

IONIZING RADIATION EFFECT ON THE POLYCARBONATE COLUMN TO BE USED IN THE ^{99}Mo - $^{99\text{m}}\text{Tc}$ GENERATOR

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ABSTRACT

Radiopharmaceutical is a substance that, due to its pharmaceutical form, activity and radiation energy, can be used for diagnosis and treatment of living beings, may be administrated by oral or parenteral routes. Radiopharmaceuticals for diagnosis are composed by radionuclides those emit gamma radiation, such as, technetium-99m, iodine-123, indium-111, gallium-67 and thallium- 201, among others. The ^{99}Mo - $^{99\text{m}}\text{Tc}$ generator is a closed system, composed by a chromatographic column of aluminum oxide (Al_2O_3), in which is introduced a known activity of ^{99}Mo , it disintegrates in the column and originates the $^{99\text{m}}\text{Tc}$. When sterile saline solution (NaCl 0.9%) flows through the column, only $^{99\text{m}}\text{Tc}$ in the form of sodium pertechnetate ($\text{Na}^+\text{TcO}_4^-$) is collected in the eluent, while ^{99}Mo remains adsorbed in the alumina column. Now a day this column is made of borosilicate type 1 glass. This study envisages a research to characterize polycarbonate (PC) column irradiated in saline solution to mimic ^{99}Mo - $^{99\text{m}}\text{Tc}$ generator use condition. The effect of radiation dose on the column of PC EB irradiated in the presence of saline solution was studied by HPLC with fluorescence detector in order to investigate bisphenol A (BPA) release. A protocol was developed to perform the HPLC analysis of PC irradiated samples. A calibration curve was prepared from 5 to 500 $\mu\text{g L}^{-1}$ (ppb). It was possible to observe BPA on saline PC irradiated samples just close to the first point of calibration curve. The developed protocol and HPLC with fluorescence detector can be used to detect BPA release in saline solution with ppb amount.

1. INTRODUCTION

Bisphenol A (BPA) is a substance which is used as a component of synthetic plastics materials, for instance synthesis of polycarbonate (PC) [1,2], and also as an antioxidant in plastics, paints and adhesives [3-5]. In 2001, world production of BPA (since the 1960s in the US) was estimated at about 2.5 million tonnes [6]. Materials containing BPA have been used in many applications, for example as a varnish on the inside of metal cans and other types of packaging used for the storage of food products, beverages and pharmaceuticals as well [7-9]. The polycarbonate, Figure 1, has been used for the production of medical device components (for dialysis and oxygenation of the blood), bottles for feeding infants and cooking plates. The wide use of polycarbonate follows mainly from their particular properties - durability, high tensile strength, light weight, high tensile mode, glass transition temperature and high

melting point [10-14]. For years BPA has been treated as neutral to human healthiness however BPA detection in the natural environment, drinking water and food products (since 1990), aroused the interest of researchers. Almost at the same time a negative effect of this compound on human health was established. Consequently, the BPA has been classified by the European Commission as a substance with harmful effects on human health. Many biochemical and toxicological studies confirmed that bisphenol A have estrogenic properties and an undesirable effect on the estrogen receptor. In recent studies [15,16] BPA has been classified as a disturbing hormonal balance for humans and other animals also proved to have estrogenic activity, even at concentrations of 1 ng L^{-1} [17-20].

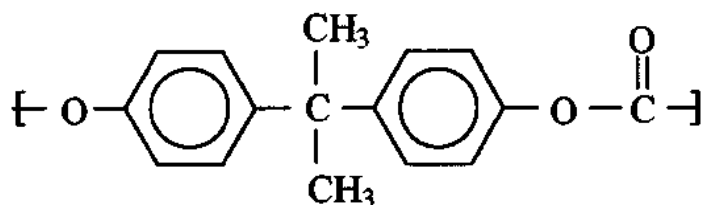


Figure 1: Chemical structure of polycarbonate ([21].

Due to the large applicability of PC, and considering its application in medical field, it is necessary to study the effect of ionizing radiation on medical devices made of PC that would be sterilized through this kind of processing [21]. One possible use would be in the column used on $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generator. The radiopharmaceuticals of technetium-99m ($^{99\text{m}}\text{Tc}$) have become, in the last 30 years important diagnostic agents used in nuclear medicine clinics, depending on a number of physical characteristics such pharmaceutical form as well as the quantity and quality of radiation. Currently, there are about 30 of these compounds being used in nuclear medicine generating a volume corresponding to 80% of examinations clinical routine a nuclear medicine service. Through $^{99}\text{Mo}/^{99\text{m}}\text{Tc}$ generating system, $^{99\text{m}}\text{Tc}$ element can be easily available in hospital nuclear medicine or service. The generator is a closed system comprising a chromatographic borosilicate glass column with aluminum oxide (Al_2O_3), on which is deposited a known activity of ^{99}Mo . In the column, ^{99}Mo disintegrates and gives $^{99\text{m}}\text{Tc}$. Sterile saline (NaCl 0.9%) is forced to pass through the column, collecting in the liquid eluent mostly $^{99\text{m}}\text{Tc}$ in the form of sodium pertechnetate ($\text{TcO}_4^- \text{Na}^+$), while the ^{99}Mo remains adsorbed to the alumina column, Figure 2 [22].

Physical and chemical properties of polymeric materials can be modified by ionizing radiation exposure, gamma rays, x rays and electron beam. Both crosslinking and degradation occur by main chain scission during radiation processing of polymers, however, one to another predominates in some irradiated materials [23]. Shintani [24] has observed bisphenol A release when PC containing BPA in its molecular structure was sterilized using gamma rays. This release should be avoided to protect human health against compounds that causes risk and in order to keep environment free of deterioration [25].

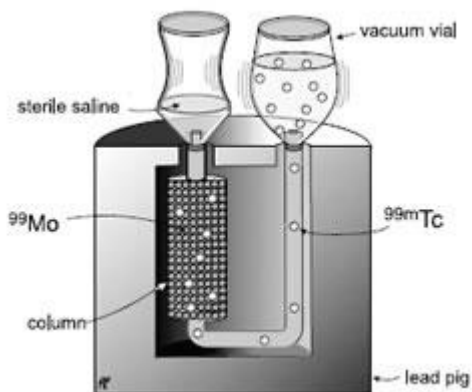


Figure 2: Generator of ^{90}Mo - $^{99\text{m}}\text{Tc}$ chromatographic column type IPEN-TEC [22].

When the radiation energy absorbed is bigger than the bond energy between the atoms of the polymer chain, occurs the homolytic cleavage of the bond and consequently there is the formation of free radicals. This formation is commonly expected in the radiolysis of all organic molecules. In the organic solids they may remain entrapped after irradiation. These radicals may cause the appearance of color in the polymer. The EPR technique may be used to observe the formation of radicals due to the interaction of radiation with the polymer and the subsequent decay of radicals by reactions between radicals or the air itself.

The column used in ^{99}Mo / $^{99\text{m}}\text{Tc}$ generator is currently made of borosilicate glass and the objective of this study is the characterization of polycarbonate column to replace the actual column used. In this paper will be presented preliminary results of the effect of ionizing radiation in irradiated polycarbonate in saline solution.

2. Experimental Part

2.1. Preparation of samples

It was taken from a polycarbonate plate, samples 25 mm long and 2 mm thick, supplied by the Radiopharmacy Center, IPEN, which were used in the preparation of the experiment.

The PC samples for electron paramagnetic resonance assays (EPR) were emerged in saline solution concentration of 9mg/mL (0.9%) supplied by HypoFarma placed in EPR purity quartz tubes.

For HPLC preliminary measurements, PC samples were cut into square peace, each sample with approximately 1 g using Mettler AB304-S model. PC samples were put into vials and 10 mL saline solution 9mg/mL(0,9%) of HypoFarma was added to each sample separately.

2.1.1. Irradiation

The set PC sample containing the saline solution and the quartz tube was irradiated with gamma rays from cobalt 60 sources of the Multipurpose Gamma Irradiator CTR-IPEN with absorbed radiation dose of 25 kGy, dose rate 15 kGy h⁻¹ in the presence of air and at room temperature. Immediately after the irradiation, the sample was kept in dry ice, at temperature of 195K before start measurements. Samples for HPLC measurements were irradiated with 25 kGy and 200 kGy.

2.1.2. Electron Paramagnetic Resonance

Two samples were prepared in quartz tubes containing PC one no irradiated and the other irradiated samples, both tubes were sealed with parafilm in the presence of air at atmospheric pressure and room temperature. The EPR spectra of the samples were obtained at room temperature with a Bruker EMX machine model X-BAND. Microwave power 0.6325 mW, 1 scan, modulation field 1G, center field 3525G, width 500G.

2.1.3. High Efficiency Liquid Chromatography

For BPA analysis in saline solution it was used High Efficiency Liquid Chromatography Jasco, automatic injector (AS-2059); quaternary pump (PU-2089); column oven (CO-2060); fluorescence detector (FP-2020): excitation 227 nm, emission 313 nm; chromatographic column SHODEX C18-4D (4.6 ID mm X 150 mm L); mobil phase acetonitrile:water, 70:30; isocratic programmed for 7 minutes;

2.1.4. Results and Discussion

The effects of ionizing radiation will be presented in some properties of the PC and also in its molecular structure. The EPR studies were performed using 25 kGy that is the conventional sterilization dose which can visibly observe a color change in the PC.

2.1.5. Formation of Radicals

The EPR is based on the paramagnetic resonance phenomenon of electron. At resonance conditions, a material which has electron with resultant magnetic moment which is not null and in the presence of an external variable magnetic field, absorbs the energy of a microwave excitation is fixed. As organic radicals have unpaired electron, being paramagnetic specie it is possible to observe them by this technique.

With the aim of EPR spectra it is possible to study the formation of radicals in the PC radiolysis and their decay of PC samples irradiated in the presence of air and saline solution.

In Figure 1 observed the EPR spectrum of irradiated PC with 25 kGy radiation absorbed dose. Even though most of EPR studies of PC had been performed at low temperature, here in this study it was possible to observe a strong signal, maybe possibly due to absence of air because PC was immersed in saline solution during irradiation. This information could be complemented by the observation of the gas evolution results of relative concentrations of CO and CO₂ found of 65.4% and 33.8%, respectively, using mass spectrometry by Hama and Shinohara [26] for PC γ -irradiated at room temperature to a radiation dose of 54 kGy.

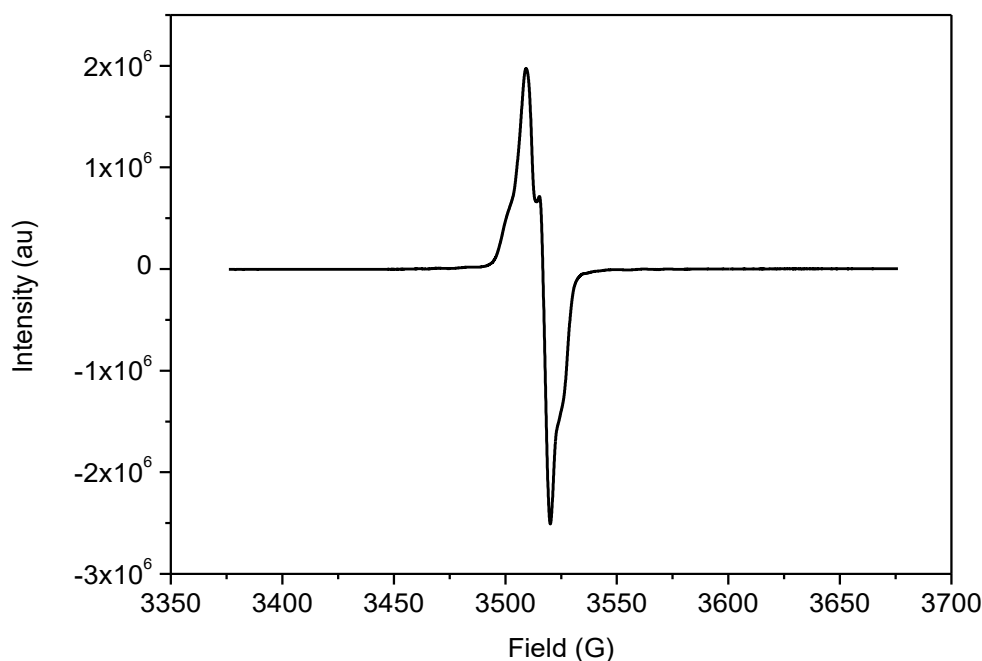


Figure 3: EPR spectrum of Polycarbonate irradiated in saline solution with 25 kGy in the presence of air.

Some papers can be found about ESR studies of irradiated polycarbonate in air, inert atmosphere, vacuum, but no results on PC irradiated in saline solution has been presented.

Hama and Shinohara [26] observed at least three kinds of paramagnetic species were produced in PC γ -irradiated at 77 K. Their PC sample became dark green after 7 kGy radiation absorbed dose, processed at low temperature, vacuum and bleached after temperature increase and visible light exposure. In this study, PC sample irradiated at room temperature became light green.

Furthermore, microwave power increase induced change on the shape of line of PC signal of the cited authors' study [26]. The following reactions of carbonate groups scission were proposed by them to the radicals observed by EPR.

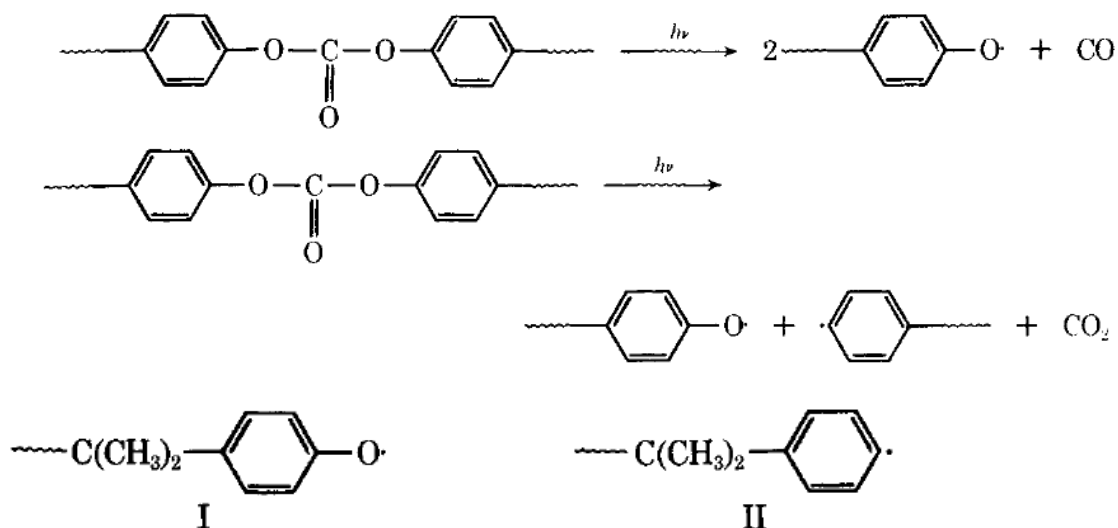


Figure 4: Scission of polycarbonate induced by g-radiation, leading to the formation of radical I phenoxy and II phenyl groups [26].

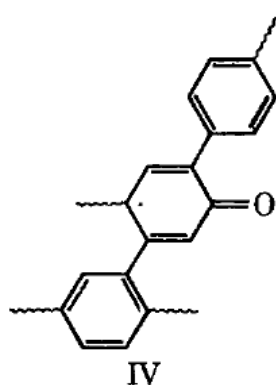


Figure 5: Polyenyl type radical [26]

It was observed in literature the decay of radicals through time after irradiation with increasing temperature. So, we intend to study PC' radical s behavior afterwards.

2.1.6. Preliminary results of quantification of BPA

It was necessary to develop a protocol analysis by liquid chromatography high performance for quantification of BPA at low concentrations of ppb order. A calibration curve using a standard of known concentrations was prepared. The patterns of chromatograms are shown in Figure 6.

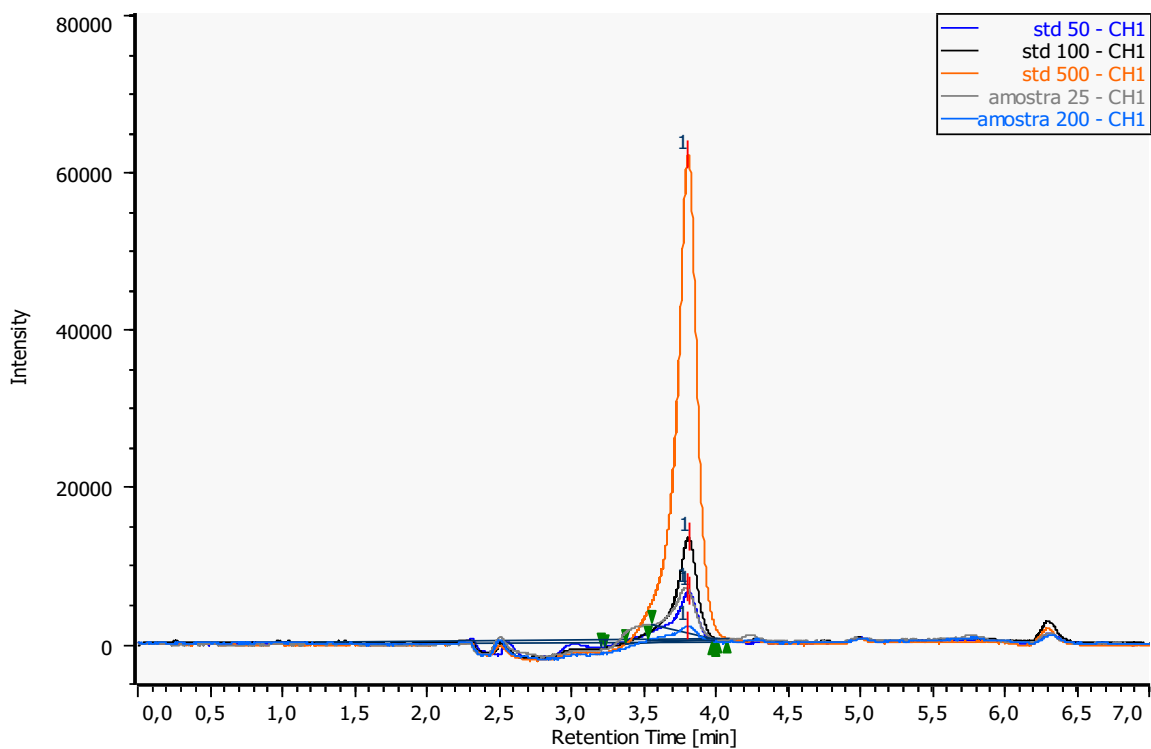


Figure 6: Chromatogram of BPA at concentrations from 50 to 500 $\mu\text{g L}^{-1}$

Areas were obtained from the peaks shown in Figure 6, these values are presented in Table 1.

Table 1: Values of peaks area of the obtained elution patterns of BPA

Concentration ($\mu\text{g mL}^{-1}$)	Area
50	81296
100	136494
500	656909

The values in Table 1 were used to prepare the calibration curve shown in Figure 7.

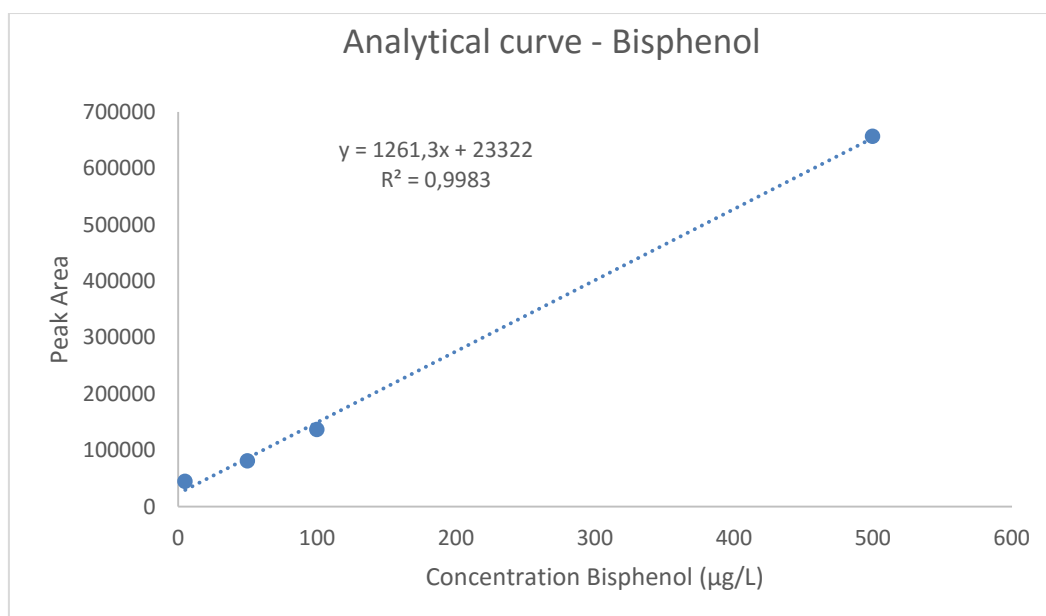


Figure 7: HPLC calibration curve of BPA.

With the results of the preliminary analysis and patterns of response curve indicates that the protocol developed for the study of BPA by HPLC can suitably be used for the BPA release study at concentrations in the order of $\mu\text{g L}^{-1}$ (ppb) of irradiated PC saline solution. The results of analyzes of PC saline solutions of the irradiated samples were compared with the calibration curve and, the values are shown in Table 2.

Table 2: Saline solution used in Polycarbonate irradiation at radiation absorbed doses of 25 and 200 kGy.

Samples	Area	Concentration ($\mu\text{g L}^{-1}$)
25 kGy	56998	26,7
200 kGy	13264	Below the detection limit

The pharmacokinetic study published by The American Chemistry Council showed that concentrations of BPA in the blood were much lower for oral doses than for other routes of administration, such as injection in the abdominal cavity (intraperitoneal) or under the skin (subcutaneous) [26]. As PC studied here will be eluted with saline solution that will be injected, it is important to analyze BPA release. Further information about testing of potential for trace levels of BPA to migrate from polycarbonate into food and beverages. Those tests were performed under conditions that are typical of how polycarbonate products are actually used. The results indicated that migration of BPA, when it is detected, is generally less than 5 parts per billion [26]. In this study limit detection was considered below 8 parts per billion.

3. CONCLUSIONS

EPR can be used to study PC stable radicals at room temperature, considering sterilization absorbed dose of a medical device. Preliminary results of BPA calibration curve and irradiated PC, concerning BPA release in saline solution, seems that the developed HPLC protocol can be used to detect and quantify BPA.

Further studies about color change of irradiated PC and radicals decay through time will be done.

Additionally, more analysis has to be performed to establish this HPLC protocol as routine way to quantify BPA in saline solution.

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