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Molecular structure effects on the post irradiation diffusion in polymer gel dosimeters

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HIGHLIGHTS

- A chemical system based on itaconic acid and N-N′ methylenebisacrylamide was presented.
- A chemical point of view of the results of the irradiated dosimeters was done.
- A modified monomer was synthesized modifying an itaconic acid molecule.
- Effects on the dosimetric behavior in these new materials were tested.
- Post-irradiation diffusion on the itaconic acid based dosimeters was analyzed.

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ABSTRACT

Polymer gel dosimeters have specific advantages for recording 3D radiation dose distribution in diagnostic and therapeutic medical applications. But, even in systems where the 3D structure is usually maintained for long periods of time after irradiation, it is still not possible to eliminate the diffusion of the different species in the regions of dose gradients within the gel. As a consequence, information of the dose loses quality over time. In the pursuit of a solution and to improve the understanding of this phenomenon a novel system based on itaconic acid and N-N′-methylene-bisacrylamide (BIS) is hereby proposed. Effects of changes in the chemical structure of the monomers over the dosimetric sensitivity and over the post-irradiation diffusion of species was studied. In this study, one of the carboxylic groups of the itaconic acid molecule was modified with aniline to obtain molecules with similar reactivity but different molecular sizes. Then, dosimeters based on these modified species and on the original ITA molecules were irradiated in an X-ray tomography apparatus at different doses up to 173 Gy. Afterwards, the resulting dosimeters were characterized by Raman spectroscopy and optical absorbance in order to study their feasibility and capabilities as dosimetric systems, and by optical-CT to analyze the post irradiation diffusion.

1. Introduction

Polymer gel dosimeters have specific advantages for recording 3D radiation dose distribution representing a key factor for most of the therapeutic and diagnostic radiation techniques (Baldock et al., 2010; Doran, 2009). Radiation-induced polymerization and crosslinking reactions that take place in dosimeters have been studied for different monomers like acrylamide and N-N′-methylene-bisacrylamide (BIS) and most recently for less toxic monomers like N-isopropyl acrylamide (NIPAM) and BIS (Chiu et al., 2014; Huang et al., 2013). The resulting dosimeters presented a linear response with radiation and proved to be excellent candidates for measuring three-dimensional dose distributions, which is a fundamental characteristic of dosimetry systems, as stated by Gore and Kang (Gore and Kang, 1984) on their studies on Fricke

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Gel dosimeters. An important aspect of this development was to stabilize the geometric dose information by incorporating the aqueous Fricke solution into a gel matrix and setting the bases for almost all modern dosimetry systems. Later on, Maryanski et al. (1993) proposed a new type of dosimeters where polymerization of a monomer and cross linker species was induced by radiation. Upon irradiation, water molecules dissociate into OH and H radicals that break the double C=C bonds of co-monomers, the resulting co-monomer radicals interact with other co-monomers and produce a chain reaction to form 3D polymer networks that are spatially retained in a gelatin matrix. The amount of formed polymer is related to the absorbed dose received by the polymer gel. The degradation of the spatial dose information because of ion diffusion represents the main limitation for Fricke gel dosimetry (Baldock et al., 2001). However, the use of polymers instead of ionic species considerably lowers the diffusion effects and if a proper formulation of the dosimetric system is selected, then the irradiation assays and dose distribution measurements can be carried out on different times without losing sensitivity or spatial distribution quality.

In this work a new polymeric system consisting of: (1) a monomer (itaconic acid), (2) a cross linking agent (BIS) acting as radiation induced reactants, (3) agarose or gelatin to maintain spatial distribution upon radiation, and (4) an oxygen scavenger molecule (Tetrakis hydroxymethyl phosphonium chloride THPC) to prevent oxygen free radical polymerization inhibition, is studied. These are the typical constituents of a polymeric dosimeter, however, because of itaconic acid nature that could prevent the gelatin gelification, a phosphate based buffer solution was used instead of water for the preparation of the dosimeters. The monomers ITA and BIS have been already studied for hydrogel formation and the polymerization induced by other radical initiation methods has been demonstrated (Caykara and Akcakaya, 2007).

The diffusion of species in a solution or gelatin matrix depends on several phenomena, chemical interactions, polymer entanglement, molecular size, mesh size, among them (Cherdhirankorn et al., 2009; Masaro and Zhu, 1999). Most of these properties are inherent to each chemical system and can't be varied for a specific dosimeter. Nevertheless, if similar monomer molecules are selected for the dosimeters preparation relevant information can be obtained from their differences upon irradiation.

The main objective of this work is to establish a methodology to study the relationship between the molecular structure of the monomers and the post irradiation changes in polymer gel dosimetric systems. For that purpose different particular goals were defined, first to study the performance of a new polymeric dosimetric system based on itaconic acid and BIS (ITA-BIS). Also, the chemical modification of the itaconic acid molecule by a coupling reaction with aniline is studied (modified ITA). Finally, a methodology to correlate the post irradiation diffusion effects in polymeric dosimeters is applied to the ITA-BIS dosimeters and compared with the preliminary results obtained for dosimeters prepared with the modified ITA and BIS.

2. Materials and methods

2.1. Itaconic acid chemical modification

The synthesis of the new monomer was performed through the formation of an amide bond mediated by a carbodiimide reaction. For that purpose, itaconic acid ($\geq$ 99% purity) and aniline ($\geq$ 99.5% purity) purchased from Sigma-Aldrich® were used as reactants, N-(3-dimethylaminopropyl)-N′-ethylcarbodiimide hydrochloride (commercial grade) was used as carboxyl and amine-reactive zero-length cross linker together with N-hydroxysuccimide (98%) (NHS) to enhance the coupling efficiency. Both reactants were also purchased from Sigma-Aldrich®. The solvent used as reaction medium and also for the dosimeters preparation was a buffer solution with equimolar quantities of sodium phosphate monobasic and sodium phosphate dibasic with analytical grade. The molar ratio ITA:Aniline was 1:5 to assure the reaction of most of the itaconic acid. However EDC (1-Ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride) was used as the limiting factor in the reaction in order to avoid the reaction of both acid groups in the ITA molecules, by keeping the molar ratio ITA:EDC above 2:1. The reaction extent was measured by UV–vis spectroscopy recorded with a Shimadtzu spectrophotometer UV-260 from 290 to 550 nm every two minutes for a total time of 80 min. Fourier transform infrared spectroscopy (FTIR) was used to analyze the reaction products and reagents and to confirm the ITA-Aniline coupling reaction, A Nicolet 5-SXC FT-IR spectrophotometer was used to obtain the spectra. FTIR spectra were recorded in a spectral range of 4000–400 cm^{-1} with a resolution of 4 cm^{-1}; 64 scans were run for each sample.

In order to purify the final product a temperature induced crystallization process was carried out obtaining a solid product by cooling the liquid product from ambient temperature to 4 °C for 48 h. The solid product was then filtered and washed twice with the supernatant and then twice with milli-Q grade water at 4 °C, this procedure was repeated 3 times. Considering that the melting point of aniline is −6.3 °C and that the rest of the reagents are soluble in water, is reasonable to expect an efficient separation of the desired product with the described procedure. Afterwards, the solid material was vacuum filtered using a Büchner flask set-up and finally, the resulting crystals were dried at 37 °C until constant weight. FTIR spectroscopy was used to evaluate the chemical composition of the crystals.

The overall coupling yield calculated from a molar balance for the limiting reactant as: (modified ITA moles / original ITA moles x100) was 32.5%, which was expected because of the specific conditions that were selected to ensure the modification of only one acid group of the ITA molecule at the expense of reducing the reaction yield. The obtained product requires a subsequent purification in order to obtain a product of comparable quality to the other reagents used in this work. Nevertheless, it is still suitable for a qualitative comparison and dosimetric feasibility tests.

2.2. Gel dosimeter preparation

For the ITA-BIS based dosimeters preparation the quantities presented in Table 1 were used, first Gelatin 300 Bloom purchased from FLUKA was mixed at ambient temperature and heated up to 50 °C for 30 min, then the temperature was lowered to 37 °C to avoid polymerization of the monomers during the dosimeter preparation. BIS was mixed for 15 min and then the ITA was incorporated and stirred for another 15 min. Finally, 10% v/v of the buffer solution with THPC also at 37 °C was incorporated and the

Table 1
Dosimeter compositions.

Itaconic Acid Based Dosimeter		Modified Itaconic Acid Based Dosimeter	
Component	**Mass % (gr/gr x 100)**	**Component**	**Mass % (gr/gr x 100)**
Buffer solution	90.13 ± 0.01	Buffer solution	90.62 ± 0.01
Gelatin	5.13 ± 0.01	Gelatin	5.14 ± 0.01
ITA	3.04 ± 0.01	Modified ITA	3.06 ± 0.01
BIS	1.59 ± 0.01	BIS	1.02 ± 0.01
THPC	0.10 ± 0.01	THPC	0.10 ± 0.01