Radiation Physics and Chemistry 101 (2014) 53–58

Contents lists available at ScienceDirect

Radiation Physics and Chemistry

journal homepage: www.elsevier.com/locate/radphyschem

Radiation-induced change of optical property of hydroxypropyl cellulose hydrogel containing methacrylate compounds: As a basis for development of a new type of radiation dosimeter

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HIGHLIGHTS

- White turbidity appeared even at 1 or 2 Gy of ^{60}Co γ-ray irradiation.
- Haze could be used as an index of the degree of white turbidity.
- UV–vis spectroscopy indicated multiple mechanisms leading to white turbidity.

ARTICLE INFO

Article history:
Received 12 March 2014
Accepted 2 April 2014
Available online 13 April 2014

Keywords:
Hydrogel
Hydroxypropyl cellulose (HPC)
Methacrylate
White turbidity
Dosimeter
Haze

ABSTRACT

Hydrogels with matrix of a cellulose derivative, hydrogel of hydroxpropyl cellulose (HPC), containing two of methacrylate compounds (2-hydroxyethyl methacrylate (HEMA) and poly(ethylene glycol) dimethacrylate (9G)) were irradiated with ^{60}Co γ-rays. The gels become white with irradiation, and thus, could be candidates of a new type of radiation dosimeter utilized in radiation therapy because the gels become white with irradiation and can be confirmed directly by human eyes even at low doses of 1–2 Gy. Radiation-induced change of optical properties, haze value and UV–vis absorption spectrum, of the irradiated gels was measured. Dose response of the white turbidity appearance was different for different compositions of the methacrylate compounds as well as for different dose rates. The degree of the radiation-induced white turbidity was quantified by measuring haze value, showing linear dose response in low dose region (<2 Gy). We also analyzed the gels with a UV–vis spectrometer and HEMA- and 9G-rich gels gave different spectral shapes, indicating that there are at least two mechanisms leading to the white turbidity. In addition, dose rate dependence was smaller for 9G-rich gels than HEMA-rich gels in the range of 0.015–1.5 Gy/min.

1. Introduction

Nowadays, cancer is one of the major reasons of human deaths and its therapy with ionizing radiations is being spread thanks to high quality of life (Foray and Balosso, 2008). It is required in radiation therapy to control dose, and planned dose should surely be given to cancer, with reducing dose given to normal tissues surrounding the target as much as possible in order to reduce risk of radiation hazards such as secondary carcinogenesis, necrosis, etc. For this purpose, several kinds of irradiation methodologies have been developed, e.g. IMRT (intensity modulated radiation therapy), SRT (stereotactic radiotherapy), BNCT (boron neutron capture therapy), a scanning irradiation system, irradiation with a rotating gantry system, charged particle irradiations, brachy therapy, and so on. Such a development enables us to plan complicated dose distributions in human bodies (Foray and Balosso, 2008; Noda and Kamada, 2010). It is well studied whether a three-dimensional dose distribution actually given in a phantom is sufficiently accurate compared to that planed in advance to the irradiation. However, there is no useful and convenient tool capable to confirm dose distributions in patients' bodies. Gel dosimeters have been expected to be a promising tool for such a validation because their densities, atomic compositions and mean excitation potentials are almost equivalent to those of human bodies as well as because radiation-induced chemical changes are fixed inside gel matrices (Baldock et al., 2010; McJury et al., 2000).

Gel dosimeters utilizing radiation-induced polymerization of vinyl monomers are called as *"polymer gel dosimeters"*. Most of

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http://dx.doi.org/10.1016/j.radphyschem.2014.04.004
0969-806X/

them can be categorized into two types: PAG- and MAG-types. The PAG (polyacrylamide gel) type contains acrylamide or similar compounds as the vinyl-type monomers while the MAG (methacrylic acid gel) type contains methacrylic acid and similar compounds. In 2001, ascorbic acid was introduced in polymer gel dosimeters as an oxygen scavenger, which realized *"normoxic"* polymer gel dosimeters (Fong et al., 2001). Another oxygen scavenger, tetrakis(hydroxymethyl)phosphonium chloride (THPC), was proposed next year by De Deene et al. (2002). The oxygen scavengers reduced complications in manufacture of polymer gel dosimeters and realized normoxic gel dosimeters such as nPAG and nMAG. It is known that sensitivities of most of proposed gel dosimeters have, more or less, dose rate dependences (Jirasek, 2006). Sensitivities of polymer gel dosimeters are, in most cases, evaluated as increase of R_2 value with unit dose, $R_2/D\ s^{-1}\ Gy^{-1}$. Here R_2 is defined as the reciprocal value of the relaxation time T_2 in magnetic resonance measurements. De Deene et al. (2006) investigated the sensitivities of PAG, nMAG, and nMAG dosimeters in the dose rate range from 0.25 to 4 Gy/min. The sensitivities of the dosimeters commonly decrease with increasing dose rate. The decreasing percentage in the dose rate range was 6% for PAG, 4% for nPAG, and 34% for nMAG. Thus, generally speaking, dose rate dependences of MAG-type dosimeters are rather significant compared to those of PAG-type dosimeters. Recently, Vandecasteele et al. (2011) examined dose rate dependences of radiochromic leucodye micelle hydrogel dosimeters, LMD1–3 and LCS. Although their gel dosimeters are different from polymer gel dosimeters of PAG- and MAG-types in terms of reaction mechanisms as well as of the way of dose determination, all of their dosimeters also showed dose rate dependences. Their sensitivities, which were evaluated based on the absorbances measured at around 587–636 nm, decreased with increasing dose rate from 0.5 to 4 Gy/min. The decreasing percentages of the sensitivities were 42% for LMD1, 24% for LMD2, 36% for LMD3 and 35% for LCS.

There are still a few points to be improved as follows. First, hydrogels of gelatin need appropriate temperature management because they can soften with increasing temperature and could release water during storage. Chemical gels, which have covalent bonding between matrix polymers, are more stable in terms of shape or conservation of solvent than physical gels, such as gelatin and agarose gels, which have only week hydrogen bonding. It has already been shown that a cellulose derivative prepared with a radiation crosslinking technique (Tamada and Maekawa, 2010) can be utilized for polymer gel dosimeters (Hiroki et al., 2013). Second, spatial dose distributions are read out from irradiated gel dosimeters normally by using magnetic resonance apparatuses such as MRI or NMR. These apparatuses are huge and expensive. If chemical changes induced by ionizing radiations in gel dosimeters are visible and easily quantified, such dosimeters are more convenient. Some gels of cellulose derivatives prepared with a radiation crosslinking technique are much more transparent than gelatin or agarose gels, and it is quite easy to see radiation induced polymerizations inside the gel matrix (Hiroki et al., 2013). Third, vinyl-type monomers used in the polymer gel dosimeters are rather toxic. There are some attempts to use less toxic monomers (Hiroki et al., 2013; Senden et al., 2006); however, there is still a room to hope for much less toxic monomers.

In this study, it was aimed to observe radiation-induced change of optical properties of hydroxypropyl cellulose (HPC) hydrogels containing methacrylate compounds because such a chemical system is proposed as a new type of polymer gel dosimeter (Hiroki et al., 2013), which has a potential to reduce the above-mentioned weaknesses. From the viewpoint of toxicity as well as of sensitivity toward irradiations, two methacrylate compounds, 2-hydroxyethyl methacrylate (HEMA) and poly(ethylene glycol) dimethacrylate (9G), were selected as polymerizing monomers with irradiation. The present paper will show dose response of white turbidity evolution by using optical measurements such as haze measurement and UV–vis spectroscopy, and discuss composition dependence, dose rate effect, and mechanism leading to visual change.

2. Experimental

2.1. Chemicals

Hydroxypropyl cellulose (HPC), viscosity of which in 2 wt% aqueous solution at 20 °C is in the range of 1000–5000 cP, and 2-hydroxyethyl methacrylate (HEMA) of Wako 1st Grade were purchased from Wako Pure Chemical Industries Ltd. Poly(ethylene glycol) dimethacrylate (9G) of 536 g/mol in averaged molecular weight and 80 wt% aqueous solution of tetrakis(hydroxymethyl) phosphonium chloride (THPC) were purchased from Shin-Nakamura Chemical Co., Ltd. and Tokyo Chemical Industry Co., Ltd., respectively. Chemical structures of HPC, HEMA and 9G are shown in Fig. 1. All chemicals were used without further purification, and polymerization inhibitor, hydroquinone monomethyl ether (MEHQ) in HEMA (250 ppm) and 9G (100 ppm), was not removed. Ultrapure water (>18.3 MΩ cm) from a Milli-Q system was used throughout all the processes of both radiation crosslinking of HPC and manufacture of gel samples.

2.2. Manufacture of gel samples

In the present study, gel samples went through three steps: (i) manufacture, (ii) irradiation, and (iii) analysis. Note that ionizing radiations were used not only in step (ii) but also in step (i) in order to prepare chemically bonded gel matrices of HPC. An electron beam of 2.0 MeV was used in step (i) while ^{60}Co γ-rays were used in step (ii).

Powders of HPC were dispersed into ultrapure water at the concentration of 20% in weight and kneaded for at least 30 min, giving paste like state of HPC–water mixture. After 1-week storage at 4 ± 1 °C in a refrigerator, the paste like mixture was pressed, with the pressure of approximately 18 MPa for 30 min, into a sheet of 1 mm thickness (150×150 mm^2). The sheet was packed in a PE/nylon package after purging air, and immediately irradiated with the electron beam at room temperature. The sheet was put on a conveyer system and irradiated with the current of 2.0 mA. The speed of the conveyer was set at 4.16 m/min, corresponding to the dose rate of 5 kGy per one-time passage through an irradiation field. All the sheets were repeatedly passed through the irradiation field 4 times, giving total dose of 20 kGy.

The irradiated sheet was stored in the refrigerator for 1 week to wait stabilization of radiation-induced crosslinking reactions. Subsequently, it was taken out from the package and cut into small pieces (20×30 mm^2), and washed by dipping them into ultrapure water for 1 week or longer with refreshing water every day. The washed small pieces were dried in vacuum at 40 °C for at least 1 day. The swelling ratio of radiation-crosslinked HPC was measured gravimetrically to be 16.6 ± 0.3. In other words, the concentration of radiation-crosslinked HPC in a sufficiently swollen state is 5.7 ± 0.1% in weight. Such gel properties can be varied by

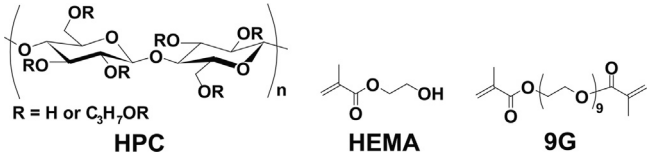

Fig. 1. Chemical structures of HPC, HEMA and 9G.