



# The effect of radiofrequency electromagnetic radiation on rat liver tissue and serum paraoxonase (PON1)

✉ Mehmet Cihan Yavas<sup>a,\*</sup>, ✉ Asuman Kilitci<sup>b</sup>

<sup>a</sup>Mardin Artuklu University, Faculty of Medicine, Department of Biophysics, Mardin, Türkiye

<sup>b</sup>Duzce University, Faculty of Medicine, Department of Pathology, Duzce, Türkiye

## ARTICLE INFO

### Keywords:

Electromagnetic field  
Liver  
Mobile phone  
Paraoxonase  
Radiofrequency

Received: Aug 22, 2023

Accepted: Oct 02, 2023

Available Online: 25.10.2023

DOI:

[10.5455/annalsmedres.2023.08.210](https://doi.org/10.5455/annalsmedres.2023.08.210)

### Abstract

**Aim:** The development of technology increases the rate of everyone having a smartphone. Therefore, the possible biological effects of these devices are of concern. In this study, we aimed to investigate the effect of 2100 MHz radiofrequency electromagnetic radiation on rat liver tissue and serum paraoxonase 1 level.

**Materials and Methods:** Within the scope of the study, a 2100 MHz radiofrequency electromagnetic radiation model was created. In our study, we used Sprague Dawley male rats. Two groups were made as sham-control and exposure group (5 h a day for 2 weeks). Liver tissue and serum paraoxonase were studied.

**Results:** The paraoxonase 1 value of the exposure group was higher than the sham control group, and did not have statistically important difference in the comparison of exposure and sham control groups ( $p>0.05$ ). Did not have important difference in histopathological parameters of rat liver tissue ( $p>0.05$ ).

**Conclusion:** Although it seems that radiofrequency radiation does not cause liver damage, more detailed studies with short- and long-term exposure are needed.



Copyright © 2023 The author(s) - Available online at [www.annalsmedres.org](http://www.annalsmedres.org). This is an Open Access article distributed under the terms of Creative Commons Attribution-NonCommercial-NoDerivatives 4.0 International License.

## Introduction

Electromagnetic fields - regardless of the range of frequency bands - have become a part of our daily lives today and are used more and more. The prevalent use of wireless communication systems in the last 30 years and mobile phone (MP) use is the leading one [1]. Radiofrequency electromagnetic fields (electric and magnetic fields) affect tissues as a result of their interaction with biological systems. These two effects (thermal and non-thermal) have been demonstrated, but the possible effects on biological systems are still uncertain. Radiofrequency electromagnetic energy sources; it is frequently used in communication, industry, and health fields [2]. Radiofrequency radiations emitted from MP can trigger oxidative harm by raising lipid peroxidation and oxidative stress [3].

Many studies report that paraoxonase (PON) is associated with oxidative stress [4]. The PON family, which are among the antioxidant enzymes: involve PON one, PON

two, and PON three. Paraoxonase enzyme types are essential enzymes whose physiopathological roles are investigated in neurodegenerative and cardiovascular diseases. PON one (PON-1) is primarily expressed in the liver and has been reported to be connected to high-density lipoprotein [5]. PON 1 is an antioxidant member that contributes to the defense system by hydrolyzing peroxidases [6]. The PON gene family also makes important contributions as an endogenous free radical scavenger in the human body [7].

In some studies, it is reported that 2100 MHz radiofrequency radiation (RF-R) does not cause a significant change on the liver tissue [8], and in some studies, it causes oxidative damage in the liver [9]. Therefore, this experimental study was carried out to detect the effects of 2100 MHz radiofrequency electromagnetic radiation (RF-EMR) on possible histopathological and serum PON activity on rat liver tissue.

## Materials and Methods

Before the start of this study, permission was obtained from the local ethics committee of animal experiments of Gazi University (G.Ü. ET. 20.026. Decision Date:

\*Corresponding author:

Email address: [mcihanyavas@gmail.com](mailto:mcihanyavas@gmail.com) (✉ Mehmet Cihan Yavas)

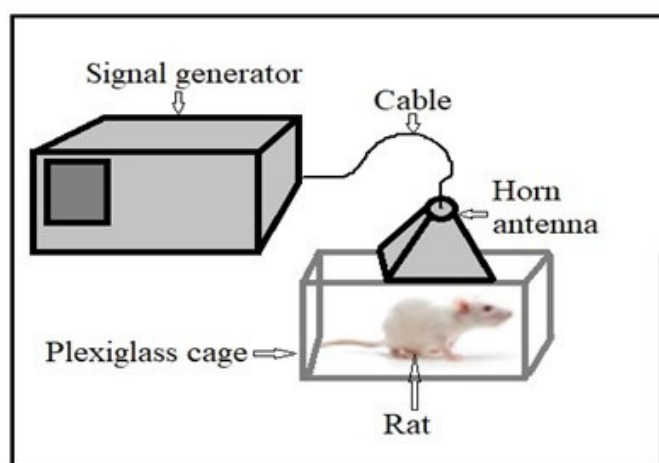
28.05.2020). Later, the study was carried out at Gazi University GÜDAM center. In our study, it has been continued in line with the Guidelines for the Care and Use of Laboratory Animals.

#### Animal and exposure design

The experiment was carried out according to ethical procedures. 14 male Sprague Dawley rats were randomly divided into two equal groups. Sham-control n=7 and exposure group n= 7. The sample size in experimental animals was taken as reference to the study of Doğan et al. [25]. The animals were kept in the 12 / 12 light/dark period, in the 21 - 23°C, humidity in the range of 45-50, and access to water and pellets food was provided. The exposure group was exposed to RF-EMR exposure for 14 days and 5 hours a day in the plexiglass cage. The sham-control was in the plexiglass cage and no exposure was created. In the study, exposure signals were created with a generator device (R&S®SMBV100A, Germany), and with the help of a horn antenna (Schwarzbeck, 9120 L3F, Germany) (as seen in Figure 1). Electric field measurement was performed with EMR-300 Broadband RF Survey Meter (Pfullingen, Germany) electromagnetic field measuring meter. The average value of the electric field was measured as 38.95 V/m with the measuring instrument. SAR values for the whole body and liver tissue are given in Table 1. For the specific absorption rate calculations, the 3D volumetric pixel model of the animal model was designed, and the broadband horn antenna was modeled [10].

**Table 1.** SAR analysis values.

Body part-SAR	10g	1g
Whole body	305.5 mW/kg	720 mW/kg
Liver	214 mW/kg	665 mW/kg



**Figure 1.** The schema of 2.1 GHz RF-EMR exposure device set up.

#### Measurement of PON activity

As a result of the study, rat blood taken from the intracardiac route was centrifuged at 4 minutes and 1000 rpm.

Serum samples obtained were analyzed application the entirely automated method improved by Rel Assay Diagnostics (cat. no. RL0031, Mega Tip, Gaziantep, Turkey) and using commercial kits purchased. According to this method, two different substrates were analyzed for PON activity. The analysis of the absorbances (37°C, 412 nm) was carried out with the aid of a spectrophotometer. PON results are presented as U / L. [11, 12].

#### Histopathologic examination

The samples of the excised liver tissue were fixed in 10 % neutral buffered formol. Tissues to be analyzed were kept overnight for follow-up. Sections of 4 micrometer thickness were taken from the tissues embedded in paraffin blocks. After deparaffinization and rehydration, staining with hematoxylin and eosin was achieved. In addition, Masson trichrome staining was performed to better evaluate fibrosis. Histopathological uncovering were evaluated beneath the light microscope by the pathologist who did not know the experimental groups. Histopathological scoring was made proportion to the loftiest area. By semi-quantitative semiquantitative analysis; (0= None (0%), 1= Minimal (0-10%), 2= Mild (10-30%), 3= Moderate (30-50%), 4= Severe (more than 50%)) 4 categories were determined and the parameters were scored accordingly. We evaluated the variables "necrosis, fibrosis, hepatocyte damage (cellular changes), inflammation, congestion, bleeding and hepatic cord disorganization" to determine possible damage that may occur as a result of exposure.

#### Statistical analysis

The data set in the study was interpreted using the SPSS Statistics for Windows, version 21.0, (IBM Corp., Armonk, N.Y., USA) program. The shapiro - wilk and kolmogorov - smirnov tests were supported whether the variables were normally distributed or not. Explanatory statistics for the variables are given as mean  $\pm$  standard deviation, min and maximum. Independent t-test was used to compare the groups. The Mann-Whitney-U test was used to evaluate the histopathological scores of the two groups. Results were evaluated significant at  $p < 0.05$ .

#### Results

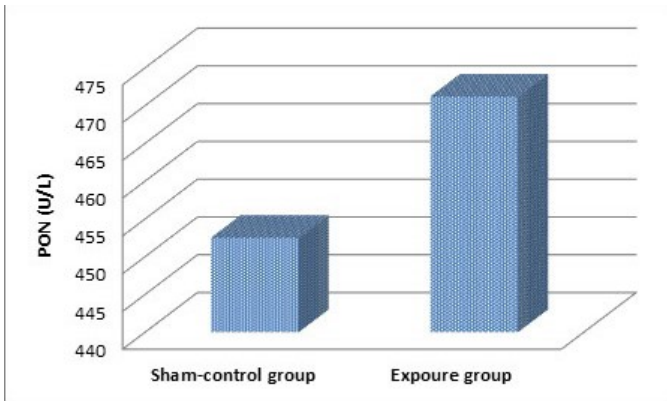
There was no statistically important difference in PON 1 data among the sham-control and exposure groups included in the study ( $P > 0.05$ ). In the study, it was determined that the PON 1 level of the exposure group increment in compoarision to the sham-control group. Group

**Table 2.** Serum paraoxonase 1 (PON1) data obtained from the groups.

PON (U/L)	Mean $\pm$ SD	Min	Max	p-value
Sham-control group	452.57 $\pm$ 81.47	319	574	0.602
Exposure group	471.28 $\pm$ 43.50	420	537	

PON:Paraoxonase, SD: Standard Deviation, Min: Minimum, Max: Maximum.





**Figure 2.** Paraoxonase (PON1) distributions of the groups.

comparison results for PON 1 are given in Table 2 and Figure 2.

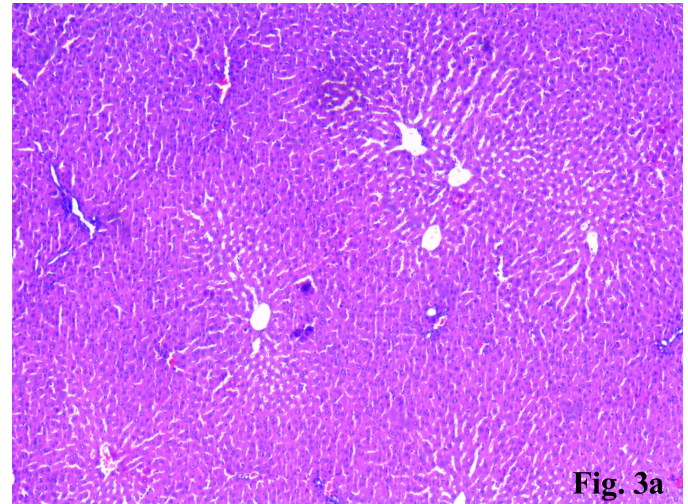
In histopathological scoring, congestion between groups ( $p=0.710$ ) was  $p>0.05$ . There was no significant difference in all observation scoring results of hepatocyte damage - cellular changes, hepatic cord disorganization, inflammation, hemorrhage, necrosis and fibrosis (mtc) parameters ( $p=0.999$ ,  $p>0.05$ ). (In the Mann Whitney U test analysis) (Figure 3).

### Discussion

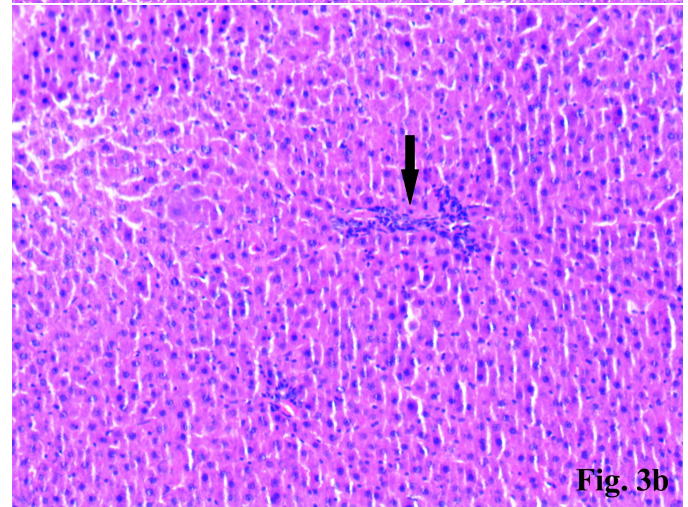
Many different scientific reports over the biological affects of electromagnetic fields have been published for the last 10 years, and discussions continue to increase [13]. The time people are exposed to electromagnetic radiation is increasing, and further research may reveal the possible negative effects of cell phones and base stations [14]. It is emphasized that exposure to electromagnetic fields originating from MP for 6 minutes per day is more dangerous than other electromagnetic sources [15]. Researchers investigating the effects of static and electromagnetic fields on in vitro human serum paraoxonase-1 activity indicated that PON1 activity could be affected by pharmacological, environmental, and lifestyle factors as well as various agents such as age and gender, and PON1 activity increased with increasing magnetic field intensity [16]. It is stated that 900 MHz radiofrequency exposure can induce inflammatory changes in liver tissue [17]. It has been reported that 1800 MHz RF-EMR can cause oxidative and nitrosative damage in liver, brain and kidney tissues after chronic exposure [18].

Considering the findings of serum PON activity in our study, it is seen that it can be affected by the short-term RF EMF originating from MPs. Contrary to the literature, In our study, there was no statistically significant change in the histopathology of the rat liver, although there were some minor changes in the exposure group when comparison to the sham-control group.

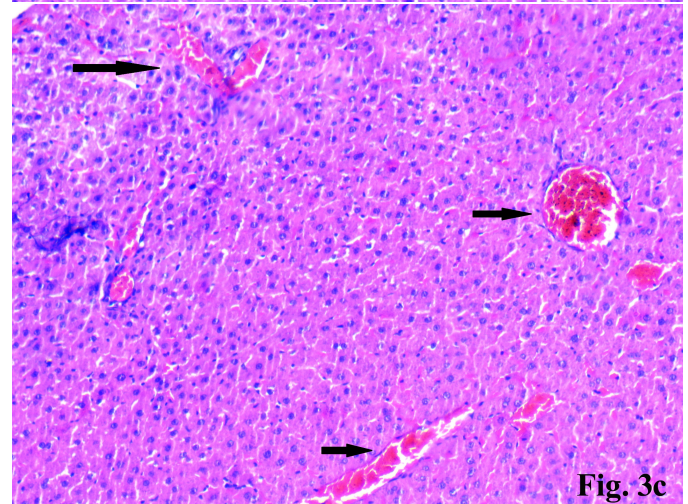
The researchers applied 15 minutes of exposure on the rabbits for 7 and 14 days. In the study data of the researchers, they reported that exposure of experimental animals to 1800 MHz GSM-like RFR in the whole body may cause oxidative stress and alter in some blood chemistry variable [19]. Wistar albino rats were continuously exposed to



**Fig. 3a**



**Fig. 3b**



**Fig. 3c**

**Figure 3.** Histopathological pictures of the sham-control and exposure group. Fig 3a: Liver tissue of rat from sham-control group (H&E, x50). Fig 3b: Focal inflammatory cell infiltration in the liver parenchyma of the rat from the exposure group (H&E, x100). Fig 3c: Congested vascular and sinusoid structures in the liver tissue of the rat from the exposure group (H&E, x100).

a 2100 MHz RF-EMF for 30 days. The immunohistochemical analysis findings in the study reported that there was an augmented apoptotic index in the exposure group com-

parison to the control group [20]. In a study investigating the influence of mobile cell on oxidative stress parameters (Wistar rat, blood analysis on the 15th and 30th days); It has been stated that there are many changes in biochemical parameters, so radiofrequency fields originating from mobile phones can be subversive and have many adverse influence on tissues and enzyme operate [21]. It has been reported on Wistar rats that 60 Hz, 0.5 mT very low-frequency electromagnetic field significantly increased antioxidant serum activity (paraoxonase, HDL, total antioxidant status) in a single exposure of 4 hours [22]. The researchers reported that 1 hour of 900 MHz RF electromagnetic radiation for 3 weeks a day did not have a significant effect on the serum paraoxonase values of rats [23]. Researchers investigating the paraoxonase activity of exposure to ionizing radiation at disparate times and doses reported that PON1 activity levels reduction in individuals with long-term exposure to radiation [24]. When the results of our study were examined, no statistically important difference was establish between the exposure and sham-control groups. In the light of the literature findings, an increase in the PON activity of the exposure group was found in the study, which is similar to our study findings. We hypothesize that the increase in PON activity may be due to the short-term effects of the RF-EM field originating from the mobile cell and this may have increased as a response to a protection mechanism. Our study differs from other studies because it evaluates both liver and PON1 together. Therefore, we believe that it will be a guide to radiofrequency electromagnetic radiation applications.

## Conclusion

In conclusion, it was observed that there was no important alteration in PON1 activity and rat liver tissue after short-term RF-EMR exposure. It is thought that this is an effect of the body's protection mechanism or that short-term exposure does not have an effect.

## Acknowledgment

We thank Prof. Korkut YEGİN and Bahriye SIRAV for their scientific contribution.

## Conflict of interest

The authors declared that there was no conflict of interest regarding the study.

## Financial disclosure

The authors did not receive any funding in this study.

## Ethical approval

This study was approved by Gazi University Local Ethics Committee (G.Ü. ET. 20.026. Decision Date: 28.05.2020).

## Authorship contributions

M.C.Y.: Conception, design, literature, materials, supervision, fundings, data collection, review, writing, critical, review. A.K.: Materials, literature, data collection and processing, analysis and interpretation, review, review, Critical.

## References

1. Wiart J, Watanabe S, Wu T, Joseph W, Lee KA. Electromagnetic fields (EMF) exposure. *Ann Telecommun.* 2019;74:1-3. 2019.
2. Challis LJ. Mechanisms for interaction between RF fields and biological tissue. *Bioelectromagnetics.* 2005;26(S7):98-106. 2005.
3. Dasdag S, Bilgin HM, Akdag MZ, Celik H, Aksen F. Effect of long term mobile phone exposure on oxidative-antioxidative processes and nitric oxide in rats. *Biotechnol Biotechnol Equip.* 2008;22(4):992-7.
4. Motta S, Letellier C, Ropert M, et al. Protecting effect of vitamin E supplementation on submaximal exercise-induced oxidative stress in sedentary dogs as assessed by erythrocyte membrane fluidity and paraoxonase-1 activity. *Vet J.* 2008;181:288-95.
5. Bacchetti T, Ferretti G, Sahebkar A, The role of paraoxonase in cancer. *Seminars in Cancer Biology.* 2019;56:72-86.
6. Atay AE, Kaplan MA, Evliyaoglu O, Ekin N, Isikdogan A. The predictive role of Paraoxonase 1 (PON1) activity on survival in patients with metastatic and nonmetastatic gastric cancer. *Clin Ter.* 2014;165(1):e1.
7. Elkiran ET, Mar N, Aygen B, Gursu F, Karaoglu A, Koca S. Serum paraoxonase and arylesterase activities in patients with lung cancer in a Turkish population. *BMC cancer.* 2007;7(1):1-8.
8. Tuncal S, Önal AK, Aydoğan F, Unsal V, Yumuşak N, Büyükcatalay E. et al. The effects of 2100 MHz radio frequency radiation on thyroid tissues. *West Indian Med J.* 2021;69(1):51.
9. Sharma A, Shrivastava S, Shukla S. Oxidative damage in the liver and brain of the rats exposed to frequency-dependent radiofrequency electromagnetic exposure: biochemical and histopathological evidence. *Free Radic Res.* 2021;1-12.
10. www.cst.com, CST AG Germany (last accessed August 15th, 2020).
11. Sehitogulları A, Aslan M, Sayır F, Kahraman A, Demir H. Serum paraoxonase-1 enzyme activities and oxidative stress levels in patients with esophageal squamous cell carcinoma. *Redox Rep.* 2014;19(5):199-205.
12. Cebeci E, Oner FA, Usta M, Yurdakul S, Erguney M. Evaluation of oxidative stress, the activities of paraoxonase and arylesterase in patients with subclinical hypothyroidism. *Acta BioMed.* 2011;82(3):214-22.
13. Saliev T, Begimbetova D, Masoud AR, Matkarimov B. Biological effects of non-ionizing electromagnetic fields: Two sides of a coin. *Prog Biophys Mol Biol.* 2019;141:25-36.
14. Magiera A, Solecka J. Mobile telephony and its effects on human health. *Rocz Panstw Zakl Hig.* 2019;70(3):225-34.
15. Panagopoulos DJ. Comparing DNA damage induced by mobile telephony and other types of man-made electromagnetic fields. *Mutat Res Rev Mutat Res.* 2019;781:53-62.
16. Abdi S. Effects of static and electromagnetic fields on human serum paraoxonase-1 activity in vitro. *J Basic Res Med Sci.* 2018;5(2):21-6.
17. Mortazavi SM, Owji SM, Shojaei-Fard MB, et al. GSM 900 MHz microwave radiation-induced alterations of insulin level and histopathological changes of liver and pancreas in rat. *J Biomed Phys Eng.* 2016;6(4):235-242.
18. Berköz M, Arslan B, Yıldırım M, Aras N, Yalın S, Çömelekoğlu Ü. 1800 MHz radio-frequency electromagnetic radiation induces oxidative stress in rat liver, kidney and brain tissues. *East J Med.* 2018;23(2):71.
19. Ozgur E, Kismali G, Guler, G, Akcay A, Ozkurt G, Sel T, Seyhan N. Effects of prenatal and postnatal exposure to gsm-like radiofrequency on blood chemistry and oxidative stress in infant rabbits, an experimental study. *Cell Biochem Biophys.* 2013;67(2):743-51.
20. Çeliker M, Özgür A, Tümkaya L, Terzi S, Yılmaz M, Kalkan Y, Erdoğan E. Effects of exposure to 2100 MHz GSM-like radiofrequency electromagnetic field on auditory system of rats. *Braz J Otorhinolaryngol.* 2017;83(6):691-6.
21. Eslami E, Fatahian S, Shahaniipour K. Assessment of the cell-phone radiations effects on anti-oxidative and renal parameters in rat. *Toxicol Environ Health Sci.* 2019;11(4):278-82.
22. Seifrad S, Farzampour S, Nourbakhsh M, Amoli MM, Razzaghy-Azar M, Larijani B. Effects of extremely low frequency electromagnetic fields on paraoxonase serum activity and lipid peroxidation metabolites in rat. *Diabetes Metab Syndr.* 2014;13(1):85.

23. Bilgici B, Akar A, Avcı B, Tuncel OK. Effect of 900 MHz radiofrequency radiation on oxidative stress in rat brain and serum. *Electromagn Biol Med.* 2013;32(1):20-9.
24. Serhatlioglu S, Gursu MF, Gulcu F, Canatan H, Godekmerdan A. Levels of paraoxonase and arylesterase activities and malondialdehyde in workers exposed to ionizing radiation. *Cell Biochem Funct.* 2003;21(4):371-5.
25. Doğan İ, Doğan N. Estimation of sample size with resource equation method in experimental animal studies. *Türkiye Klinikleri J Biostat,* 2020;12(2):211-217.