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Effect of inorganic salts and matrix crosslinking on the dose response of polymer gel dosimeters based on acrylamide

David Chacón[a,b], Miriam Strumia[c,d], Mauro Valente[a,e,f], Facundo Mattea[a,c,d,*]

[a] Universidad Nacional de Córdoba, Facultad de Matemática, Astronomía, Física y Computación, Laboratorio de Investigación e Instrumentación en Física Aplicada a la Medicina e Imágenes por Rayos X, LIIFAMIR⊗, Córdoba, Argentina
[b] Departamento de Física, Universidad Nacional, Heredia, Costa Rica
[c] Universidad Nacional de Córdoba, Facultad de Ciencias Químicas, Departamento de Química Orgánica, Córdoba, Argentina
[d] Instituto de Investigación y Desarrollo en Ingeniería de Procesos y Química Aplicada, IPQA, CONICET, Córdoba, Argentina
[e] Instituto de Física E. Gaviola, IFEG, CONICET, Córdoba, Argentina
[f] Centro de Física e Ingeniería en Medicina, CFIM & Departamento de Ciencias Físicas, Universidad de La Frontera, Temuco, Chile

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ABSTRACT

The use of additives in polymer gel dosimeters to enhance their sensitivity or to improve their performance is of great importance for their application in radiomedicine. Inorganic salts have been used as additives with this purpose; however, their presence in the dosimeters induce severe modifications in their mechanical properties and consequently in their capabilities to maintain a stable dose distribution with time. Most studies in this area conclude in the need to use chemical modifications of the species responsible for the mechanical properties of the dosimeters, which in most cases is a gelatin matrix. In this study, a covalent crosslinking of the gelatin matrix of PAGAT dosimeters doped with different inorganic salts, namely $MgCl_2$, $CaCl_2$ and $MnCl_2$ has been carried out. The mechanical properties, X-ray sensitivity and dose distribution stability in these materials were compared to those of PAGAT. The results indicated a compromise between the crosslinking of the gelatin structure and the sensitivity of the dosimetric material. Therefore, the proper selection of the degree of crosslinking and the inorganic salt concentration must be considered. An enhanced dosimeter was obtained by adding $MgCl_2$ with a 1 M concentration and by crosslinking the gelatin matrix with glutaraldehyde at a 0.08% w/v concentration. This material presented a 75% enhanced sensitivity relative to PAGAT and similar temporal stability and spatial stability in 2D dose distributions.

1. Introduction

One of the main tasks for a medical physicist is to control the dose distribution in radiotherapy treatments and in patient radiation protection during diagnostic radiology. Gel dosimetry has the potential to be great tools in these applications, because unlike common dosimeters, such as ionization chambers, thermoluminescent dosimeters and films, they don't have any limitations to record and maintain spatial dose distribution. Additionally, gel dosimetry has the advantage of providing, not only quantitative information on the delivered dose, but also a three-dimensional dose distribution with high resolution (Ibbott, 2004). Among the different types of gel dosimeters, polymer gel dosimeters (PGDs) have been proposed and used in the last decades because of their low post-irradiation diffusion compared to other systems like Fricke Gel dosimetry (Baldock et al., 2010). Since 1993, when the first polymer gel dosimeter (PGD) was proposed (Maryanski et al., 1993), different types of monomers and compositions have been suggested and studied (Titus et al., 2016; Rabaeh et al., 2008) to obtain a dosimetric system with the optimal dose-response, temporal and spatial stability, energy and dose rate independency and with preparation methods simple enough to be used in clinical applications.

In the last five years, the use of inorganic salts to enhance the sensitivity of PGDs to radiation has been investigated. Initially, in 2012 Hayashi et al. (2012) showed that there was a clear effect on a methacrylic-acid-based PGD with the addition of some inorganic salts. They observed an increase in the R2-dose sensitivity when $MgCl_2$ was incorporated in the PGD. In their results, it was found that the polymerization rate increased with the addition of inorganic salts by measuring temperature changes caused by the exothermic polymerization reactions during the irradiation. The authors suggested that this effect was correlated with the hydration properties of metal cations such as (Li^+, Na^+, K^+ and Mg^{+2}), which promotes the mobility and reactivity of

* Corresponding author. Universidad Nacional de Córdoba, Facultad de Ciencias Químicas, Departamento de Química Orgánica, Córdoba, Argentina.
E-mail addresses: fmattea@gmail.com, fmattea@fcq.unc.edu.ar (F. Mattea).

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the radicals involved in the polymerization reactions and also on their termination rate. Similar effects were reported from the same authors with a polyacrylamide based gel (PAGAT) (Hayashi et al., 2013), where an increase in the nuclear magnetic resonance (NMR) response of the dosimeters was reported. However, a significant depression of the gels melting point caused by the addition of inorganic salts represented a great drawback for the application of these materials (Al-Jarrah et al., 2016). They concluded that some type of crosslinking agent should be used in the gelatin matrix of the PGDs to avoid it. The melting point depression and changes on the mechanical properties of gelatin matrix have been reported for different applications and related to changes in the electrostatic properties of the gel (Haug et al., 2004; Sarabia et al., 2000).

The use of formaldehyde in different PGDs to increase their melting point has been studied by several authors (Fernandes et al., 2008; Aziz et al., 2013; Pavoni and Baffa, 2012) obtaining an increase in the melting point of about 40 °C. Recently, glutaraldehyde (GTA), a less toxic crosslinking agent than formaldehyde, has been studied (Romero et al., 2016) with the aim of improving the thermal stability of PGDs. This study showed that, if concentrations lower than 0.50% w/v of GTA were used to crosslink the gelatin matrix, its thermal stability was significantly improved and an increase of the elastic modulus up to 100 times was achieved at 37 °C. In addition, the analytical responses of crosslinked and unmodified itaconic acid based dosimeters (Mattea et al., 2015) were compared with no significant differences between each other.

The main goal of the present study is to evaluate the effect of inorganic salts and GTA on a polymer gel dosimeter based on acrylamide (PAGAT). For this purpose, the rheological characterization of different dosimetric systems with and without inorganic salts and GTA was carried out to evaluate the elastic properties of the material together with the dosimetric response to X-ray radiation. In this study, the ions selection was based on their ionic radius and on their effect on the structure of water according to Y. Marcus (2009). In this way, $MgCl_2$, $MnCl_2$ and $CaCl_2$ were selected because of their higher capability on forming water structures as depicted in Fig. 1.

2. Material and methods

2.1. PGD manufacturing

Acrylamide based gels (PAGAT) were manufactured based on the method described by Venning et al. (2005) using 89% w/w of ultrapure deionized water, 5% w/w of gelatin (250 Bloom purchased from FLUKA), 3% w/w of N, N' methylene bisacrylamide (BIS, 99% purchased from Sigma Aldrich®), 3% w/w of acrylamide (AAm, 99% purchased from Sigma Aldrich®) and 10 mM of Tetrakis(hydroxymethyl)phosphonium chloride (THPC, 80% solution purchased from FLUKA). Briefly, 90% of the water used in the dosimeters was mixed with the gelatin for 10 min at room temperature and stirred at 250 rpm. Afterwards, the temperature was set to 45 °C with constant stirring until a homogenous solution was obtained. Then, BIS was incorporated and the whole solution was mixed for 15 min at 45 °C. Next, the temperature was lowered to 37 °C and the AAm was incorporated. The whole solution was mixed at 37 °C for 30 min and the THPC was added with the remaining 10% of the water at 35 °C. The obtained solution was kept at this condition for 2 min. Two types of dosimeters were prepared with the obtained material, first PMMA cuvettes of $10 \times 5 \times 40\ mm^3$ were filled with the sensitive material and used for the dosimetric response analysis, and then PMMA layer containers of $50 \times 50 \times 5\ mm^3$ were prepared and used to study dose distribution characteristics in the dosimeters. Finally, the containers were sealed and stored at 4 °C until their irradiation. For materials containing inorganic salts, a 1 M solution of the specific salt ($MgCl_2$, $CaCl_2$ or $MnCl_2$) was used instead of water. Furthermore, for crosslinked gels, glutaraldehyde (GTA, 50% w/w purchased from Sigma Aldrich®) was incorporated after the THPC at the last minute of the preparation. Table 1 summarizes the different concentrations and materials used in this study. For the rheological characterization the dosimetric materials were placed in cylindrical containers suitable for the analysis.

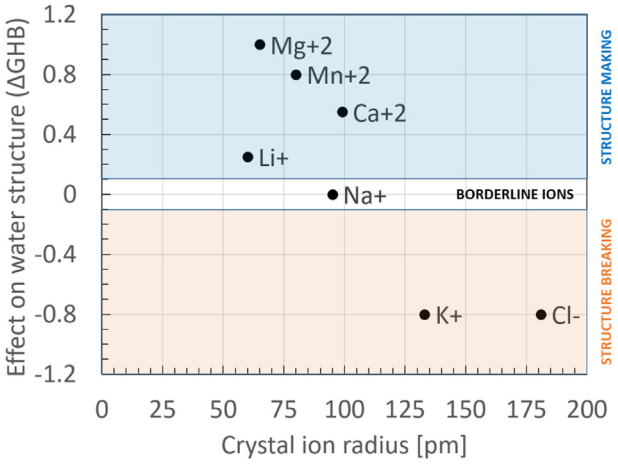

Fig. 1. a) Effect on the structure of water vs crystal ionic radius.

2.2. Irradiation

The different sets were irradiated in an X-ray tube with a W anode connected to a Siemens Kristalloflex generator with a maximum power of 3 kW, described elsewhere (Valente et al., 2016). The electrical current range of the generator goes from 5 to 50 mA and the voltage range from 20 to 60 kVp. In the irradiation experiments the incident beam was collimated to a $5 \times 5\ cm^2$ square geometry, using an electrical current of 44 mA, voltage of 44 kVp, a source-to-phantom distance of 800 mm and a collimator to sample distance of 10 mm. In order to improve absorbed dose uniformity, the cuvette dosimeters were irradiated with a "Box"-like technique using four opposite and parallel fields with a dose rate of 100 cGy/min. All irradiations were carried out by triplicate and at a controlled temperature of 25 °C. For the layer type dosimeters, the irradiations were carried out with the same beam quality using a circular collimator with a diameter of 15 mm and a dose rate of 120 cGy/min at 25 °C. The delivered dose of each dosimeter was set to have similar responses in each material. Therefore, PAGAT dosimeters were irradiated with a dose of 10 Gy, and materials containing inorganic salts, with or without GTA crosslinking, were irradiated with a dose of 5 Gy.

Table 1
PGDs used in this study.

Set	PGD	Inorganic Salt	GTA concentration	Dose Range
			(%w/v)	(Gy)
P1	PAGAT	–	–	0–16
P2	PAGATMg	$MgCl_2$	–	0–10
P3	PAGATCa	$CaCl_2$	–	0–12
P4	PAGATMn	$MnCl_2$	–	0–12
P5	PAGAT(Liq) [a]	–	–	0–12
G1	PAGAT + GTA26	–	0.26	0–18
G2	PAGAT + GTA15	–	0.15	0–18
G3	PAGAT + GTA8	–	0.08	0.10
PG1	PAGATMg + GTA26	$MgCl_2$	0.26	0–18
PG2	PAGATMg + GTA15	$MgCl_2$	0.15	0–15
PG3	PAGATMg + GTA8	$MgCl_2$	0.08	0–10

[a] The PAGAT(Liq) was stored at 35°C until its irradiation to keep it in a liquid state.