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A new approach to optimize the genipin gel dosimeter formulation

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► ***Original article***

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ABSTRACT

Background: In this work, we investigated the effect of adding 0.3% w/w of the non-toxic substance agarose to the dosimeter formulation of genipin radiochromic gel, which was named LCA-GENA (Low Concentration Agarose-GENipin and Agarose) gel dosimeter. ***Materials and Methods:*** A compact linear accelerator with a beam quality of 6 MV and a dose rate of 200 cGy/min irradiated the produced gel dosimeters in a dose range of 0-10 Gy. A UV-Visible spectrophotometer was used to read out the irradiated gel dosimeters. Calibration curves for both absorbance peak and area-under -spectrum responses were investigated. Furthermore, the physical and radiological characteristics of the new formulation were investigated. ***Results:*** The results showed that the dose sensitivity of the LCA-GENA gel dosimeter under the irradiated conditions is $(8.4 \pm 0.15) \times 10^{-3}$ cm^{-1} Gy^{-1}. Results showed adding the abovementioned percentage of agarose will increase the melting point of the genipin gel dosimeter from 24°C to 28°C. Also, an investigation of the radiological properties of the novel formulation revealed that this radiochromic gel is water equivalent. ***Conclusion:*** From the obtained results, it is verified that adding 0.3% w/w agarose to the genipin gel dosimeter leads to an increase in the melting point of the original genipin gel dosimeter, easier fabrication, and lower price than that of higher agarose concentrations. The mentioned features make this gel suitable for dosimetry applications in clinical and radiotherapy environments.

INTRODUCTION

Gel dosimeters have many advantages, including tissue equivalency, sensitivity to different types of radiation with different doses and energies, registering the dose distribution in three-dimensional and two-dimensional, being independent of the direction of the radiation, etc. [1-5]. Due to the mentioned characteristics, these dosimeters might be used for various applications, such as dosimetry in the radiotherapy environment or verification of treatment plans [6-10]. When gel dosimeters are exposed to radiation, structural and chemical changes occur, which can be recorded using magnetic resonance imaging, X-ray CT (Computed tomography) scan, optical CT, spectrophotometry, etc. [11-13]. Gel dosimeters are mainly divided into radiochromic and polymer types, and each group has specific advantages and disadvantages [14, 15]. Genipin is a hydrolytic product of geniposide found in the fruit (gardenia jasminoides ellis). The structure of genipin was discovered in 1960 using nuclear magnetic resonance spectroscopy data and chemical degradation experiments [16]. Genipin is a natural cross-linker for gelatin. Genipin can bind to different amino acids that constitute the gelatin and form blue pigments.

When genipin cross-links with gelatin, the color of the solution slowly changes from transparent to blue, and the gel will become darker over time [17]. This blue hydrogel is radiochromic and can be scanned by optical CT and spectrophotometer [18]. This gel will turn pale (pale blue) under irradiation and have a light absorption peak near 600 nm, which a spectrophotometer can measure. It is verified that the diffusion effect does not occur in the genipin gel dosimeter after exposure [19]. However, this issue is one of the limiting features of many gels, especially ferric and polymer gels [20, 21]. In 2011, Georgia *et al.* calculated the radiological properties of Genipin dosimeter gel for electron and photon beams and concluded that this gel dosimeter is the water equivalent from a dosimetry point of view [22]. In 2016, Jarrah *et al.* investigated the effects of adding inorganic salts and glucose on this gel's dosimetric response and physical properties [23]. It has also been shown that the response and sensitivity of the Genipin gel dosimeter depend on the reading temperature. One of the disadvantages of genipin gel dosimeters is the low melting point of this gel, which melts at a temperature of 24° C [24]. It has been reported that in many therapeutic environments, we face temperatures of 21-24 degrees [25]. The low melting point of the genipin gel dosimeter will severely limit the use of these dosimeter gels in many therapeutic and dosimetry applications. In addition,

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this low melting point in making and transporting the gel can cause serious problems.

In the previous research, some specific percentages of the agarose additive were investigated to solve this problem, named the GENA (GENipin and Agarose) gel dosimeter [26]. Also, it is shown that the sensitivity of the GENA gel dosimeter is independent of energy and dose rate [27]. Agarose is a non-toxic polysaccharide polymer with a melting point of 90 ^{0}C. This substance increases the gel's strength and has a more robust gelation process than gelatin. The basis of adding this non-toxic substance to increase the melting point of dosimeter gels is extracted from the research used by Abtahi *et al.* for the MAGIC (Methacrylic acid, Ascorbic acid, Gelatin, Initiated by Copper) polymer gel dosimeter [4]. Previously, the use of formaldehyde to increase the melting point of magic polymer gel dosimeters has been investigated and studied by Pavoni and Bafa [28], but formaldehyde is a highly toxic and carcinogenic substance. This toxic substance is not recommended for modifying the formulation of gel dosimeters for the reasons above.

In this research, the effect of adding a small concentration of agarose to genipin gel to modify the formulation of this dosimeter gel has been investigated. The new formulation was named LCA-GENA (Low Concentration Agarose-GENA) gel dosimeter. The LCA-GENA offers cost advantages over the previous formulation and boasts lower production complexities.

MATERIALS AND METHODS

Fabrication of the LCA-GENA gel dosimeter

Davies and colleagues introduced the composition for producing genipin dosimeter gels without any additives; however, their formulation had the drawback of a low melting temperature [19]. In the current study, a minor quantity of agarose was incorporated into their formulation to address the issue of low melting temperature.

For this purpose, a formulation was prepared using 96% w/w ultra-pure water (high-purity grade, high-pressure liquid chromatography grade, obtained from the Direct-Q 3 UV water purification system by Millipore, France). The formulation also included 3.7% w/w gelatin (Porcine Skin, Type A, 300 Bloom, Sigma Aldrich, USA), 100 mM sulfuric acid (Merck, Ltd., Germany), and 50 μM genipin cross-linker (Merck, Ltd., Germany). Furthermore, 0.3% w/w agarose (Merck, Ltd., Germany) was incorporated into the formulation.

The method of incorporating agarose into the gelatin matrix (gelatin-agarose) is based on the research conducted by Abtahi *et al.* to develop the MAGICA (MAGIC and Agarose) polymer gel dosimeter. Hence, the agarose is dissolved in 30% w/w water, while gelatin is dissolved in 70% w/w water [4].

70% w/w water was poured into a balloon (round -bottomed, TGI Glassware, Germany) to produce the LCA-GENA gel dosimeter. The balloon was sealed with aluminum foil (14 μm thickness, Toshna company, Iran) to prevent the photo-induced cross-linking of genipin and gelatin during manufacturing. The sealed balloon is positioned in a Pyrex water bath (Cocotte Ovale Pyrex, France, 4.5 Lit, -40°C + 300°C). The water bath was placed on a heater stirrer. Gelatin was added to the water, poured into the balloon, and soaked for ten minutes. Then, the gelatin water mixture temperature was increased to 45 °C. The mixture was stirred until the gelatin was dissolved completely. The temperature of the solution was checked using a thermometer placed in the water bath.

The agarose solution was prepared in a 250 ml beaker (Novin Pyrex, Iran) on a separate heater stirrer. 30 % w/w water was poured into the beaker to produce an agarose solution. The agarose was added to the water, and the mixture temperature was raised to 90 °C. Then, let the agarose is dissolved in the water completely. Afterward, the temperature of the agarose solution decreased to 45°C. At this temperature, the agarose solution was added to the gelatin solution.

Then, the genipin was added, and the mixture temperature was increased to 70°C. After 5 hours, the color of the solution changes from clear white to blue. Afterward, in a dark room (to prevent light irradiation to the gel made), the solution was poured into spectrophotometer cuvettes (1 ×1 ×1 ×4.5 cm3, made of polystyrene, Guangzho JET Bio-filtration Products, Ltd, China). Furthermore, two centrifuge vials (length 118.54 mm, maximum and minimum diameter 17.53 mm and 15.62 mm) were filled to measure the melting point.

Cuvettes were protected from ambient light using 5 mm thick aluminum foil. The cuvettes and vials are placed in a refrigerator at 4 ^{0}C for at least 24 hours. In the previous research, different concentrations of agarose, such as 0.5, 0.7, and 0.9% w/w, were investigated [26]. This research investigated the effect of 0.3% w/w agarose concentration on the GENA gel dosimeter's response, sensitivity, and radiological and physical properties. The modified GENA gel dosimeter was named LAC-GENA (Low Agarose Concentration GENA).

Radiological characteristics

A 25 ml pycnometer (Hubbard-Carmick specific gravity glass, Thomas Scientific, USA) was used to measure the mass density of the prepared LCA-GENA gel dosimeter. To calculate the electron density (ρ_e) and the number of electrons per gram (n_e), equations (1) and (2) were employed, respectively.

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$$\rho_e = \rho \cdot N_A \cdot \Sigma W_i \cdot \left(\frac{Z_i}{A_i}\right) \quad (1)$$

$$n_e = (\rho_e / \rho) \quad (2)$$

where ρ is the mass density; N_A is Avogadro's number; W_i is the weight percentage of the i-th element with atomic number Z_i and atomic mass A_i.

The effective atomic number of the desired gel dosimeter is calculated using the Maynord formula shown in equation (3):

$$Z_{eff} = \sqrt[2.94]{\sum_{i=1}^{n} a_i \cdot Z_i^{2.94}} \quad (3)$$

where ai represents the proportion of the total number of electrons attributed to each element [29].

Melting point Measurements

Two centrifuge vials filled with gel were placed in a water bath to measure the melting point of the produced gel dosimeter. Following the technique introduced by Abtahi *et al.*, three needles (hoaxing, China) are inserted into the gel and allowed to attain thermal equilibrium with the water bath's temperature (21 ± 0.5 °C) [4]. Then, the water bath temperature was increased by one degree steps. At each temperature, a waiting period of 30 minutes was observed to ensure isothermal conditions between the gel dosimeter and the water bath. The gel's loose temperature is defined as the point at which it begins to melt, but not entirely melted. At this temperature, the needles inserted into the gel are released. The melting point is the temperature at which the gel completely melts, and the phase changes from solid to liquid [4].

Irradiation procedure

The produced gel dosimeters were exposed using a compact accelerator (Elekta, SL 25.75, England). The cuvettes were placed at a depth of 5 cm in a homemade 30 × 20 × 30 cm^3 plexiglass water phantom to ensure full scattering conditions. The phantom was made using the standards described in the references [29, 30]. Irradiation parameters were a field size of 12×12 cm^2, gantry rotation of 90 degrees, a source-to-surface distance of 96.5 cm, a beam quality of 6 megavolts, and a dose rate of 200 cGy/min. Doses of 2, 4, 6, 8, and 10 Gy were delivered to the center of the cuvette, respectively. The maximum error of delivered radiation dose was ± 0.03 Gy. Three samples were irradiated for each absorbed dose, and three were left unexposed as blanks/controls. Irradiation took place at a temperature of 20 ± 0.5°C. Figure 1 demonstrates images of three samples with various absorbed doses.

Readout technique

The samples were readout 12 hours post-irradiation. A spectrophotometer (Camspec, M350, Double beam UV-Visible spectrophotometer, England) read the irradiated and blank samples. A 450-800 nm wavelength range was applied to scan the gel dosimeters. The samples were read at a temperature of (20 ± 0.5°C).

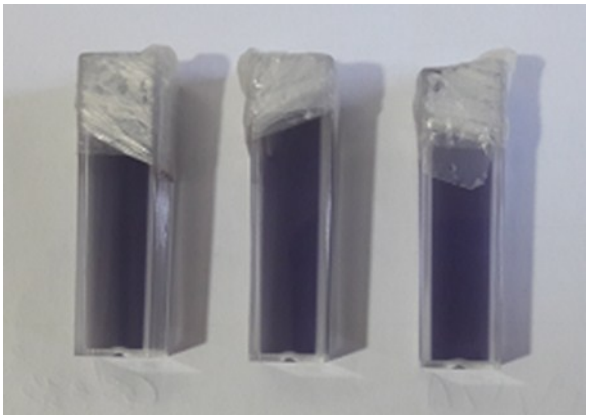

Figure 1. Cuvettes containing LAC-GENA gels are exposed to 0, 4, and 10 Gy from right to left, respectively.

To produce a calibration curve, absorbance peaks (AP) of curves with different absorbed doses were plotted as a function of the absorbed dose. The calibration curve's slope is considered the gel dosimeter's sensitivity [4]. Besides this, another parameter called the AUS (area under the absorption spectrum) was investigated. The AUS values for irradiated gels are obtained using equation (4) [31]:

$$(AUS) = \int_{\lambda_1}^{\lambda_2} \text{absorbance}_{(\lambda)} d\lambda \quad (4)$$

where the start wavelength of λ_1 and the final wavelength of λ_2 were 450 and 800 nm, respectively.

R-square and Adjusted R-square are applied to evaluate the goodness of the linear fit. As these parameters get closer to one, the linearity response of the gel dosimeter gets better. Interested readers refer to reference [32] for more details about the goodness of fit parameters.

Dose resolution

The dose resolution (D_Δ^P) was previously introduced as the minimal discrimination of two detectable absorbed doses, with a specific confidence level of p [33]. The dose resolution was calculated by equation (5).

$$D_\Delta^P = K_P \sqrt{2} \frac{\sigma_a}{\alpha} \quad (5)$$

where K_P is the coverage factor. The coverage factor for confidence levels of 52%, 68%, and 95% are reported as 0.71, 1, and 1.96, respectively [33]. σ_a is the standard deviation of response, and α is the dose sensitivity of the LAC-GENA gel dosimeter.

According to eq. (5), dose resolution and minimum detectable dose (MDD) can be affected by the exposed LAC-GENA gel dosimeters' standard deviation and dose sensitivity.

When the absorbed dose approaches zero, the dose resolution is defined as the minimum detectable dose (MDD).

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Statistical analysis

In this research, statistical analysis of the results was done using SPSS software (IBM SPSS@ Statistics) with Tukey and 2-tailed tests [32]. Interested readers are referred to ref. [34] for more descriptions about used statistical analysis.

RESULTS

Dose-AP response of LAC-GENA gel dosimeter

The maximum absorption value for the LAC-GENA gel dosimeter occurs at a wavelength of 601 ± 1.51 nm. For instance, the absorbance spectrum of the LAC-GENA gel dosimeter for a specific absorbed dose is demonstrated in figure 2. The AP-sensitivity of this gel dosimeter was (8.4 ± 0.15) × 10^{-3} cm^{-1} Gy^{-1}. The goodness of fit parameters of R^2 and adjusted- R^2 for linear fit to dose-AP data are 0.981 and 0.976, respectively. Equation (6) shows the relationship between the LAC-GENA gel dosimeter response and the absorbed dose.

$$Absorbance = (-0.0084 \times Dose) + 1.008 \quad (6)$$

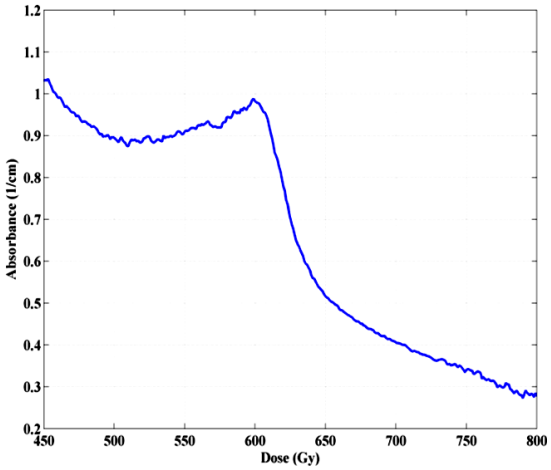

Figure 2. The absorbance spectrum of the LAC-GENA gel dosimeter for a 2 Gy absorbed dose. The absorbance peak occurs at a wavelength of 601 nm.

AUS response of LAC-GENA gel dosimeter

Figure 4 displays the AUS response of the LAC-GENA gel dosimeter. The AUS sensitivity of the radiochromic LAC-GENA gel dosimeter is equal to 1.805 nm. cm-1 Gy-1. Equation (7) shows the relationship between the AUS response of the gel dosimeter to different absorbed doses. R^2 and adjusted R^2 for AUS response were 0.981 and 0.976, respectively.

$$AUS = (-1.805 \times Dose) + 235.7 \quad (7)$$

Melting piont of genipin-agarose gels dosimeter

It was observed that the needles sunk into the gel dosimeter at 27°C, but the gel had not completely melted. At 28°C, the gel was completely melted, and its phase changed from solid to liquid. Therefore, a temperature of 27 °C is considered the loose temperature, and a temperature of 28 °C is the melting point of the LAC-GENA gel dosimeter. This temperature is suitable for many dosimetry garboards in clinical and radiotherapy environments.

Radiological characteristics of genipin-agarose gels dosimeter

The elemental compositions of the made gel dosimeter, water, and soft tissue are reported in table 1. The results show that the hydrogen component of the LAC-GENA gel dosimeter is close to the water's hydrogen component, and this difference is equal to 1.4%. However, the oxygen component for the produced gel is less than water. Since the total photon cross-section of oxygen and carbon is identical, the total, partial composition of carbon and oxygen can be considered a substitute for water.

The mass density, effective atomic number, number of electrons per gram, and electron density of the produced gel dosimeter, water, and soft tissue are reported in table 2.

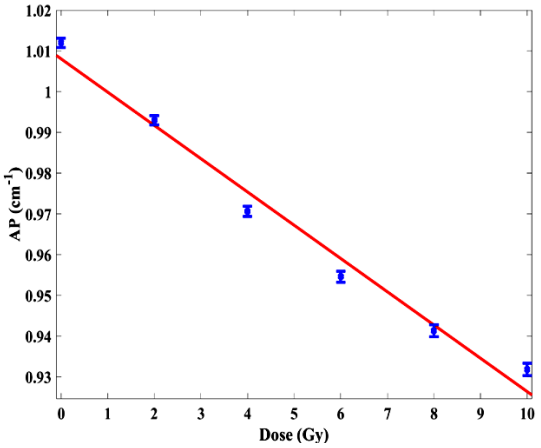

Figure 3. The linear fit to LAC-GENA gel dosimeter's dose-absorbance peak (AP) in a dose range of 0-10 Gy. Error- bars indicate the standard deviation in AP at each absorbed dose. Response decreasing is due to the dosimeter bleaching upon irradiation.

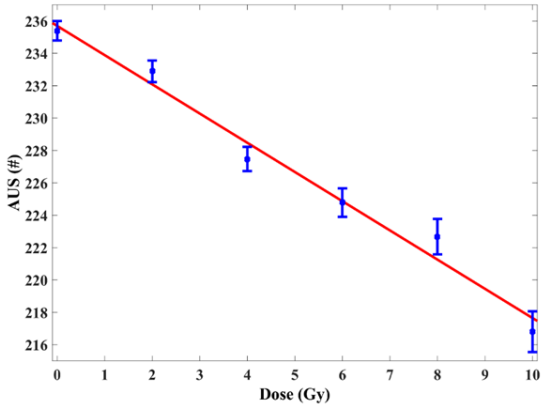

Figure 4. The linear fit for area unser spectrum (AUS) response of LAC-GENA gel dosimeter as a function of absorbed dose in a dose range of 0-10 Gy. Error- bars indicate the standard deviation in AUS at each absorbed dose.

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Table 1. Elemental composition of LAC-GENA gel dosimeter, water, and soft tissue. WH, WN, WC, WO, and WS indicate weight percentages of hydrogen, nitrogen, carbon, oxygen, and sulfur, respectively. W(C+O) shows the total weight percentages of oxygen and carbon.

Material type	W_H (%)	W_N (%)	W_C (%)	W_O (%)	$W_{(C+O)}$ (%)	W_S (%)
LAC-GENA	11.05	0.65	1.65	87.32	88.97	0.32
Water	11.2	-	-	88.8	88.8	-
Soft tissue	10.2	3.4	14.3	70.8	85.1	0.3

Table 2. Effective atomic number (Zeff), mass density (ρ), electron density (ρe), and number of electrons per gram (ne) for LAC-GENA gel, water, and soft tissue.

Material type	Z_{eff}	ρ (gr/cm^3)	ρ_e (cm^{-3})	n_e (gr $^{-1}$)
LAC-GENA	7.45	1.003	3.38×10^{23}	3.37×10^{23}
Water	7.51	1	3.34×10^{23}	3.34×10^{23}
Soft tissue	7.34	1.04	3.44×10^{23}	3.31×10^{23}

Dose resolution

The changes in dose resolution as a function of absorbed dose are depicted in figure 5. As shown in figure 5, the dose resolution of the LAC-GENA gel dosimeter varied from 0.375 to 0.515 Gy for a 0-10 Gy dose range. Also, the minimum detectable dose (MDD) is 0.428 Gy for the investigated LAC-GENA gel dosimeter.

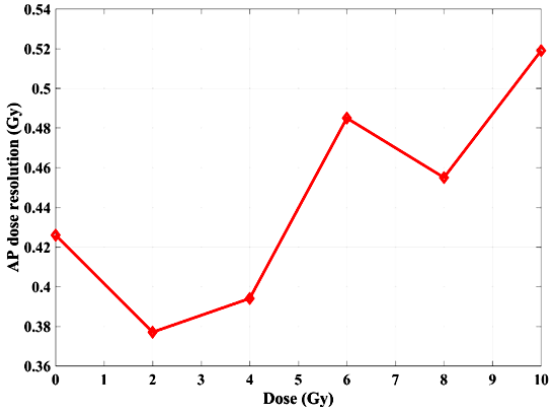

Figure 5. Absorbance peak (AP) dose resolution variation of LAC-GENA gel dosimeter vs. absorbed dose. The lines connecting the points are drawn only for the guidance of the eyes and have no physical meaning.

DISCUSSION

The results showed an AP-sensitivity of 8.4×10^{-3} cm^{-1} Gy^{-1} for LCA-GENA gel dosimeter. An original radiochromic genipin gel dosimeter was previously investigated by Davies *et al.* [19]. They reported a sensitivity value of 5.7×10^{-3} cm^{-1} Gy^{-1} for the Genipin radiochromic gel dosimeter. The dose sensitivity of the LAC-GENA gel dosimeter investigated in this research was 30.3% higher than the sensitivity value of the gel dosimeter investigated by Davies *et al.* Also, the dose sensitivity of the original genipin gel dosimeter produced in a similar condition to the current research was equal to 8.6×10^{-3} cm^{-1} Gy^{-1} [26]. The dose sensitivity of the LAC-GENA gel dosimeter is 2.3% less than the original genipin gel dosimeter, but statistical analysis revealed that this difference is insignificant ($p > 0.05$). A radiochromic leuco crystal violet (LCV) gel dosimeter was investigated by Xie *et al.* [35]. They obtained a dose sensitivity of 6.31×10^{-3} cm^{-1} Gy^{-1} for the mentioned radiochromic gel dosimeter. The dose sensitivity value of the LAC-GENA gel dosimeter is 22.8% higher than that of the Leuco crystal violet gel dosimeter. An orange Fricke gel dosimeter was investigated by Gallo *et al.* [36]. They have reported a dose sensitivity of 77×10^{-3} cm^{-1} Gy^{-1} for this dosimeter gel, which is noticeably higher than the dosimeter sensitivity of the radiochromic LAC-GENA gel dosimeter. A leuco malachite green (LMG) dye gel dosimeter was investigated by Jordan [37]. He showed that the dose sensitivity for this radiochromic gel dosimeter is equal to 4.4×10^{-3} cm^{-1} Gy^{-1}. The sensitivity of the LAC-GENA gel dosimeter produced in this research is 90.9 % higher than the sensitivity of the gel dosimeter presented by Jordan. Therefore, the dose sensitivity of the LAC-GENA gel dosimeter of this research is more than that of previously produced genipin gel, leuco crystal violet gel, and leuco malachite gel, but it is less than of orange Fricke gel dosimeters for gamma-rays.

The results showed that the area under spectra (AUS) response is more sensitive than the absorption reading parameter. This parameter increases the dose sensitivity of the radiochromic LAC-GENA gel dosimeter by 220.7 times. Also, the higher sensitivity of the AUS reading parameter compared to the absorption reading parameter has been investigated and confirmed by Abtahi *et al.* for the PAGATUG (Poly Acrylamide, Gelatin, And Tetrakis, Urea, Glucose) polymer gel dosimeter [31]. This increase in sensitivity is equal to 120.9. Hence, the dose sensitivity increment factor for the radiochromic LAC-GENA gel dosimeter is 1.83 times higher than that of PAGATUG polymer gel dosimeters. The more interesting readers are referred to ref [26, 27]. Our previous research demonstrated that the AUS sensitivity of the original genipin gel dosimeter was 1.72 nm. cm^{-1} Gy^{-1} [26]. The AUS sensitivity of the LAC-GENA gel dosimeter in the current study was better than that of the original genipin gel by 4.7%. Hence, adding 0.3% w/w agarose can improve the AUS sensitivity of the genipin gel.

The results showed that the melting point of the genipin-based gel dosimeter increased by four degrees Celsius by adding 0.3% w/w of agarose. This result can be compared with that reported by Jarrah *et al.* [23]. They showed that by adding 5% w/w glucose to the formulation of genipin gel, its melting point could be increased up to 28 degrees Celsius. They also showed that by increasing the weight percentage of gelatin from 4% w/w to 7% w/w, the melting point of genipin gel could be increased to 27 degrees. In this research, using only 0.3% w/w agarose additive, it was shown that the melting point

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of the genipin gel dosimeter could be increased up to 28 degrees Celsius, which seems an easier and cheaper method than the previous procedure. Also, our previous study verified that higher agarose concentrations could increase the melting point of the genipin gel dosimeter more effectively [26]. However, this research's lower utilized concentration of agarose additive led to easier fabrication, lower price, and suitability for many clinical and radiotherapy dosimetry applications.

The difference between the total percentage of carbon and oxygen of the LAC-GENA gel dosimeter and the oxygen percentage of water is only 1.9%. However, the oxygen in the produced gel is less than water. Gorgiara *et al.* calculated the weight percentages of the radiochromic genipin gel dosimeter components using the Monte Carlo code [22]. For this gel dosimeter, they have reported weight percentages of 11.05, 1.522, 0.5216, 86.96, and 0.3108 for hydrogen, carbon, nitrogen, oxygen, and sulfur components, respectively. From comparing the LAC-GENA gel dosimeter with the Genipin gel dosimeter, differences of 0%, 7.8%, 1.9%, 0.4%, and 0.3% for hydrogen, carbon, nitrogen, oxygen, and sulfur components are obtained, respectively. Hence, it confirmed that the LAC-GENA gel dosimeter is more equivalent to soft tissue than the dosimeter of genipin gel.

From the comparison of the results obtained from Gorgiara *et al.*'s research, it can be concluded that the electron density, effective atomic number, and number of electrons per gram of genipin gel dosimeter are equal to that of the LAC-GENA gel dosimeter and the difference in the mass density of genipin gel dosimeter and LAC-GENA gel dosimeter is only 0.2%. A nitroblue tetrazolium (NBT) pluronic gel dosimeter was investigated by kwiatos *et al.* [38]. Comparing their obtained results with water showed that the differences between the effective atomic number, number of electrons per gram, mass density, and electron density of the NBT gel dosimeter and water are 2.6%, 0.3%, 3.1%, and 2.9%, respectively. These results verified that the LAC-GENA gel dosimeter has more water-equivalent behavior than the NBT pluronic gel dosimeter. Also, from the obtained data, the difference in effective atomic number, mass density, electron density, and number of electrons per gram is 0.8%, 0.3%, 1.1%, and 0.9%, respectively, between LAC-GENA gel dosimeter and water are obtained. From the obtained results, it can be concluded that the LAC-GENA gel dosimeter is a water-equivalent dosimeter.

The dose resolution fluctuation for the original genipin gel dosimeter in a dose range of 0-10 Gy was reported to be 29.2% [26]. However, the dose resolution fluctuation for the LAC-GENA gel dosimeter in the same dose range dose range was 17.7%. Hence, the LAC-GENA gel's dose resolution variation is less than the original genipin gel dosimeter for the mentioned dose range. Davies *et al.* reported the dose resolution of the genipin gel dosimeter varies between 0.8-1 Gy for a 0-10 Gy dose range [19]. The MDD of the genipin gel dosimeter was reported to be 0.8 Gy [19]. Hence, it can be concluded that the dose resolution of the newly produced LAC-GENA gel dosimeter is better than that of the genipin gel dosimeter produced by Davies *et al.*. On the other hand, the MDD of the LAC-GENA gel dosimeter is better than that of the genipin gel by 46.5%.

A VIPAR (N-vinylpyrrolidone argon) gel dosimeter was investigated by Kozicki *et al.* [39]. They reported the dose resolution of this gel dosimeter varies between 0.65-1.35 Gy. Also, a MAGIC gel is investigated by Hurley *et al.* [40]. They reported the dose resolution of the mentioned gel dosimeter is less than 0.5 Gy for 0-10 Gy doses. A leuco crystal violet (LCV) micelle gel dosimeter was investigated by Babic *et al.* [41]. They reported the dose resolution varies between 0.08-0.12 Gy. Hence, the dose resolution of the LAC-GENA gel dosimeter is better than that of the original genipin gel, previously produced genipin gel, VIPAR, and MAGIC gel dosimeters but worse than that of the LCV gel dosimeter.

CONCLUSION

It is shown that the addition of 0.3% w/w agarose to the genipin gel formulation can increase the melting point of the original genipin gel dosimeter from 24 °C to 28 °C. Also, results revealed that adding 0.3% w/w agarose does not significantly change the genipin gel's dose sensitivity and water equivalency.

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***Author contribution*:** S.M.M.A., Conceptualization; Supervision; Methodology; Formal analysis; Visualization; Writing - Review & Editing; Investigation; Funding acquisition. F.B., Methodology; Validation; Formal analysis; Data Curation; Investigation. D.S., Supervision; Investigation; Writing - Review & Editing.

***Conflicts of interest*:** None.

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