pnas.93.25.14474.
38. Wood, J.L. pH-controlled hydrogen-bonding. *Biochem. J.* **1974**, *143*, 775–777, doi:10.1042/bj1430775.
39. López-Saucedo, F.; Alvarez-Lorenzo, C.; Concheiro, A.; Bucio, E. Radiation-grafting of vinyl monomers separately onto polypropylene monofilament sutures. *Radiat. Phys. Chem.* **2017**, *132*, 1–7, doi:10.1016/j.radphyschem.2016.11.006.
40. Li, B.; Brown, K. V; Wenke, J.C.; Guelcher, S.A. Sustained release of vancomycin from polyurethane scaffolds inhibits infection of bone wounds in a rat femoral segmental defect model. *J. Control. Release* **2010**, *145*, 221–230, doi:10.1016/j.jconrel.2010.04.002.