Three-dimensional radiochromic and polymer gel dosimeters with Pluronic F-127 matrix – a review of current research

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Abstract. A co-polymer of poly(ethylene oxide)-block-poly(propylene oxide)-block-poly(ethylene oxide) (Pluronic F-127, PEO-PPO-PEO) was proposed as a physical gel matrix, substituting gelatine for three-dimensional polymer gel dosimeters and as a matrix for the preparation of new radiochromic gel dosimeters. Two polymer gel dosimeters and seven radiochromic gel dosimeters were obtained with this new matrix. In this review we summarise the main advantages of using Pluronic F-127 for manufacturing radiation dosimeters and the best performing new Pluronic dosimeters.

1. Introduction
Pluronic F-127 was used for two purposes in our previous research. The first was to propose the substitution of a natural gelatine polymer with a synthetic co-polymer matrix in polymer gel dosimeters. The second purpose was to propose new radiochromic gel dosimeters, with respect to the existing ones [1-4], on the basis of this co-polymer and tetrazolium salts. The goals were to achieve dosimeters of improved thermal and optical properties with respect to gelatine-based dosimeters, and in case of radiochromic dosimeters, to obtain systems recording dose distributions with no diffusion of irradiated parts over time after irradiation. In most similar system referred to in the above publications, radiochromic dosimeters are prone to losing dose distribution information over time.

A few gelling agents have been used for manufacturing three-dimensional (3D) polymer gel and radiochromic dosimeters [5]. In 1993, Maryanski et al [6] proposed the first polymer gel dosimeter with agarose that fixed a dosimetric solution by the formation of a physical gel. Soon afterwards, it was discovered that gelatine outperformed agarose by better transparency of the gel matrix, easier preparation of the gel in lower temperatures than in the case of agarose and the formation of a more even gel [7]. Since that time, most researchers have used gelatine as a matrix for polymer and radiochromic gel dosimeters. Nevertheless, the gelatine matrix has one disadvantage, namely, a low gel–sol transition temperature (~30 °C) that limits the temperature range in which non-irradiated and irradiated samples can be stored and transported. Also, it is clear from our studies that an aqueous solution of this natural
polymer of gelatine degrades over time after preparation, which is inconvenient if gelatine-based dosimeters are designed for a long period of use [8, 9].

Several studies have been performed on modifications of gelatine matrix to ensure better thermal stability. For instance, a modified MAGIC [10], MAGIC–f, contained formaldehyde that shifted the melting point to 69°C [11, 12]. However, a disadvantage of formaldehyde is its toxicity [13]. In another approach, Abtahi et al [14] mixed gelatine with agarose in MAGIC–A, which led to the melting point of such a matrix being 60°C but decreased the dose sensitivity with respect to MAGIC. Poly(vinyl alcohol) was also used as a matrix in a PAGAT dosimeter [15], and the new gel dosimeter was called PVABAT [16]. The melting point of PVABAT increased to 80°C. The authors reported that the linear dose range for this gel was 30–45 Gy, while for PAGAT it was 0–7 Gy.

Over the last two years, research has been performed on both substituting gelatine matrix with the physical matrix made of a synthetic co-polymer of poly(ethylene oxide)-block-poly(propylene oxide)-block-poly(ethylene oxide) (Pluronic F-127) in polymer gel dosimeters and on the development of the new radiochromic gel dosimeters with Pluronic F-127 matrix [9, 17-19]. The results of these studies are summarised in this communication.

2. Features of Pluronic F-127
The reasons behind the choice of the Pluronic F-127 copolymer for 3D dosimetry are as follows: (i) the exceptional transparency of Pluronic physical gels, which can be compared to that of clear water, (ii) the phase behaviour of Pluronic, which exists in sol and gel form, and is related to its concentration and presence of co-solutes [20] – this affects the manufacturing of gel dosimeters, (iii) the stability of gels over different temperature ranges, which is also related to the phase behaviour and concentration of Pluronic, (iv) Pluronic F-127 is a synthetic, non-toxic co-polymer that is used in biomaterials research [21] and is US Food and Drug Administration (FDA) approved [22], and (v) Pluronic does not degrade over time, unlike gelatine aqueous solutions [8, 9].

The exceptional transparency of Pluronic gel was assessed with UV-Vis spectrophotometric measurements. In brief, Pluronic gels (23 and 25%) exhibited much lower absorbance from gelatine solutions (5, 7.5 and 8%) over the wavelength range of 300-700 nm [9, 17]. The absorbance of Pluronic gels was six-to-ten times lower than gelatine gels at 400 nm and 1.5-times lower at 730 nm. Gels consisting of 23% and 25% Pluronic showed similar absorbance. In addition, gelatine in solution is susceptible to degradation. The aging of gelatine was a subject of studies by other researchers [23-25], who reported gelatine to be a very sensitive compound to environmental changes. Our findings of gelatine aging are reported elsewhere [8, 9].

The phase diagram for Pluronic F-127 [20] revealed that the higher the concentration of this copolymer, the broader the temperature range over which its solution remains as a physical gel. For instance, a 25% gel is stable in the temperature range of ~20-85 °C [20]. The gel-sol transition occurs below and above these temperatures. This phase diagram is affected by other substances present in Pluronic gel. The specificity of the sol-gel-sol transition of Pluronic gels makes it attractive in terms of keeping a gel dosimeter with a Pluronic matrix stable at temperatures far above room temperature in contrast to gelatine gel dosimeters.

3. Polymer gel dosimeters with Pluronic F-127
The following polymer gel dosimeters were examined for substitution of gelatine with a Pluronic F-127 matrix: methacrylic acid containing MAGAT gels [26], acrylamide containing PAGAT gels [15, 26], N-isopropylacrylamide containing NIPAM gels [27] and N-vinylpyrrolidone containing VIP [28] and VIC [29].

Substitution of gelatine with Pluronic was impossible in MAGAT and VIC polymer gel dosimeters due to the incompatibility between methacrylic acid (MAGAT) and Pluronic, or a too high concentration of dosimeter components (VIC). Alternatively, PAGAT (6 and 9% T), NIPAM (different % T) and modified VIP allowed proper Pluronic-based polymer gel dosimeters to be obtained. In contrast to Pluronic-containing PAGAT (6% T) and modified VIP gels, NIPAM containing a Pluronic matrix did
not respond to irradiation. A comparison of the new Pluronic-based polymer gel dosimeter properties are shown in Table 1. Their main feature is that the dose sensitivities of both new gels were ~33% higher than their corresponding compositions containing a gelatine matrix. The Pluronic matrix ensures improved transparency and stability in contrast to the gelatine-based gel dosimeters. The new gel dosimeters’ thermal stabilities assessed by \( T_{gel} \) values (Table 1) are 4.4–56.7 °C (VIP3-Pluronic) and 10.1–56.7 °C [9]. Note that the thermal transitions start and end at lower and higher temperatures, respectively, than \( T_{gel} \). Differential scanning calorimetry (DSC) results showed two gelatine-based dosimeters, a VIP gel dosimeter [28] and VIC [29] to be stable at 0–26 °C and 0–29.5 °C, respectively (the upper values correspond to initiation of the gel-sol transition) [8, 9]. Our recent studies showed also that substituting oxygen scavengers in VIC dosimeters (copper sulfate and ascorbic acid) with tetrakis(hydroxymethyl)phosphonium chloride (THPC) causes chemical crosslinking of gelatine, which impacts on the thermal stability of this gel (VIC-T). DSC studies showed its stability at about 0–80 °C [8].

Table 1. Comparison of VIP3-Pluronic with PAGAT2-Pluronic: 0.47 T NMR derived calibration characteristics and DSC measured thermal properties (VIP3-Pluronic: 25% Pluronic, 4% \( N,N' \)-methylenesiacrylamide, 4% \( N \)-vinylpyrrolidone, 10 mM THPC, 4% tert-butanol; PAGAT-2-Pluronic: 23% Pluronic, 3% acrylamide, 3% \( N,N' \)-methylenesiacrylamide, 10 mM THPC).

|                | Threshold dose [Gy] | Linear dose range [Gy] | Dynamic dose range [Gy] | \( R^2 = a \times D + R_{2,0} \) |
|----------------|---------------------|------------------------|-------------------------|-------------------------------------|
|                |                     |                        |                         | \( a \)         \( R_{2,0} \) \( R^2 \) |
| VIP3-Pluronic  | 0.5                 | 0.5–30                 | 0.5–>50                 | 0.1010    1.249  0.999             |
| PAGAT2-Pluronic| 0.5                 | 0–20                   | 0–>50                   | 0.0913    1.052  0.988             |

|                | DSC               | \( T_{gel, onset} \) [°C] | \( T_{gel} \) [°C] | \( T_{gel, end} \) [°C] | \( T_{gel, onset2} \) [°C] | \( T_{gel2} \) [°C] | \( T_{gel, end2} \) [°C] |
|----------------|-------------------|---------------------------|--------------------|--------------------------|--------------------------|------------------------|--------------------------|
| VIP3-Pluronic  | DSC               | 1.6                       | 4.4                | 13.8                     | 55.2*                    | 56.7*                  | 58.8*                    |
| PAGAT2-Pluronic| DSC               | 5.7                       | 10.1               | 21.4                     | 55.2*                    | 56.7*                  | 58.8*                    |

*Data for 25% Pluronic F-127. No such results for second transition was observed for VIP3-Pluronic and PAGAT2-Pluronic [9]. The upper temperature of thermal stability for VIP3-Pluronic and PAGAT2-Pluronic is assumed to be around \( T_{gel2} \) given in Table 1 for 25% Pluronic F-127.

4. Radiochromic gel dosimeters with Pluronic F-127

New radiochromic gel dosimeters were manufactured with the Pluronic F-127 matrix and the following tetrazolium salts: 2,3,5-triphenyltetrazolium chloride (TTC), tetrazolium violet, blue tetrazolium chloride, nitro blue tetrazolium chloride (NBT), tetranitro blue tetrazolium chloride, thiazoyl blue tetrazolium bromide and a representative of leuco dyes - leuco malachite green (LMG) [17-19]. The main feature of the tetrazolium salt-Pluronic radiochromic gels is the conversion of the salts into water insoluble formazans of different colours inside the Pluronic matrix (Figure 1). This is in contrast to LMG-Pluronic, where a water soluble dye is formed. However, the Pluronic matrix prevents the formazan molecules from diffusion, aggregation and sedimentation. This, in turn, relates to an extraordinary maintaining of a 3D dose distribution integral over a long time after irradiation with the diffusion coefficient equal to 0 mm²/h [17, 19].

The first tetrazolium salt-Pluronic radiochromic dosimeter reported was that with TTC [17]. The following experiments revealed that different tetrazolium salts can be used for manufacturing such dosimeters. However, some of them were unstable over time after preparation or revealed low dose sensitivity. The one of the highest dose sensitivity was NBT-Pluronic (Figure 1), which was composed
of 0.0818% NBT (1 mM), 25% Pluronic F-127 and 0.136 × 10^{-2}% sodium formate. This gel was equivalent to water.

The most important characteristic of the NBT-Pluronic gel was: (i) the average dose sensitivity of 0.0047 ± 0.1 × 10^{-4} (Gy cm)^{-1}, (ii) insensitivity to changes in the dose rate for photons of different energies, (iii) ~12% difference in the dose sensitivity between the gel irradiated with 12 MeV electrons and photons, (iv) linear and dynamic dose ranges between <1 and ≥150 Gy and (v) the dose threshold below 1 Gy [18]. DSC results showed that this NBT-Pluronic gel is stable in the temperature range of ~9.5‒57 °C.

![Figure 1. A view of NBT-Pluronic gel dosimeter in a water phantom before (a) and after (b) irradiation to 60 Gy (field size 2×2 cm²). A region of NBT conversion after irradiation can be seen (pointed with a red arrow) as a rectangular shape of red-violet colour coming from the formation of water insoluble NBT formazan.](a) (b)

5. Conclusions

Pluronic F-127 has been shown to be a very good physical matrix for manufacturing some 3D polymer gel dosimeters and 3D radiochromic dosimeters based on tetrazolium salts. The best compositions for polymer gel dosimeters are VIP3-Pluronic and PAGAT2-Pluronic, whereas for radiochromic gel dosimeters – NBT-Pluronic.

Pluronic matrix ensures improved optical properties and thermal stability for both types of dosimeters and improved dose sensitivity of polymer gel dosimeters with respect to their corresponding gelatine-based compositions. By using a Pluronic synthetic matrix, the longevity of dosimeters is enhanced with respect to gelatine gel dosimeters, where gelatine degrades in solution over time after preparation.

6. References

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