The effect of mixed dopants on the stability of Fricke gel dosimeters

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Abstract. Auto-oxidation and fast diffusion in Fricke gels are major drawbacks to wide-spread application of these gels in 3D dosimetry. Aiming to limit both processes, we used mixed dopants: the ferric-specific ligand xylenol orange with a ferrous-specific ligand (1,10-phenanthroline) and/or a bi-functional cross-linking agent (glyoxal). Markedly improved auto-oxidation stability was observed in the xylenol orange and phenanthroline doped gel at the expense of increased background absorbance and faster diffusion. Addition of glyoxal limited the diffusion rate and led to a partial bleaching of the gel. It is conceivable that these two new compositions may find useful practical application.

1. Introduction

The ferrous sulfate – gelatin 3D dosimeter (Fricke gel) has historically suffered from two major drawbacks: relatively fast diffusion of the radiation product (ferric iron, Fe^{3+}) following irradiation [1-3] and significant auto-oxidation of the ferrous iron (Fe^{2+}) during storage [4]. More recently, as fast optical scanning has become available, the diffusion rate in Fricke – xylenol orange gels, following short irradiation protocols, has been deemed acceptable [5]. Arguably, therefore, the auto-oxidation becomes a more important factor that limits both the useful dose range and shelf life of Fricke gels.

It has previously been shown that introduction of ligands that bind strongly to Fe^{2+}, like 1,10-phenanthroline, alone or in combination with formaldehyde, in a Fricke gel leads to spontaneous reduction of the product following irradiation [6]. The effect was attributed to the increased redox potential of the iron-phenanthroline complex. Conversely, xylenol orange, which is the current dopant of choice in Fricke gels, does not bind to Fe^{2+}, but forms a strong complex with the Fe^{3+}, thus decreasing the redox potential of the system. Therefore, the addition of xylenol orange likely favors auto-oxidation of the ferrous iron. In our study, we tested the properties of Fricke gels doped with xylenol orange, phenanthroline and/or glyoxal as a cross-linking agent. To our best knowledge, and from two previous reviews of the system [6, 7], such use of xylenol orange with ferrous-specific ligands and cross-linkers has not been investigated.

2. Materials and methods

Stock solutions were prepared using analytical grade reagents (supplied by Sigma-Aldrich): H_2SO_4, Fe(NH_4)_2(SO_4)_2·6H_2O, 1,10-phenanthroline (Pn), xylenol orange disodium salt (XO) from Fluka, NaCl, and glyoxal (Gx). For each gel (25.0 g), the required amounts of the stock solutions were added together and adjusted to 12.5 g with de-ionized water, followed by 12.5 g of warm (50 – 60 °C) 10% solution of type A porcine gelatin (300 bloom from Sigma-Aldrich), which was prepared at 80 °C. The
warm gel was poured into poly(methyl methacrylate) cuvettes (10 mm path length, square cross-section), closed with polypolypropylene cuvette caps and let to solidify in a refrigerator at 10 °C. All gels contained 5% gelatin, and the following compositions were tested (concentrations in mM): **FXG** (H₂SO₄/NaCl/Fe²⁺/XO = 50/1.0/0.1/0.1), **FXGxG** (H₂SO₄/NaCl/Fe²⁺/XO/Gx = 50/1.0/0.1/0.1/10), **FXPnG** (H₂SO₄/NaCl/Fe²⁺/XO/Pn = 25/1.0/0.1/0.3), **FXPnGxG** (H₂SO₄/NaCl/Fe²⁺/XO/Pn/Gx = 25/1.0/0.1/0.3/10).

Irradiations were performed using a Co-60 source (Eldorado 6, Atomic Energy of Canada Ltd.) at the London Regional Cancer Program (London, Canada). For sensitivity and stability determination the cuvettes were irradiated in full. For diffusion measurement, the top halves of the cuvettes were shielded with a lead block and a dose of 10 Gy was delivered to the bottom halves. The cuvettes were irradiated at 22 °C, transported at 4 °C for a period of 1.5 hours after irradiation, and scanned at 22 °C. Optical absorbance readings of the fully irradiated cuvettes were performed at 585 nm with a GENESYS 10S UV-Vis spectrophotometer (Thermo Scientific). The half-irradiated gels were imaged using a Vista10 conebeam optical CT scanner (Modus Medical Devices Inc., London, Canada), with an amber LED source, filtered at 590±2 nm. Time course images were taken regularly for the following 4.5 hours. For long term storage, the gels were kept in a cool environment (at 10 °C).

The light transmittance profiles of the diffusion cuvettes were obtained with image processing software (ImageJ, version 1.44p). The data was fitted to an approximation of the complementary error function in order to determine the diffusion parameter (n, mm²), whose increase over time (t, h) gives the diffusion coefficient (D, mm²·h⁻¹) [8]:

\[
D = \left( \frac{\sqrt{4 - 1}}{4 \cdot \ln 2} \right) \frac{n}{t} = 0.212 \frac{n}{t} \tag{1}
\]

3. Results

3.1. Dose response and chemical stability

Figure 1 shows the dose response in the tested gels immediately after irradiation and, in the same gels, eight days later. All compositions, except FXPnG, show significant change in their absorbance.

![Figure 1: Dose response: 3 hours after irradiation (solid lines, filled symbols) and 8 days after irradiation (dashed lines, open symbols).](image)

Figure 2 presents the effect of long-term storage in a cool environment (10 °C) on the background absorbance of the gels (2a), and the initial dose response (2b). Not given in the figure is the linearity of the dose response: all four compositions gave linear response (R² > 0.995) for the first 21 days after irradiation (22 days after preparation), and R² > 0.989 after 50 days (51 days after preparation).
Addition of phenanthroline led to an approximately 40% decreased sensitivity and increased background absorbance. Nevertheless, for FXPnG, both characteristics of the gel remained very stable: there was minimal apparent auto-oxidation for the first week of storage and practically constant dose response for at least three weeks. The presence of glyoxal had minimal initial effect on both background absorbance and sensitivity. However, partial bleaching of the gels was seen in the following days. Auto-oxidation was eventually apparent in approximately a week for FXGxG and three weeks for FXPnGxG. The initial dose response decreases monotonically in those gels.

3.2. Diffusion coefficients and summary of results

The change of the diffusion parameter \((n)\) versus time is presented in figure 3.

![Figure 3: Diffusion parameter \((n)\) at 22 °C, starting approximately 1.5 hours after irradiation.](image)

The diffusion coefficients, estimated from equation (1) and the linear fits from figure 3, are given in table 1, together with a summary of the other characteristics of the gels.
Table 1: Summary of the results.

| Gel code    | Bkgd. abs. mAU·cm⁻¹ | Dose response mAU·Gy⁻¹·cm⁻¹ | Diff. coeff. mm²·h⁻¹ | Auto-oxidation during storage | Dose response after irradiation |
|-------------|----------------------|-----------------------------|----------------------|------------------------------|--------------------------------|
| FXG         | 224                  | 46.4                        | 0.86 ± 0.02          | fast                         | unstable                       |
| FXGxG       | 258                  | 49.0                        | 0.87 ± 0.06          | bleaching at first           | decreasing                     |
| FXPnG       | 444                  | 27.5                        | 1.10 ± 0.11          | slow                         | stable                         |
| FXPnGxG     | 482                  | 28.5                        | 0.77 ± 0.08          | bleaching at first           | decreasing                     |

4. Discussion and conclusions

The compositions of the tested gels were chosen on the basis of screening experiments and a review of the published literature [1-3, 6, 7]. Glyoxal, which is a di-aldehyde, was preferred as a cross-linker over the mono-functional and less stable formaldehyde. The sulfuric acid concentration was based on previous investigations [7] and preliminary testing of the stability of the ferrous-phenanthroline complex. Sodium chloride was used as an additive that may minimize the effect of organic impurities.

As stated in the beginning, given the advances in fast optical scanning, the auto-oxidation in Fricke gels may be considered one of their main disadvantages. We have shown that addition of phenanthroline and xylene orange, i.e. FXPnG, yields a very chemically stable gel. Compared to FXG, the radiation sensitivity of the gel is decreased but still adequate for clinical applications. However, the initial background absorbance is almost doubled, and the diffusion rate is increased by 30%. In order to decrease the initial background absorbance, we suggest that the gelatin solution be pre-treated, as suggested in the literature [3].

Introduction of glyoxal in FXPnGxG led to a drastic decrease of the diffusion rate without affecting the sensitivity of gel initially. Instead of auto-oxidation, bleaching of the gel was observed during storage; in a few days the background of the gel stabilized and in several weeks auto-oxidation was seen. That effect may be useful for clinical applications but requires further research. FXGxG showed nearly identical diffusion rate as FXG, indicating that the cross-linking ability of glyoxal may be affected by pH. During storage FXGxG behaved in a similar manner as FXPnGxG, but on a shorter time-scale.

Overall, both FXPnG and FXPnGxG show interesting properties that may be advantageous in clinical settings.

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6. References

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