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Invited Article

# Effect of D-(+)-Glucose on the Stability of Polyvinyl Alcohol Fricke Hydrogel Three-Dimensional Dosimeter for Radiotherapy

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D-(+)-glucose (Glc) was added to the original Fricke polyvinyl alcohol–glutaraldehyde–xylenol orange (FPGX) hydrogel dosimeter system to make a more stable FPGX hydrogel three-dimensional dosimeter in this paper. Polyvinyl alcohol was used as a substrate, which was combined with Fricke solution. Various concentrations of Glc were tested with linear relevant fitting for optimal hydrogel production conditions. The effects of various formulations on the stability and sensitivity of dosimeters were evaluated. The results indicated that D-(+)-Glc, as a free radical scavenger, had a great effect on stabilizing the dose response related to absorbency and reducing the auto-oxidization of ferrous ions. A careful doping with Glc could slow down the color change of the dosimeter before and after radiation without any effect on the sensitivity of the dosimeter.



## 1. Introduction

The Fricke solution was firstly used as a kind of dosimeter for radiotherapy in the 1980s because of its good sensitivity to radiation including x-rays and gamma rays. The ferrous ions ($Fe^{2+}$) in Fricke solution turn into ferric ions ($Fe^{3+}$) [1] by oxidization under ionizing radiation, and the change from $Fe^{2+}$ to $Fe^{3+}$ can be investigated with UV–visible spectroscopy [2]. In order to stabilize the dose distribution of a Fricke solution dosimeter, the Fricke solution is incorporated into a gel matrix so that the dose distribution can be measured in three dimensions using magnetic resonance imaging or optical computed tomography [3]. With the development of three-dimensional dosimeters, stabilizing the geometric dose information by incorporating the aqueous Fricke solution into a gel and adding additives have become two important aspects for improving the stability and the sensitivity of the dosimeters.

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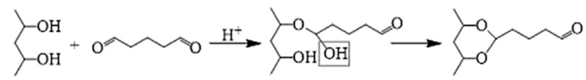
A number of gel systems have been used as the substrate of gel dosimeters. Among these, agarose [1] and gelatin [4] are the popular choices, but they have disadvantages in preparation and transparency which limit their application in Fricke gel dosimeters. Recently, polyvinyl alcohol (PVA), considered as a tissue-equivalent gel system, has been reported in use as a gel matrix [5]. As a common water-soluble polymer, PVA is often used in the film and adhesive industries. Compared with other organic gel materials, it has advantages such as being obtainable with tight manufacturing tolerances, low impurity levels, nontoxicity, and it can be prepared in the presence of oxygen. Besides, when mixed with Fricke solution, a PVA-made gel matrix can be analyzed by either optical computed tomography or magnetic resonance imaging detection methods because of its good transparency and stable performance.

In order to improve the stability of the dimensional dose information, some additives are used in Fricke gel dosimetry and the most common one is xylenol orange (XO), a chelator that forms two or more coordination bonds with central ferrous or ferric ions. Ferrous ions bind to XO forming a colored complex ($XO–Fe^{2+}$) in the visible range which can be measured spectrophotometrically (Fig. 1) [6].

After adding XO into the system, the diffusion of the ferric ions become slow [reaction Eqs. (2–8) in Fig. 2] [7]. This is due to the formation of a complex which is much bulkier than the "free" ferric ions [8]. However, adding XO also alters the absorption spectra of the Fricke gels so that irradiated gels give visible color development [8]. We have already done immense amounts of research on Fricke PVA–glutaraldehyde (GA)–XO (FPGX) hydrogel dosimeters [9–12], in which the gel was cross linked by GA [reaction Eq. (1) in Fig. 2].

Although the FPGX gel dosimeter is inexpensive and easy to prepare, the auto-oxidation of ferrous ions is still a problem which might eventually affect the spatial dose information. During our research, we found that D-(+)-glucose (Glc) could not only act as a reducing agent to decrease the auto-oxidation of ferrous ions, but it could also be the chelator after being oxidized into D-gluconic acid [13–15]. The reaction equations are given [reaction Eqs. (9–12) in Fig. 2]. In this experiment, we attempted to study the stabilization and dose response of FPGX gel dosimeters by changing the concentration of Glc.



(1)

$$H_2O \rightsquigarrow H\cdot + OH\cdot \quad (2)$$

$$H + O_2 \longrightarrow HO_2\cdot \quad (3)$$

$$Fe^{2+} + OH\cdot \longrightarrow Fe^{3+} + OH^- \quad (4)$$

$$Fe^{2+} + HO_2\cdot \longrightarrow Fe^{3+} + HO_2^- \quad (5)$$

$$HO_2^- + H^+ \longrightarrow H_2O_2 \quad (6)$$

$$2Fe^{2+} + H_2O_2 \longrightarrow 2Fe^{3+} + OH\cdot + OH^- \quad (7)$$

$$Fe^{3+} + XO \longrightarrow Fe^{3+}\text{–}XO \quad (8)$$

$$\text{Glucose} + O_2 + H_2O \longrightarrow \text{Gluconic acid} + H_2O_2 \quad (9)$$

$$H^+ + GH_4^- \longleftrightarrow HGH_4 \quad (10)$$

$$Fe^{2+} + GH_4^- \longleftrightarrow FeGH_4^- \quad (11)$$

$$Fe^{3+} + GH_4^- \longleftrightarrow FeGH^- + 3H^+ \quad (12)$$

**Fig. 2 – Reaction equations.**

## 2. Materials and methods

### 2.1. *Gel preparation*

All chemicals used in this study were analytical grade and supplied by Sinopharm Chemical Reagent Co., Ltd (Shanghai, China). Ultrapure water from a Milli-Q Integral 5 water purification system was used in all preparation.

The basic hydrogel dosimeter formulation was according to our former experiment [9–12]. The mixture solutions with 30 mM sulfuric acid, 0.15 mM ammonium ferrous sulfate [$Fe(NH_4)_2(SO_4)_2\cdot 6H_2O$], 0.015 mM XO, 0.025% weight/weight GA, 10% weight/weight PVA, and a series concentration of D-(+)-Glc (0 mM, 0.015 mM, 0.03 mM, 0.075 mM, 0.15 mM, 0.3 mM, 0.75 mM, and 1.5 mM) were prepared under nitrogen atmosphere. The prepared solutions were filled into the polystyrene cuvettes (10 mm, 10 mm, 45 mm), sealed with polytetrafluoroethylene caps, and kept in a dark place at 5°C for 10 hours. All experiments were repeated three times under the same conditions.

### 2.2. *Irradiation experiments*

Irradiation was performed by $^{60}Co$ with a dose rate of 0.3 Gy/min under 25°C (at Shanghai Institute of Measurement and

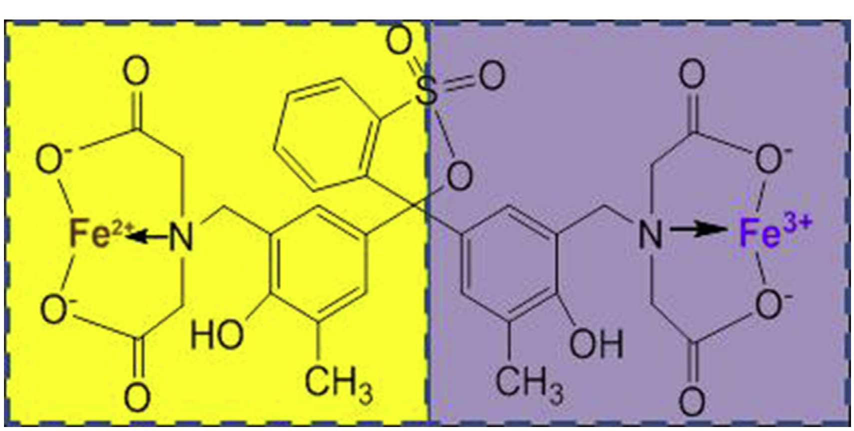



**Fig. 1 – The reaction principle of xylenol orange and $Fe^{2+}/Fe^{3+}$.**