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Enhancing Fricke Xylenol Gel Dosimeter's Response to Radiation with Optimized Preparation Methods

Shajid Syed Mohamed[1], Abhijit Mandal[1*], Kalyan Mondal[1], Gogul Priean V[1], Bratindranath Mukherjee[2], Praveen Chandra Pandey[3], Himanshu Mishra[1], Ritusha Mishra[1], Ganesh Kumar Patel[1], Ankur Mourya[1], Lalit Mohan Aggarwal[1], Sunil Choudhary[1]

1. Department of Radiotherapy and Radiation Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India.
2. Department of Metallurgical Engineering, Institute of Technology, Banaras Hindu University, Varanasi, India.
3. Department of Physics, Institute of Technology, Banaras Hindu University, Varanasi, India.

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ABSTRACT

Introduction: The fundamental principle of the Fricke gel dosimeter involves the oxidation of ferric ions upon exposure to radiation. However, a significant limitation of this dosimeter is the post-irradiation diffusion of ferric ions, which can result in the degradation of spatial dose information.

Material and Methods: Gels were prepared using 300 bloom gelatin, deionized water, sulfuric acid, ferrous ammonium sulfate, and xylenol orange dye (Sigma-Aldrich). The solution was then poured into 10 ml plastic cuvettes.. The gel samples were refrigerated at various temperatures for 1 to 10 days and irradiated within a water bath environment utilizing a telecobalt unit (Phoenix, Theratronics) employing parallel opposed beams. Spectrophotometric analysis at a wavelength of 585 nm was used to measured optical density changes with dose.. This procedure was repeated across gel formulations prepared under differing pH conditions.

Results: The gel's optimum pH value, which was stored for 10 days at 5° C, showed a linear response up to 10 Gy, although the storage time was longer than that of the gels with low (0.3) and high pH (1.3). The auto oxidation rate was determined and found to be less for non-irradiated gel batches stored at 5° C in relation to the gel samples at room temperature and freezing temperature.

Conclusion: The dose response of the dosimeter is highly dependent on its pH, composition, alkaline residuals, and pre-irradiation storing conditions.. We observed the optimum pH is 1, at which the dosimeter shows a maximum response. Storing gel samples at 5°C notably reduces the Fe^{2+} to Fe^{3+} auto-oxidation rate.

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Introduction

Radiation Therapy is one of the conventional modalities of treating cancer patients. Evolution in technology made the treatment delivery safe, accurate, and with minimal toxicity to unaffected healthy tissues [1]. Radiation dosimetry stands as a keystone in the field of radiotherapy, ensuring the accurate and safe delivery of therapeutic radiation doses to achieve optimal treatment outcomes. Accurate radiation dose measurement has a critical role in the field of radiation dosimetry, accomplished through dosimeters. The importance of precise dose delivery to patients highlights the significance of accurate dosimetry. This accuracy makes sure that the treatment is going as expected.

Numerous dosimeters, including ionization chambers, diodes, films, and thermoluminescent dosimeters, excel at measuring absorbed doses. However, despite their precision, widespread availability, and extensive study, these methods are limited to two-dimensional (2D) measurements of dose data [2]. Gel dosimeters offer a distinct advantage by enabling dose measurement in three-dimensional (3D) geometry. Among the commercially available gel dosimeters, the Fricke Xylenol Gel dosimeter emerges as notable, evolving from traditional Fricke solutions through the incorporation of a gelatin matrix [3, 4].

The dosimeter is based on the oxidation process of ferrous ions (Fe^{2+}) in ferrous ammonium sulfate to ferric ions (Fe^{3+}) when exposed to ionizing radiation. It is easy to prepare with consistency and tissue equivalent that itself acts as a phantom and dosimeter at the same time. It has better spatial dose resolution comparable to film dosimeters [5]. Fricke Xylenol Gel (FXG) dosimeter can be used in dose measurement for small fields, and the result is well agreed with the ionization chamber [6]. All these advantages are very significant in the verification of complex intensity modulated plans, especially in case of high dose gradient situations. The major limitations of the

*Corresponding Author: Tel: +91 9415221531; Email: abhijit.mandal1@bhu.ac.in

dosimeter include autoxidation of pre-irradiated gel samples and post-irradiation diffusion of ferric ions, which results in the loss of spatial stability.

In recent years, there's been growing interest in improving the performance of radiation dosimeters by optimizing their preparation methods. One dosimeter that has attracted attention for its potential to offer precise and responsive dose measurements is the Fricke Xylenol Gel (FXG) dosimeter. However, we still don't fully understand how different preparation methods affect the dosimeter's sensitivity. This study aims to explore this by looking at things like pH levels, the dosimeter's ingredients, and how it's stored. By doing this, we hope to find new ways to make the FXG dosimeter work even better for practical uses, like in radiation therapy. This research enhances the understanding of dosimetry principles and offers potential improvements in radiation therapy.

In this study, the FXG dosimeter was prepared with 270 bloom gelatine, which is easily available and cheaper compared to gelatine 300 bloom, which is imported, and the strength of the gel used doesn't create any impact on the outcome [7, 8]. The study involves preparing gels under different preparations and analysing their response to radiation dose. This investigation aims to pinpoint the optimal conditions that result in heightened sensitivity to radiation. By modulating the pH levels and refrigeration parameters of FXG prior to irradiation, we can extract valuable insights into the optimal preparatory conditions for practical applications.

Materials and Methods

FXG preparation

The Fricke gel dosimeter (FXG) is composed of an aqueous acid solution of ferrous sulfate and xylenol orange (XO) embedded in a gelatinous matrix. Specifically, the FXG contains 4% (weight/volume) gelatin derived from porcine skin (300 bloom, Sigma-Aldrich), 0.4 mM ferrous ammonium sulfate (FAS), 50 mM sulfuric acid, and 0.1 mM xylenol orange. This formulation is an optimized version of the traditional Fricke solution, incorporating 270 bloom gelatin (as the gelling agent) and xylenol orange (as the metal ion indicator) to enable 3D dose measurement. The FXG system consists of two main components: the gel, which makes up 75% of the total volume, and the active chemicals, which account for the remaining 25%. The composition of the gel mixture and their molecular weight were given in Table 1, according to the Sigma Aldrich manual. Before preparation, the beaker was washed properly with washing solutions (ketone) and finally placed in the hot air oven for 10 minutes to remove the alkaline residuals, since ketone evaporates in 40°C. Gelatin was dissolved in deionized water and heated to 45°C so that it would completely dissolve. The stock reagents were prepared in another beaker and maintained at a temperature of 35°C in an ultrasonic cleaner water bath. The final FXG dosimeter was prepared by infusing the stock solutions into the gel solutions at 35°C and kept stirred for 5 minutes, as shown in Figure 1. The prepared solutions were then transferred to 10 ml plastic containers and kept at 5°C for 24 hours.

Adjusting the pH of the gel samples

The pH of the gel samples was adjusted by increasing either the concentration of Gelatin or the concentration of Sulfuric acid. However, the chosen gelatin concentration of 4% (w/v) was sufficient to reduce the post-irradiation diffusion of ferric ions after time, resulting in the loss of spatial dose information [9]. The most convenient way is to change the acid concentration to adjust the pH of the gel samples. Subsequently, the gel mixture was augmented with 40mM of sulfuric acid. This sequential procedure was iterated for sulfuric acid concentrations of 50 mM and 60 mM.

Table 1. Composition of the reagents used in the preparation of the FXG dosimeter.

Composition	Molecular Formula	Molecular weight (g/mol)
Gelatin	$(C_{17}H_{32}N_5O_6)X$	402.47
Ferrous Ammonium Sulfate exahydrate	$(NH_4)_2SO_4.FeSO_4.6H_20$	392.13
Xylenol Orange tetra sodium salt	$C_{31}H_{28}N_2O_{13}SNa_4$	760.6
Sulfuric acid	H_2SO_4	98.08

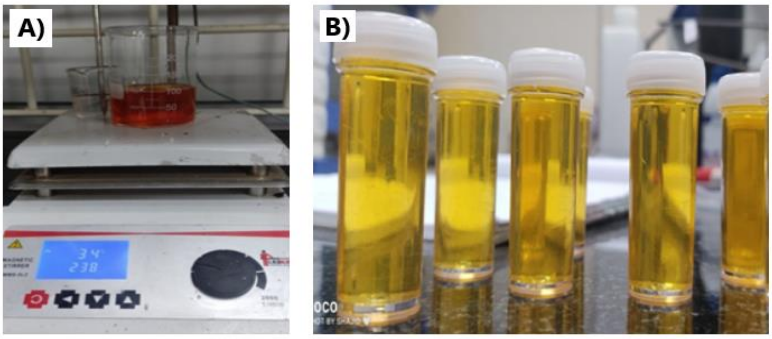

Figure 1. A) Infusion of Fricke solution. B) Freshly prepared gel samples in 10 ml in gel solutions at 35°C

Measuring pH

After preparation, the pH of the solutions was determined using a digital pocket pH meter. At first, the meter was calibrated by mixing the buffer powder of pH value 4.01 in 250 ml of distilled water. It was stirred well until the powder dissolved completely in the water. Then, the pH meter was dipped into the beaker containing the solution, and the pH value was noted. Corresponding to the buffer solution, the pH value shown by the meter was adjusted, and then the calibrated pH meter was used to measure the pH value for the prepared FXG gel samples, which were shown in Figure 2.

Reduction in Auto-Oxidation rate

The impact of natural oxidation on ferrous ions becomes more significant at higher concentrations, as the oxidation rate is directly proportional to the square of the concentration. As a result, this increased oxidation accelerates the system's instability over time [4]. It can be minimized by storing the dosimeter at an optimum temperature before irradiation. The samples were placed at room temperature, 5°C, and below freezing temperature -18°C. The auto oxidation rate of non-irradiated gel batches was measured by spectrophotometer.

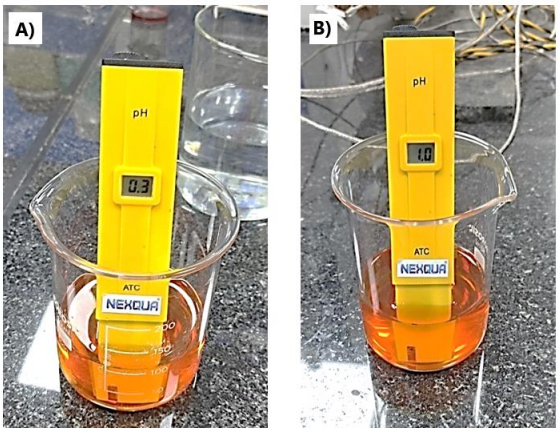

Figure 2. A) FXG gel solution with pH 0.3, B) FXG gel solution with pH 1.0

Irradiation of Fricke Gel Dosimeter

The gel samples were irradiated in a water bath using a telecobalt unit (Phoenix, Theratronics International Limited) with parallel opposed lateral beams of field size 15 cm × 15 cm in source-axis-distance (SAD) setup, which were shown in Figure 3. Perspex slabs of 10 cm thickness were kept below the water bath to account for backscatter. The gel cuvettes were irradiated with different doses ranging from 0 to 15 Gy. Fifteen gel samples were irradiated in a water bath as triplets for each dose interval. All the gel samples were kept at room temperature for 2 hours before irradiation for thermal stabilization.

Figure 3. Parallel opposed irradiation setup of gel samples in water bath of field size 15 X 15 cm^2 using telecobalt unit (Phoenix, Theratronics International Limited)

Absorption spectra analysis of the Fricke Xylenol Gel dosimeter

The optical density (OD) of the FXG was analyzed immediately after irradiation using a Jasco V-770 UV-Vis-NIR spectrophotometer, covering the wavelength range of 200 to 800 nm, with a focus on the visible region. The irradiated gels were poured into quartz cuvettes since quartz doesn't absorb any light. The data were obtained for the visible region 300-700 nm with a step size of 1 nm and the change in Fe^{3+} concentration was measured at the wavelength of 585 nm [10].

Results

The optimal concentration of the Fricke Xylenol Gel (FXG) dosimeter was 95% water, 4% gelatine, and three other chemicals make the remaining 1%, namely 0.4 mM ferrous ammonium sulfate, 0.1 mM Xylenol Orange, and 50 mM sulfuric acid. Gel samples were categorized into low, high, and optimum pH levels based on the sulfuric acid concentrations in the gel mixture (Table 2).

Table 2. Shows the corresponding measured pH value for the gel samples with different acid concentrations

Gel Mixture	Measured pH value	Range
4%Gelatin + 0.4mM FAS + 0.1mM XO + 40mM H_2SO_4	1.2-1.3	High
4%Gelatin + 0.4mM FAS + 0.1mM XO + 50mM H_2SO_4	1.0	Optimum
4%Gelatin + 0.4mM FAS + 0.1mM XO + 60mM H_2SO_4	0.3-0.5	Low

Abbreviation: FAS= Ferrous ammonium sulfate, XO= Xylenol orange, H_2SO_4= Sulfuric acid

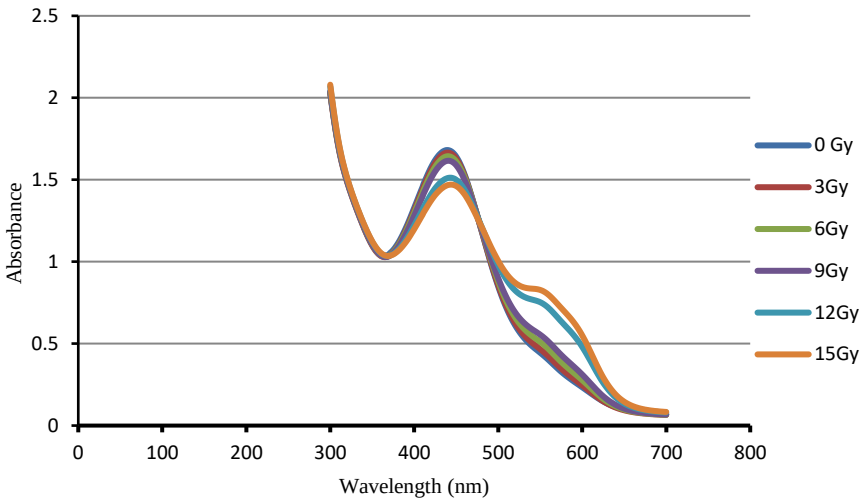

Figure 4. Absorption Spectrophotometric measurements of irradiated Gel batches of pH 1(50mM) in the wavelength region of 300-700nm.

The values obtained from the spectrophotometric measurements for visible range 300-700 nm were plotted for Fricke Xylenol Gel (FXG) dosimeter, which has been stored at 5° C for 10 days. The peak obtained at 585 nm is used for the quantification of the complex Fe^{3+} -XO that increases with an increase in absorbed dose, and simultaneously, another peak will occur at 435 nm due to the compound XO, which strongly absorbs light at 435 nm. The absorbance value at 435nm tends to reduce relatively. The spectrum clearly shows two peaks, the first one at 435 nm due to XO compound and the second one at 585 nm due to double Fe3+ - XO complex as shown in Figure 4.

At a pH of 1, the dosimeter was found to show a maximum and linear response up to a dose of 10 Gy with high correlation (R2=0.988), and it shows a sigmoidal function above 10 Gy and again increases linearly, as given in Figure 5 and 6. The change in absorbance per unit gray is 0.025 Abs/ Gy.

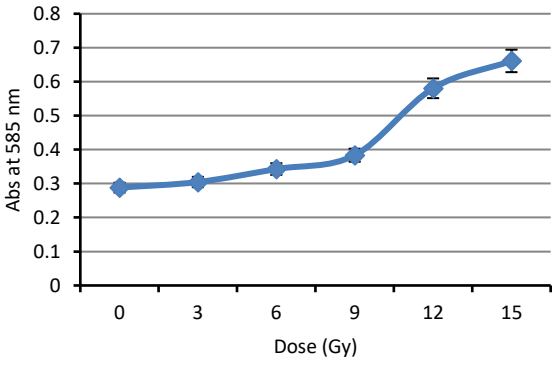

Figure 5. Absorbance (Abs) values measured at 585 nm as a function of absorbed dose for optimum pH (1)

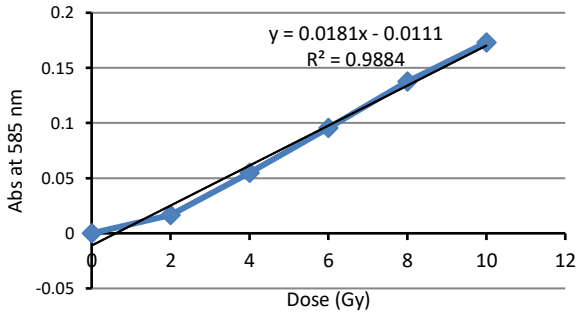

Figure 6. Absorbance (Abs) values measured at 585nm corrected for background as a function of absorbed dose in the range between 0 to 10 Gy for optimum pH (1)

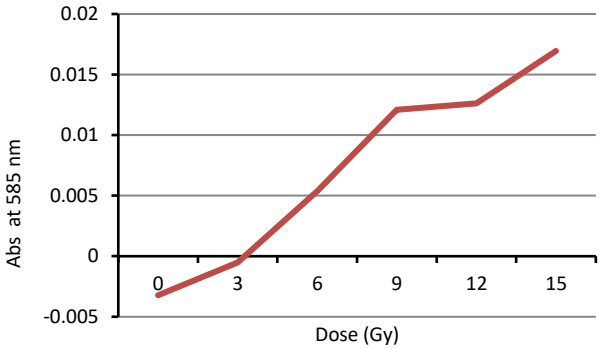

Figure 7. Dose vs corrected absorbance (Abs) for low pH.

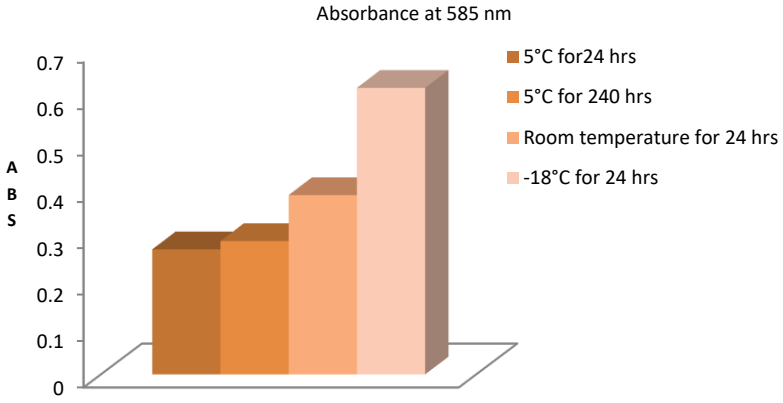

Figure 8. Autoxidation of gel samples kept at different storing temperatures.

Figure 9. High pH gel samples

At a pH of 0.3, the dosimeter exhibited reduced sensitivity to radiation exposure, as illustrated by the change in absorbance per unit gray (0.00015 Abs/Gy), as depicted in Figure 7. Additionally, Figure 8 presents the auto-oxidation rates of pre-exposed gels stored at various temperatures.

Discussion

From the Figure 4, it shows a well-defined isosbestic point occur at 480 nm, it confirms the presence of two different mechanism of light absorption in the region before and after the isosbestic point [10]. The same result was observed in the study [10].

The pH of the Fricke Xylenol Gel (FXG) samples tends to affect the dose response of the dosimeter, altering the concentration of gelatinous base, and sulfuric acid can increase or decrease the sensitivity of the dosimeter. This effect is due to the gelatin and sulfuric acid changing the pH of the gel mixture. In addition to the pH level, careful attention should be given to the quantity of gelatin employed. Research indicates that utilizing gelatin exceeding 5% of the total weight leads to two distinct outcomes. Initially, there is a noticeable increase in initial absorbance, followed by a subsequent reduction in transparency. This observation could be attributed to the heightened viscosity of the gel, subsequently impacting its fluidic characteristics [11]. Consequently, the feasibility of the gel for optical spectrophotometer readings becomes compromised, rendering it unreadable in such a context. Therefore, the concentration of gelatin and its corresponding viscosity play a pivotal role in determining the effective method for quantitative measurements.

The system exhibited heightened sensitivity to radiation, demonstrating a linear response to radiation exposure at a pH of 1. The linear dose response of FXG at radiation doses below 10 Gy provides insight for potential 3D dosimetric applications in radiotherapy [12].

High acid content strongly reduces the system sensitivity, and the change in absorbance per unit gray is 0.00015 Abs/ Gy. This may be because the excessive H^+ acid ions act as a scavenger that primarily reacts with the hydroxyl ions OH^- resulting in the formation of water molecules and failing to deprotonate XO compound. At low pH, the complex Fe^{3+}-XO would dissociate, and the H^+ acid ions readily bond with XO molecules instead of bonding with Ferric ions [13]. As a result, the final product Fe^{3+}-XO complex is not formed, since this complex only absorbs light at 585 nm to quantify the change in concentration which is relative to the dose absorbed in that medium.

At low acid concentrations, the corresponding pH value was 1.2 -1.3, in which the system shows instability, accompanied by a gradual shift of the xylenol orange color to purple, even without any exposure to radiation [4], as shown in Figure 9. The reason for this is that the Fe^{2+} ions had already undergone spontaneous oxidation, turning the gels purple [11].

FXG is sensitive in preparing conditions like chemical purity, additives, and temperature [14]. Alkaline residuals in the beaker may also affect the pH of the system, so it is necessary to clean the beaker properly, as mentioned in the gel preparation section. Due to natural oxidation over time, the Fricke gel solution experiences an increase in its absorbance values after its preparation. So, the gels prepared with the same concentration were kept below freezing temperature 0° F (-18° C) for 24 hours, and the gels were kept outside

for two hours to get equilibrium with the irradiation ambience.

Auto-oxidation occurred more rapidly in samples stored at 0°F (-18°C) for 24 hours compared to those kept at room temperature. Conversely, gel samples stored at room temperature exhibited slower auto-oxidation during the same period. Solutions stored under typical laboratory conditions, with exposure to both natural and artificial light at approximately 25°C, demonstrated a significant increase in absorbance values when compared with the solutions kept at 5°C. This increase peaked after one week of storage and was twice the level observed in solutions refrigerated at 5°C for the same duration. Notably, the rate of auto-oxidation was significantly lower in gel samples stored at 5°C for a duration of 10 days.

The novelty of this study is encapsulated in its multi-faceted investigation of the Fricke Xylenol Gel (FXG) dosimeter. By delving into the interplay of factors such as composition and pH, the study offers fresh insights into enhancing the dosimeter's performance. The identification of optimal concentrations, such as the combination of 95% water, 4% gelatine, and a strategic blend of ferrous ammonium sulfate, Xylenol Orange, and sulfuric acid, demonstrates a novel approach in achieving improved sensitivity to radiation. Furthermore, the study uncovers the role of pH as a significant determinant impacting the response of the dosimeter and the delicate balance needed to harness the best performance. It's essential to note that alkaline residuals present in the beaker can influence the pH of the system. Therefore, thorough cleaning of the beaker, as specified in the gel preparation section, is imperative to prevent unintended pH variations. The study's comprehensive assessment of temperature effects, including auto-oxidation rates at varying storage conditions, highlights the intricate variables at play and underscores the practical relevance of the findings. In essence, this research bridges scientific exploration with practical implications, paving the way for enhanced radiation dosimetry techniques and potential applications in diverse fields.

Conclusion

Measuring radiation-induced changes in the optical density of a transparent coloured gel results in a dosimetric system that is simpler, faster, and cost-effective. The optimal final concentration of the Fricke Xylenol Gel dosimeter reagents was 4% gelatin in Deionized water, 0.4 mM Ferrous Ammonium Sulfate, 0.1 mM Xylenol Orange tetra sodium salt, 50 mM Sulfuric acid contributes a pH value of 1 at which the dosimeter shows a maximum response and linear over a dose of 10 Gy. The oxidation of Fe^{2+} ions to Fe^{3+} ions in the gel samples was substantially minimized when maintained at a storage temperature of 5°C.

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