www.ecjse.com
ISSN:2148-3736
El-Cezerî Fen ve Mühendislik Dergisi
Cilt: 3, No: 3, 2016 (385-390)

El-Cezerî Journal of Science and Engineering
Vol: 3, No: 3, 2016 (385-390)

ECJSE

Research Paper / Makale

Effect of Irradiation Dose and Storage Time on the EPR Signal Intensities of Gamma Irradiated Sulfapyridine

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Received/Geliş: 27.04.2016 **Revised/Düzeltme:** 27.05.2016 **Accepted/Kabul:** 15.06.2016

Abstract: The interest in sterilizing the medicine using gamma energy is increasing. However, radiation may cause molecular degradation in the sample and thus may lead to the formation of free radicals due to high energy. This study aims to determine the radiation sensitivity of sulfapyridine (SU) irradiated with a predetermined dose using EPR spectroscopy. In the EPR spectra recorded at room temperature prior to radiation process, no EPR signal was observed. However, after the irradiation with gamma rays, EPR signal intensity increased significantly based on the irradiation dose. Mathematical functions and correlation coefficients were calculated determining the relation between the increasing radiation doses on the signal intensities of the sample. The stability of the free radicals created after the irradiation in time was investigated by recording the spectra of the sample irradiated with a dose value of 15 kGy in certain intervals. The results were found to be in good agreement with the existing literature data.

Keywords: Electron Paramagnetic Resonance (EPR), Radiation Sensitivity, Antibiotic.

Işınlama Dozunun ve Depolama Süresinin Gama ile Işınlanmış Sülfapridinin Sinyal Şiddeti Üzerine Etkisi

Özet: İlaçların gama enerjisi kullanılarak sterilizasyonuna olan ilgi artmaktadır. Ancak radyasyon yüksek enerjisinden dolayı örnekte moleküler yıkımlara sebep olabilmekte ve bu durum örnekte serbest radikaller oluşturabilmektedir. Bu çalışmanın amacı; belirli dozlarda ışınlanan sülfapridinin (SU) radyasyon duyarlılığını EPR spektroskopisi kullanarak belirlemektir. Işınlanmamış örneğin elde edilen EPR spektrumlarında hiç bir EPR sinyali gözlenmezken; gama ışınları ile ışınlanmanın ardından, artan ışınlama dozuna bağlı olarak belirgin EPR sinyalleri elde edildi. Örneğin artan radyasyon dozuna bağlı sinyal şiddetindeki artışı tanımlayan matematiksel denklemler ve korelasyon katsayıları hesaplandı. 15 kGy ışınlanmış örneğin belirli aralıklarla spektrumları kaydedilerek ışınlama işleminden sonra oluşan serbest radikallerin kararlılığı incelendi. Sonuçların mevcut literatür verileri ile uyum içinde olduğu tespit edildi.

Anahtar kelimeler: Elektron Paramanyetik Rezonans (EPR), Radyasyon Duyarlılığı, Antibiyotik.

1. Introduction

Sterilization is a process of inactivating microorganisms that can be anywhere, anytime [1]. Today, the sterilization method with radiation is often used in order to improve hygienic quality of the food, drugs and pharmaceutical raw materials, disposable medical products as well as to prolong

How to cite this article
Sütçü, K., "*Effect of Irradiation Dose and Storage Time on the EPR Signal Intensities of Gamma Irradiated Sulfapyridine"* El-Cezerî Journal of Science and Engineering, 2016, 3(3);385-390.

Bu makaleye atıf yapmak için
Sütçü, K., "*Işınlama Dozunun ve Depolama Süresinin Gama ile Işınlanmış Sülfapridinin Sinyal Şiddeti Üzerine Etkisi*" El-Cezerî Fen ve Mühendislik Dergisi 2016, 3(3);385-390.

their shelf lives and prevent food borne diseases [2-3]. Because, thanks to the powerful penetration ability of gamma rays, sterilization method with radiation can be applied to the product to be sterilized even in the final packaging stage of the product and it doesn't leave any chemical residues behind [4]. In addition, the product sterilized with gamma rays doesn't display any radioactivity and its temperature doesn't increase [5]. However, in addition to these advantages, gamma rays have also some disadvantages due to their high energies. Free radicals created in the product by gamma rays and the regulations vary from country to country in respect to method of irradiation are some of these disadvantages [6]. 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 [7]. As a result, it is necessary to investigate the radiation sensitivity of the raw materials of drugs to be exposed to radiosterilization. Electron Paramagnetic Resonance (EPR) spectroscopy is one of the leading methods used to investigate the radiation sensitivity of irradiated samples of food and drugs [8-9].

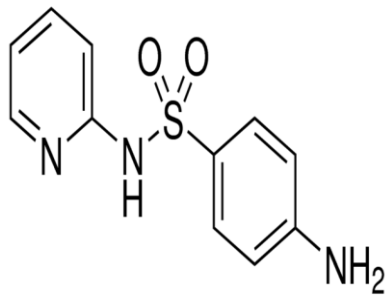
In this study, it has been aimed to determine radiation sensitivity of free radicals formed in the structure of SU drug sample using EPR technique after getting irradiated by certain doses of gamma rays.

2. Materials and Methods

SU were achieved from Aldrich-Sigma. Commercial name, chemical formula, molecular weight (g/mol) and chemical structure of SU is given in Table 1. Powder of SU (≈30 mg) were irradiated at different doses of up to 15 kGy by a ^{60}Co-γ ray source at room temperature (293K) at the Sarayköy Establishment of Turkish Atomic Energy Agency in Ankara. After the irradiation, the sample were kept in plastic bag, and left in the dark 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 1 mW, microwave frequency of 9.8 GHz, modulation amplitude 0.1 mT, magnetic field modulation frequency 86 kHz. The evolutions of the EPR signal with received radiation dose and storage time were followed by calculating the signal area determined by double integration of derivative EPR spectra. 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 sulfapyridine

1. Sulfapyridine, $C_{11}H_{11}N_3O_2S$, 249.29



3. Results and Discussions

Sulfapyridine is one of the widely used synthetic anti-microbial agent of the sulfonamide class having the bioactive p-amino group and is employed almost exclusively for the treatment of

pneumonia [10]. Sulfonamides are a major class of broad-spectrum synthetic antibiotics, widely used to treat respiratory, skin, and urinary tract infections, and as animal growth promoters [11].
In Fig. 1, the EPR spectra of SU powder irradiated at different radiation doses is presented. The values of linewidth and g factor are as follows; $\Delta H = 0.30$ mT and $g=2.0057 \pm 0.0005$, respectively. Considering the Fig.1, the signal intensity of the sample increased significantly depending on increase in irradiation doses. This proves that the increase in amount of radiation absorbed by sample also increases the number of free radicals formed in the sample [12-13]. In the calculations, although the dose of irradiation has reached up to 15 kGy, g spectroscopic splitting factor and ΔH linewidth of the sample were determined to remain approximately same. In spite of increasing radiation dose, no significant change is observed in the shapes of the signals recorded.

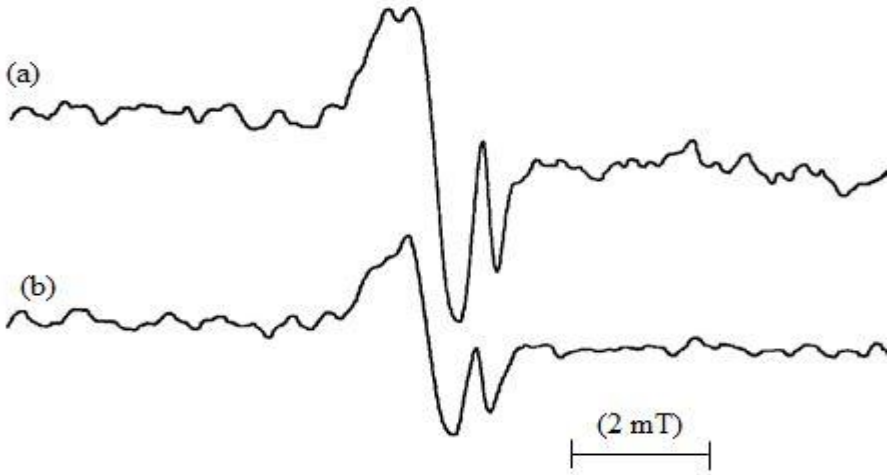


Figure 1. (a) EPR spectrum of 15 kGy irradiated SU
(b) EPR spectrum of 10 kGy irradiated SU

Aside from qualitative detection EPR can be used for dose estimation [14-15]. Therefore, the effect of increasing radiation dose on the spectra of SU was studied. The sample irradiated within certain intervals between 0-15 kGy is used in order to obtain dose-response curves. Central resonance signal change curve of SU depending on radiation dose applied is given in Fig. 2. In the Fig. 2; square signs represent experimental results; while curves connecting them represent the closest mathematical functions to experimental results.

The choice of mathematical functions is quite important to determine the amount of absorbed radiation dose by measuring peak to peak signal intensities of the samples. However, there is no single ideal method for this selection. Mathematical equations that show the best fit of the samples and correlation coefficient (R^2) are given in Table 2. This comment agree with results obtained for various kind of drugs studied before [16-17]. 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. It should be noted that no attempt has been made to force regressions through zero. Considering Table 2; the best fit of SU sample seems to be with $I = ae^{bD}$.

The signals created depending on irradiation of drugs should be capable of being tested during their shelf lives [18]. EPR spectra were recorded at room temperature within regular intervals in the daily process of 200 days. In the spectra obtained, no significant changes in the shape of EPR signals and g values were observed, while significant decrease was identified in the signal intensities. Decreased signal intensities indicate that the number of free radicals formed after irradiation also reduced. Throughout the process, sample was stored in an airtight and dark environment at room temperature. Decay curve of SU irradiated by 15 kGy is given in Fig.3. The data indicated with squares represent experimental results.

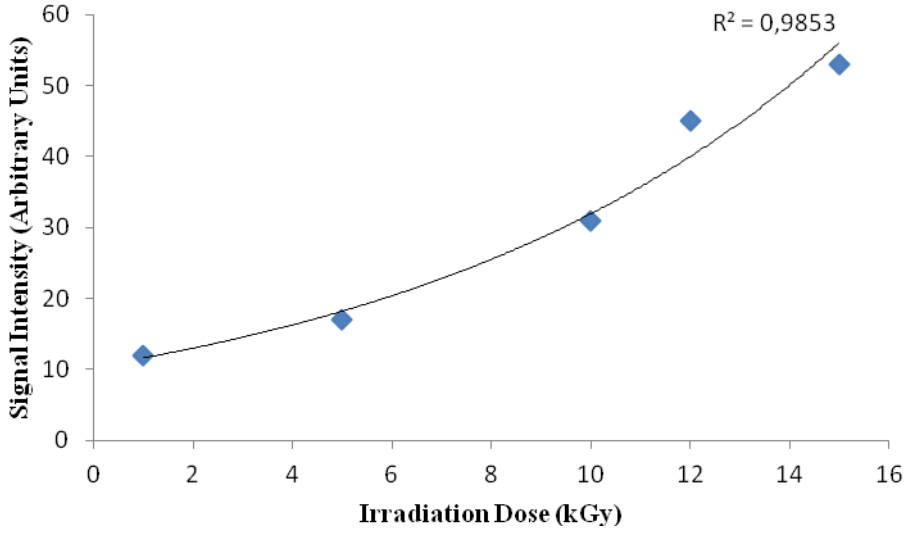


Figure 2. Dose-response curve of SU

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

Functions	**Parameters**	**R^2**
$I = ae^{bD}$	a = 10.371 b = 0.1124	0.9853
$I = aD^2+bD+c$	a = 0.1376 b = 0.8942 c = 10.293	0.9790
$I = aD+b$	a = 3.0607 b = 5.278	0.9495

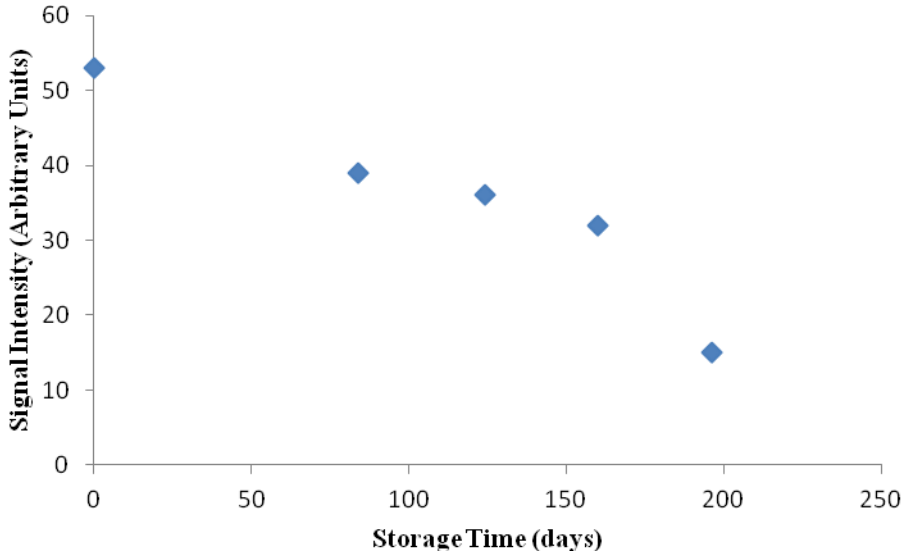


Figure 3. EPR signal intensity of SU irradiated at a dose of 15 kGy as a function of time

Considering Fig. 10, according to spectrums of SU sample recorded at the end of 124th day after irradiation, peak to peak signal intensity was reduced by 32%, whereas it was reduced by 72% at the end of the 196th day, respectively. These data show that even at the end of the 200th day, SD sample can be easily distinguished from non-irradiated sample by EPR spectroscopy method.

4. Conclusions

Since no EPR signal is observed in the non-irradiated sample and signals are clearly seen in SU spectra after irradiation, it is very obvious that free radicals are created after irradiation. Increasing irradiation dose up to 15 kGy has increased the signal intensity of the sample; however, no significant changes were observed in g spectroscopic splitting factor and ΔH linewidth. Obtaining visible signal in the spectrum of SU, which were stored at room temperature, even after 200 days of gamma irradiation shows that stable radicals are formed in this sample after irradiation process. Stable radicals formed after irradiation show that samples are not suitable for sterilization by radiation.

According to the analyses conducted, EPR spectroscopy can be used to distinguish irradiated and non-irradiated drug samples. The high correlation between experimental result of the sample on the dose-response curves and mathematical equations allows us to calculate the signal intensity of a sample obtained in any dose value.

In this dosimetric study conducted with EPR spectroscopy, radiation sensitivity of SU was determined in addition to EPR parameters of the radicals formed in the samples after irradiation.

Acknowledgements

This study was funded by Grant No.12-FF-09 of Research Fund of Dicle University (DUBAP)

References

[1] Gopal, N.G.S., 1978, Radiation sterilization of pharmaceuticals and polymers. *Radiation Physics and Chemistry*, 12, 35-50.
[2] Diehl, J.F., 2002, Food irradiation—past, present and future. *Radiation Physics and Chemistry*. 63, 211–215.
[3] Bhat, R., Sridhar, K.R. 2011, Influence of ionizing radiation and conventional food processing treatments on the status of free radicals in lotus seeds: an EPR study. Journal of Food Composition and Analysis, 24, 563-567.
[4] Ambroz, H.M., Kornacka, E.M., Marciniec, B., Przybytniak, G., 2002, Radical decay in irradiated drugs: Flutamide, ifosamide and aminglutethimide. *Journal of Radioanalytical and Nuclear Chemistry*, 254, 293-298.
[5] Basly, J.P., Basly, I., Bernard, M., 1998a, Electron spin resonance detection of radiosterilization of pharmaceuticals: application to four nitrofurans. *The Analyst*, 123, 1753-1756.
[6] Basly, J.P., Bernard, M., 1997, Radiosterilization dosimetry by ESR spectroscopy: ritodrine hydrochloride and comparison with other sympathomimetics. *International Journal of Pharmaceutics*, 149, 85-91.
[7] Delincee, H., 2002. Analytical methods to identify irradiated food—a review. *Radiation Physics and Chemistry*, 63, 455–458.
[8] Murrieta, H., Munoz, E., Adem, E., Burillo, G., Vazquez, M., Cabrera, E., 1996. Effect of irradiation dose, storage time and temperature on the ESR signal in irradiated oat, corn and wheat. *Applied Radiation and Isotopes*, 47, 1657-1661.
[9] Ambroz, H.B., Kornacka, E.M., Marciniec, B., Ogrodowczyk, M., Przybytniak, G.K., 2000, EPR study of free radicals in some drugs γ-irradiated in the solid state. *Radiation Physics and Chemistry*, 58, 357-366.

[10] Rajendiran, N., Siva, S., Saravanan, J., 2013, Inclusion complexation of sulfapyridine with a- and b-cyclodextrins: Spectral and molecular modeling study. *Journal of Molecular Structure*, 1054-1055, 215-222.
[11] Challis, J.K., Carlson, J.C., Friesen, K. J., Hanson, M.K., Wong, C.S.,2013, Aquatic photochemistry of the sulfonamide antibiotic sulfapyridine. *Journal of Photochemistry and Photobiology A: Chemistry*, 262, 14-21.
[12] Damian, G., 2003, EPR investigation of γ-irradiated anti-emetic drugs. *Talanta*, 60, 923-927
[13] Polat, M, Korkmaz, M (2006), *Journal of Pharmaceutical and Biomedical Analysis*, 40: 882-888.
[14] Basly, J.P., Basly, I., Bernard, M., 1998b, Electron spin resonance identification of irradiated ascorbic acid: Dosimetry and influence of powder fineness. *Analytica Chimica Acta*, 372, 373-378.
[15] Marralle, M., Longo, A., Panzeca, S., Gallo, S., Principato, F., Tomarchio, E., Parlato, A., Buttafava, A., Dondi, D., Zeffiro, A., 2014, ESR response of phenol compounds for dosimetry of gamma photon beams. *Nuclear Instruments and Methods in Physics Research B*, 339, 15-19.
[16] Yurus, S., Ozbey, T., Korkmaz, M., 2004, ESR investigation of gamma irradiated sulbactam sodium. *Journal of Pharmaceuitcal and Biomedical Analysis*, 35, 971-978.
[17] Tuner, H., Korkmaz, M., 2007, Radiostability of butylated hydroxytoluene (BHT): an ESR study. *Beam Interactions with Materials and Atoms*, 258, 388-394.
[18] Basly, J.P., Longy, I., Bernard, M., 1998c, Radiosterilization dosimetry by electron-spin resonance spectroscopy: Cefotetan. *Analytica Chimica Acta*, 359, 107-113.