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Investigation of radiosensitivity of gamma irradiated procaine hydrochloride in the solid state

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Abstract: Dosimetric properties of gamma-irradiated procaine hydrochloride were investigated at room temperature by Electron Paramagnetic Resonance technique. No signal was obtained on the non-irradiated samples; however significant signals were obtained from the samples irradiated with gamma at certain doses. Mathematical functions and correlation coefficients were calculated determining the relation between the increasing radiation doses on the signal intensities of the sample. The free radicals were appeared to be stable at room temperature for more than 200 days.

Keywords: Electron Paramagnetic Resonance, Gamma Irradiation, Free radicals.

Gama ile ışınlanmış katı haldeki prokain hidroklorürün radyasyon duyarlılığının incelenmesi

Özet: Gama ile ışınlanmış prokain hidroklorürün dozimetrik özellikleri, oda sıcaklığında Elektron Paramanyetik Rezonans tekniği ile incelendi. Işınlanmamış numunelerde hiçbir sinyal elde edilmezken belirli dozlarda gamma ile ışınlanan örneklerden önemli sinyaller elde edildi. Artan radyasyon dozunun örneğin sinyal şiddeti üzerine etkisini belirleyen matematiksel fonksiyonlar ve korelasyon katsayıları belirlendi. Serbest radikallerin, oda sıcaklığında 200 günden daha uzun bir süre kararlı oldukları görüldü.

Anahtar kelimeler: Elektron Paramanyetik Rezonans, Gama Işınlanması, Serbest Radikaller

1. Introduction

EPR spectroscopy is frequently used in the investigation of drugs, food and amino acids [1-6]. Controlled exposure to gamma radiation kills microorganisms in a single procedure. Ionizing radiation includes high penetrating power, low residues and the temperature of the sample is almost unchanged. Because of these properties sterilizing with ionizing radiation can be used even in the final packaging stage of the product [7]. In addition to these advantages, some harmful effects of irradiation are present. Gamma rays can cause molecular destruction due to high energies. Free radicals are formed in the sample after irradiation and regulations may vary from country to country [8]. Therefore, consumers would like to know whether the product they consume is exposed to any radiation practice; and the amount of dose in kGy if it is exposed to radiation [9]. In this context, it is necessary to distinguish irradiated samples from non-irradiated ones. EPR spectroscopy has many advantages for identifying irradiated and unirradiated samples and is one of the leading methods

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Bu makaleye atıf yapmak için
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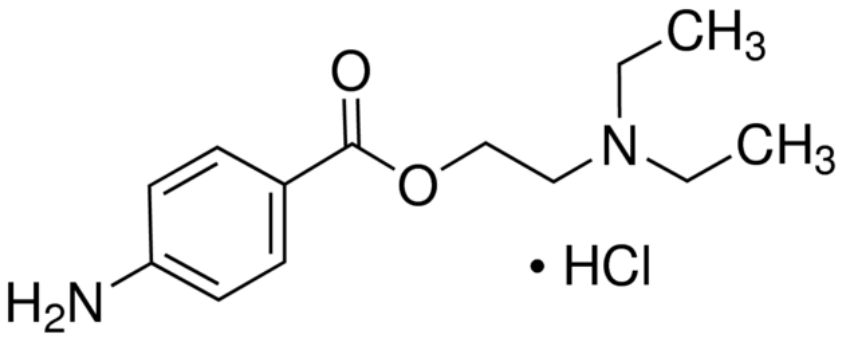
used to investigate the radiation sensitivity of irradiated samples of food and drugs [10,11]. The aim of this study is to find out whether procaine hydrochloride (PHCl) has been irradiated with ionizing radiation by EPR technique. In this paper, the variation of EPR signal intensity of the irradiated procaine hydrochloride versus irradiation dose (kGy), and storage time (days) was investigated.

2. Experimental

The sample used in this study was purchased from commercial sources. Commercial name, chemical formula, molecular weight (g/mol) and chemical structure of procaine hydrochloride is given in Table 1. Powders of PHCl (≈30 mg) were irradiated at different doses of up to 20 kGy by a ^{60}Co-γ ray source at room temperature. Irradiated samples were kept in plastic bags at room temperature. EPR measurements were carried out on samples in standard quartz EPR tubes at room temperature with a bruker model spectrometer operating at microwave power 9.48 mW, microwave frequency of 9.731 GHz, modulation amplitude 0.6 mT, magnetic field modulation frequency 100 kHz. The g factor was calibrated by comparison with a DPPH sample (g=2.0036).

Table 1 Commercial name, chemical formula, molecular weight (g/mol) and chemical structure of PHCl

Procaine hydrochloride; $H_2NC_6H_4CO_2CH_2CH_2N(C_2H_5)_2 \cdot HCl$; 272.77


3. Results and discussion

PHCl is one most effective local anesthetics that have the highest pKa level among the local anesthetics [12]. Besides procaine has been long employed as a pharmacological agent in the life sciences and clinical therapeutic studies [13]. The EPR spectrum of PHCl gamma-irradiated at 5 and 20 kGy is shown in Fig.1a and 1b, respectively. No signal was observed before irradiation. However after the irradiation the spectrum of the sample exhibits a sharp and clear EPR signal. The presence of these signals show that free radicals were formed in the structure after irradiation. The g value of the spectrum is calculated as g = 2.0034 ± 0.0005. This value agrees well with literature [14,15]. After irradiation at a dose of 20 kGy, while any change in the shape and g- factor not produced, a significant increase in signal intensity was observed.

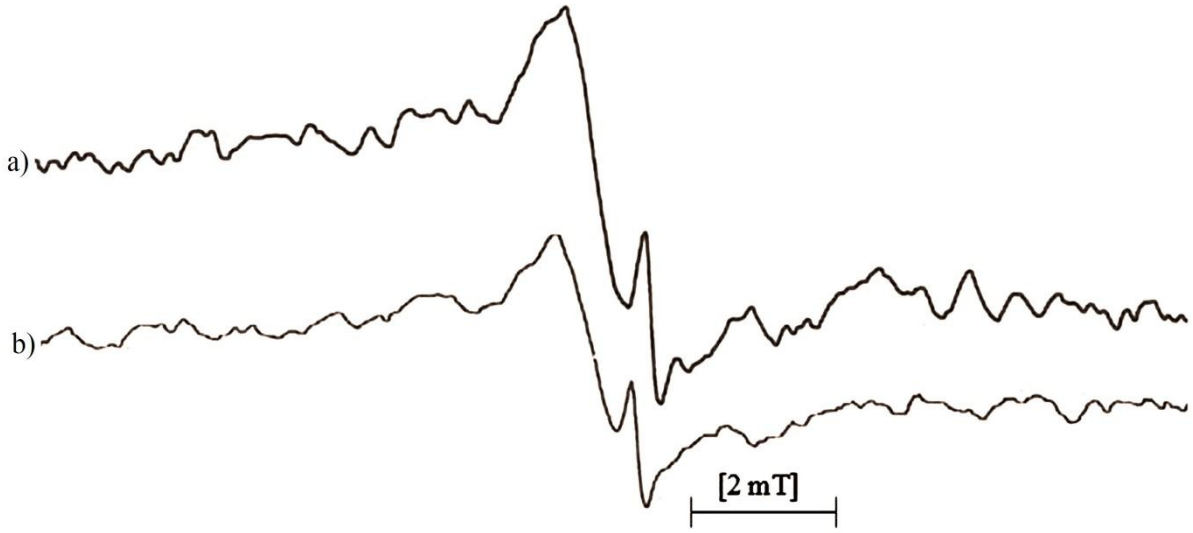


Figure 1. (a) Experimental spectrum of 20 kGy irradiated PHCl powder
(b) Experimental spectrum of 5 kGy irradiated PHCl powder

Aside from qualitative detection, EPR can be used for dose estimation [16]. Therefore, the effect of increasing radiation dose on the spectra of PHCl was studied. The samples irradiated in the dose range of 0-20 kGy were used to obtain dose-response curve of PHCl. The experimental results are shown in Fig. 2. In the Fig. 2; square signs represent experimental results; while curves connecting them represent the closest mathematical functions to experimental results.

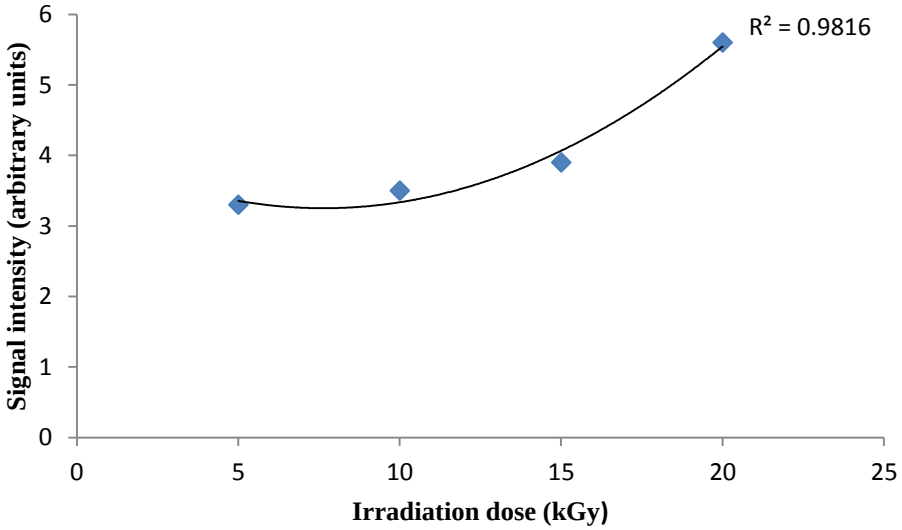


Figure 2. Dose-response curve of PHCl

It is seen, the experimental and calculated data was found to agree well with each other. Several mathematical functions were tried to describe evolution of the central EPR signal with absorbed radiation dose. Linear, exponential and polynomial functions are frequently used for this purpose [17-19]. Mathematical equations that show the best fit of the samples and correlation coefficient (R^2) are given in Table 2. In these functions, I and D are used for EPR signal intensity and treated irradiation dose in kGy, respectively and other parameters are constants to be determined. If the values calculated from these mathematical functions together with correlation coefficients are taken into consideration, the dose response curve of PHCl is explained best by polynomial function (R^2=0.9816). And the lowest correlation coefficient was calculated as 0.8105 with linear function.

Table 2 Mathematical functions calculated for dose-response curve of gamma irradiated PHCl

Functions	**Parameters**	**R^2**
$I = aD+b$	a = 0.146 b = 2.25	0.8105
$I = ae^{bD}$	a = 2.6089 b = 0.0339	0.8516
$I = aD^2+bD+c$	a = 0.015 b = -0.229 c = 4.125	0.9816

The signals created depending on irradiation of drugs should be capable of being tested during their shelf lives[18].Tests were carried out to investigate whether storage had an effect on the free radicals concentration. EPR spectra were recorded at room temperature within regular intervals in the daily process of 200 days. Decay curve of PHCl irradiated by 20 kGy is given in Fig.3.

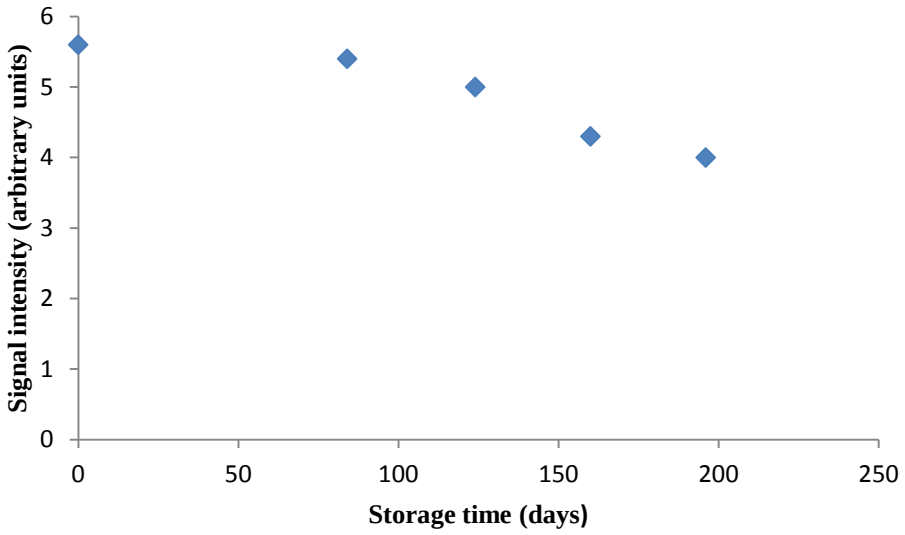


Figure 3. EPR signal intensity of PHCl irradiated at a dose of 20 kGy as a function of time

The data shown with squares in figure demonstrate the experimental results. While the signal intensity drops to 86% at the end of the 84th day, 58% of loss occurred at the end of 196 days. The results indicate that EPR spectroscopy could be used to distinguish irradiated PHCl samples from non-irradiated ones during the storage time.

4. Conclusion

Dosimetric features of gamma irradiated PHCl was investigated at room temperature. EPR signal intensity of the radical was observable for a longer time due to the stability of radical. However, further studies are needed to identify radiation sensitivity of drugs. The investigation of radiation sensitivity of the PHCl can be helpful for similar studies.

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