The characterisation of a genipin-gelatin gel dosimeter

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Abstract. Genipin cross links gelatin to slowly form a blue colour that bleaches upon irradiation. Spectrophotometric measurements of the absorbance change following irradiation to doses up to 100 Gy gives a linear dose response for certain concentrations of the gel ingredients; genipin, gelatin and sulphuric acid. Dose sensitivity increases with increasing concentrations of sulphuric acid and genipin and is also strongly dependent on the time allowed for the genipin-gelatin cross linking reaction (referred to here as blending) to take place. The optimum formulation of this gel was found for genipin concentration between 0.3 – 0.5 mM and blending time of at least 4 h.

1. Introduction
Gel dosimeters, having the ability to retain dosimetry information in three-dimensions (3D) have significant advantages in various radiotherapy applications [1]. In the Fricke-type gel dosimeter, however, ferric ions will diffuse post-irradiation where there are dose gradients within the gel [2, 3], leading to a loss in dosimetric information. Genipin, a fruit extract from \textit{Gardenia jasminoides Ellis}, is a natural cross-linker of gelatin [4] and slowly reacts during preparation to give a blue colour that bleaches quantitatively upon irradiation. It has been demonstrated that a genipin-gelatin hydrogel does not diffuse post-irradiation [5] and could also be useful in measuring surface doses [6]. The aim is to develop a non-diffusing gel dosimeter for optical CT 3D dosimetry [6, 7]. Ideally a gel dosimeter for 3D dosimetry will respond linearly with dose from 0 Gy to a chosen maximum useful for radiotherapy, allowing the dose distribution to be calibrated. This paper investigates the dose response characteristics of a genipin-gelatin gel dosimeter.

2. Methods
Gelatin (Sigma-Aldrich, G2500, \textasciitilde 300 bloom) was dissolved in water and then genipin (Wako Chemicals 078-03021) added from a stock solution. The mixture was continuously stirred in a water bath at \(45.0 \pm 0.5\, ^\circ\text{C}\). The solution slowly changed from colourless to blue and steadily darkened over time. The time allowed for genipin and gelatin to blend prior to adding sulphuric acid is referred to here as the blending time. After sulphuric acid was mixed the solution was pipetted into 1 cm plastic cuvettes and allowed to set overnight at about 4 \(^\circ\text{C}\). Samples were irradiated in a calibrated cobalt-60 Gammacell with doses up to 100 Gy. The radiation induced colour change in the gel was measured at its peak absorbance of 600 nm in a spectrophotometer (Cary 100, Varian).
As the genipin-gelatin mixture was darkening, samples were taken at regular intervals to initially observe the colour change over time. Further experiments were carried out by pouring 50 ml from a batch into a separate beaker, immediately adding sulphuric acid and preparing cuvettes. This was repeated at regular intervals to evaluate and compare the dose response as a function of blending time and a range of concentrations of genipin, gelatin and sulphuric acid.

3. Results and discussion

Figure 1 shows how the genipin-gelatin reaction darkens over time. Irrespective of the genipin concentration, the colour change reaches a plateau after approximately 48 hours.

It was found that for low genipin concentration (0.2 mM or less), a second order polynomial produced a better fit to the absorbance change readings against dose (Figure 2). At 0.1 mM, the correlation coefficients were 1.000 (polynomial) and 0.980 (linear), and at 0.2 mM, the correlation coefficients were 0.999 (polynomial) and 0.995 (linear). As the genipin concentration was increased up to 0.5 mM a linear relationship was found between 0 – 100 Gy with correlation coefficients greater than 0.999.

Dose sensitivity increases with increasing sulphuric acid concentration (Figure 3) and genipin concentration (Figure 4). As the concentration of either sulphuric acid or genipin is increased, the dose response also becomes more sensitive to the blending time. Previous work showed gel sensitivity for a linear fit of doses up to 50 Gy of approximately \(-2.3 \times 10^{-3}\) cm\(^{-1}\) Gy\(^{-1}\) [8]. In these experiments the sensitivities found ranged from -0.5 to -3.5 (\(\times \) 10\(^{-3}\) cm\(^{-1}\) Gy\(^{-1}\)). While the dose sensitivity is strongly dependent on the concentrations of genipin and sulphuric acid, only a small effect of the gelatin content was found, although results were only obtained for gelatin in the range 3 – 5 % (Figure 5). The blending time is also a dependent variable so careful control of these parameters is required to obtain a reproducible dose response of this gel.

Accurate 3D dosimetry requires optimization of the gel formulation including influence quantities such as the blending time. The optimum formulation of this gel for high sensitivity and linear dose response up to 100 Gy was found for genipin concentration between 0.3 – 0.5 mM and blending time of at least 4 h.
Figure 1. Darkening of the genipin-gelatin reaction for genipin concentrations 0.1, 0.3 and 0.5 mM. Gelatin (4.0 %) was constant and there was no acid added.

Figure 2. Dose response for various [genipin] (mM). The gel bleaches upon irradiation resulting in a decrease in optical absorbance. Gelatin (4.0 %), [H$_2$SO$_4$] (100 mM) and blending time (6.5 h) were constant.
Figure 3. Variation of dose sensitivity (cm$^{-1}$ Gy$^{-1}$) with sulphuric acid concentration and blending time. [genipin] (0.3 mM) and gelatin (4.0 %) were constant.

Figure 4. Variation of dose sensitivity (cm$^{-1}$ Gy$^{-1}$) with genipin concentration and blending time. Gelatin (4.0 %) and [H$_2$SO$_4$] (100 mM) were constant.
Figure 5. Variation of dose sensitivity (cm$^{-1}$ Gy$^{-1}$) with genipin concentration and gelatin content. 
[H$_2$SO$_4$] (100 mM) and blending time (6.5 h) were constant.

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