DOI:10.55522/jmpas.V13I3.6511 **ISSN NO. 2320–7418**

International peer reviewed open access journal

Journal of Medical Pharmaceutical and Allied Sciences

Journal homepage: www.jmpas.com CODEN: JMPACO

Research article

Effect of anticancer electromagnetic spectrums on the cancer cell line growths

Fuad H. Al-Ghamdi*[1], Ayman M Al-Qaaneh[2], Sarah Almofty[3]

[1] Department of Pharmacy Services, Johns Hopkins Aramco Healthcare (JHAH), Dhahran, Saudi Arabia
[2] Department of Allied Health Sciences, Faculty of Nursing, Al-Balqa Applied University (BAU), Al-Salt, Jordan
[3] Department of Stem Cell Research, Institute for Research and Medical Consultations (IRMC), Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia

Corresponding author Fuad H. Al-Ghamdi, ✉ fuad.ghamdi@jhah.com, **Orcid Id**: https://orcid.org/0000-0003-1565-7964

Department of Pharmacy Services, Johns Hopkins Aramco Healthcare (JHAH), Dhahran, Saudi Arabia

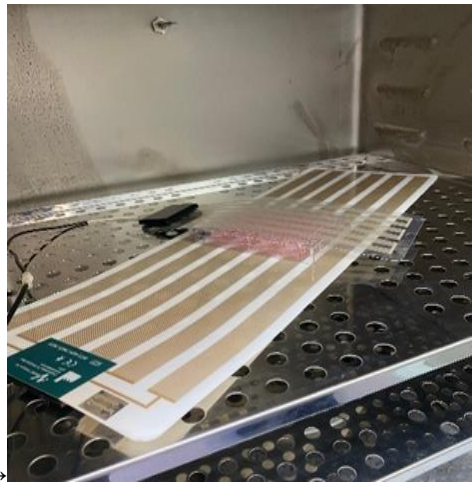
Received - 08-05-2024**, Revised** - 27-05-2024, **Accepted** - 11-06-2024 **(DD-MM-YYYY)**

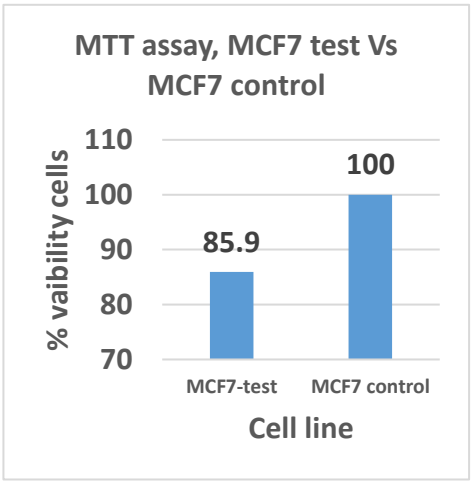
Refer This Article

Fuad H. Al-Ghamdi, Ayman M Al-Qaaneh, Sarah Almofty, 2024. Effect of anticancers' electromagnetic spectrums on the cancer cell line growths. Journal of medical pharmaceutical and allied sciences, V 13 - I 3, Pages- 6603 – 6607. Doi: https://doi.org/10.55522/jmpas.V13I3.6511.

ABSTRACT

Electromagnetic frequencies (EMF) that are generated from different electronic devices can interact with biological systems including humans. Several theories described the effects of EMF on the growth of in vitro cancer cell lines and biological systems, which revealed that EMF could inhibit cancer cell growth or decrease viability depending on the field strength and frequency. Accordingly, in this study, we are targeting to assess the effect of the anticancer-extracted electromagnetic spectrums on the growth of two types of cell lines which are the breast cancer cell line MCF-7 and human embryonic kidney HEK293 as a control cell line. Drugs digitalized electromagnetic spectrums of a mixture of anticancer medications were generated using a DigiConPro® VITATEC device emitted using the supplied antenna and applied to a 96-well culture plate containing MCF-7 and HEK293. The cell viability was performed by MTT assay after three days. The post-exposure effect of anticancers' electromagnetic spectrums was determined on the cancer cell line. Anticancers' electromagnetic spectrums were seen to cause a statistically significant (p<0.05) decrease in the growth rate relative to the control after three days of exposure to the electromagnetic spectrums. Three doses of anticancers' electromagnetic spectrums were applied as a dose per day, and each dose was running for 5 hours which induced a reduction in MCF-7 growth compared to the control group, while the HEK293 showed no statistically significant decrease in the growth rate. As a conclusion, electromagnetic spectrums of the anticancer medications may have the same effect as the chemical compound.





Keywords: Electromagnetic Frequencies, Anticancers, Exposure, Spectrums.

INTRODUCTION

This study is ongoing, we published a study with the same concept about Effect of antibiotics' electromagnetic spectrums on the bacterial growths, result was statistically significant (p<0.01) decrease in the growth rate of bacteria [1].

Many theories described the effects of electromagnetic field (EMF) on biological systems including humans as the emission of continuous waves that increase the energy of living tissues and lead to biochemical changes of molecular ions and electrons, as well as the reactive oxygen system (ROS), proteins and DNA/RNA[2-6].

The effects of these electromagnetic fields on biological systems have not been sufficiently researched due to significant heterogeneity in study designs, duration, and frequency, as well as inconsistency of results with many limitations in many studies. Also, evidence of potential adverse effects remains unclear to arrive at a conclusive explanation for the biological effect of the use of electromagnetic fields in several studies [7].

The last decade has also brought several studies in vitro and in vivo that have documented the anti-cancer effects of alternating electric fields [8–10], including low-density medium-frequency alternating electric fields, as well as moderately low-frequency modified electromagnetic fields (EMF) [11].

In addition, research on the potential therapeutic effects focused in part on the range of visible light and near-infrared, and in another part, it was conducted in very different pulse and antenna shapes based on the researchers' specific ideas [12]. The main frequencies of the latter can be found in the region of Hz to GHz. A few of these specific signals have received medical approval and have been used unchanged for many years for some therapeutic applications [13, 14].

Several studies have shown that anticancer effects have been achieved at specific frequencies (depends on the type of cancer cells) and the result has been proliferative inhibition and split spindle disorder after exposure to alternating electromagnetic fields. Furthermore, preventing important aspects of apoptosis [9, 10, 15, and 16].

There is a class of signals called PEMF (Pulsed Electromagnetic Frequencies). The used antennas are coil-like. With the signals, a steep magnetic pulse is produced by the coils, which in turn creates a pulsed electric field in the tissue that is supposed to have therapeutical benefits. Such equipment has been used for many years in the field of bone healing and related topics [13].

The rationale of our study is based on the assumption that interactions between molecules in cells are not only of a biochemical nature. We suppose that an electromagnetic part is present as well, basically consisting of the resonance frequencies (Eigen frequencies) of the reaction partners involved. Following this idea, we aimed to investigate whether the biochemical effect of specific substances on organisms might be simulated by the effect of electromagnetic waves consisting of their Eigen frequencies. In this study we did like what we did in the previous study, we present the effects of very weak broadband electromagnetic waves derived from several anticancer medications. These waves were previously obtained by placing the material during a certain time in a device dedicated to recording waves with a bandwidth of about 1 Hz to 4 GHz. After that, they were digitalized and stored in computer memory. The procedure of obtaining the signal is not part of the present study. Here we present the result of the application of the combined signal to the growth of the cancer cell line. The null hypothesis is that the application of this signal does not affect cancer cell line growth, while the alternative hypothesis is that it can significantly inhibit cancer cell line growth [1].

MATERIAL AND METHODS

Experimental Design for Electromagnetic Spectrum Generation and Exposure System

Drugs' digitalized electromagnetic spectrums of a mixture of anticancer medications waves were generated using a DigiConPro® VITATEC (Model No.: D131001) device and emitted using the supplied antenna. The antennas were positioned under and above the test 96 well cell culture plate. The exposure system was placed in an incubator at 37° C and 5% CO_2. At the same time, the control 96 well cell culture plate was not exposed to electromagnetic fields and was placed in another incubator under the same conditions to prevent any field contamination. The electromagnetic generator device DigiConPro® VITATEC was turned on for 5 hours every day for 3 days. [Figure 1].

Cell line Preparation and Culturing

Breast cancer (MCF-7) and human embryonic kidney (HEK 293) cell lines were used to study the effect of anticancers' electromagnetic spectrums on cell line growth. Cell lines were kept at -60°C, and fresh cultures were prepared for the experiment. Cells were maintained in Dulbecco's Modified Eagle Medium (DMEM), supplemented with 10% fetal bovine serum (FBS) and antibiotics (100 IU/mL penicillin and 100 µg/mL streptomycin). Cells were grown in 75 cm2 culture flasks containing 15 ml DMEM. After a few passages cells were seeded in a 96-well plate (104 cells per well) and cultured in a humidified atmosphere of 5% CO2 at 37°C. All studies used cells at 40 to 50% confluence.

The cells were prepared by using two sets of 96-well plates, one for exposing to the waves and one for control, each set contained two columns of MCF-7 and two columns of HEK293. One set of 96-well plate was placed into the Electromagnetic spectrum antenna and subjected immediately to anticancers' electromagnetic spectrums within a CO2 humidified incubator at 37°C. In contrast, the control 96-well plate was placed in the same conditions as those exposed without electromagnetic spectrum application. Cell line growth was

determined concurrently for both exposed and control by measuring the cell viability by performing MTT assay test.

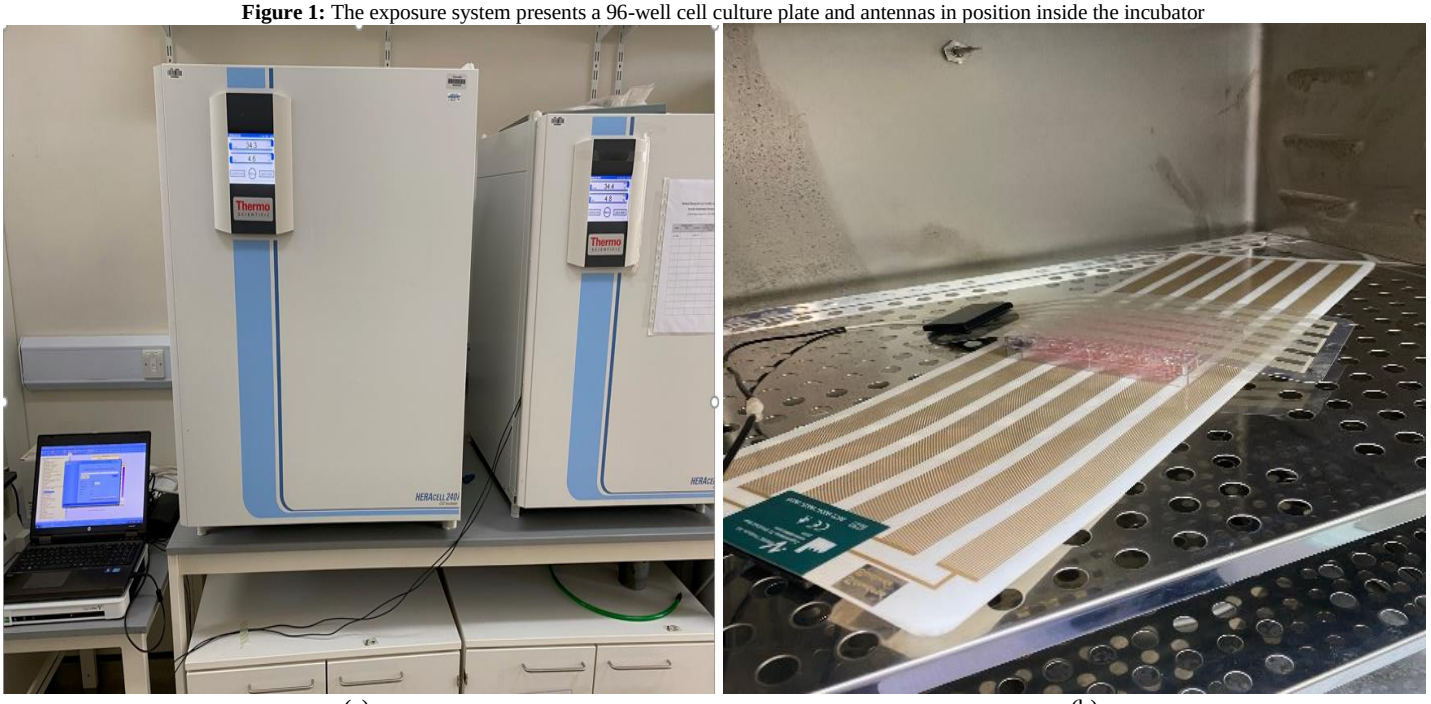
Cell Viability Assay

MTT assay was used to determine cell viability. After 3 days of incubation cells were exposed to anticancer' electromagnetic spectrums using in vitro exposure systems, applied as one dose per day, and each dose was running for 5 hours for 3 days. Untreated cells served as the control. At the end of the period of exposure, 5 mg/ml of MTT reagent was prepared in PBS and added to each well, and then all 96-well plates were incubated at 37°C in 5% CO2 for 4 h. The colored crystals of the produced formazan were dissolved in dimethyl sulfoxide (DMSO) (Sigma, USA). The absorbance was measured at 560 nm by SpectraMax M5. Cell proliferation was calculated as the ratio of the absorbance of the treated group, divided by the absorbance of the control group, multiplied by 100, to give the percentage of proliferation [17 - 19].

Statistical Analysis

Data were presented as the mean of MTT assay results for MCF7 and HEK293 vs control. Statistical significance for the change in the growth of exposed and control samples over time was evaluated using the Friedman test, t. test, the p-value was set at $p<0.01$ for all tests. All data used in the study were analyzed using SPSS 25.0 (IBM SPSS Statistics for Windows, Version 25.0 IBM Corp., and Armonk, NY, USA).

Figure 1: The exposure system presents a 96-well cell culture plate and antennas in position inside the incubator



(a) (b)

(a) The electromagnetic waves generator device DigiConPro® VITATEC. (b) The antennas are positioned under and above the test 96 well plate

RESULTS

Effects of anticancers' electromagnetic spectrums on the cancer cell line growth after 3 days of exposure (total 3 doses, 5 hours/day). The cell viability was assessed by MTT assay for both sets (exposed and control). Growth in time was found to be significant according to the Friedman test [Table 1], t. test [Table 2]

Table 1: Freidman test for Statistical significance for the change in growth over time

Cell line	N	Chi-Square	Df	P-value
MCF7 T	16	12.250	1	0.000**
HEK293 T	16	4.000	1	0.046

**p<0.01 is statistically very significant

Table 2: t. test for Statistical significance for the change in growth over time

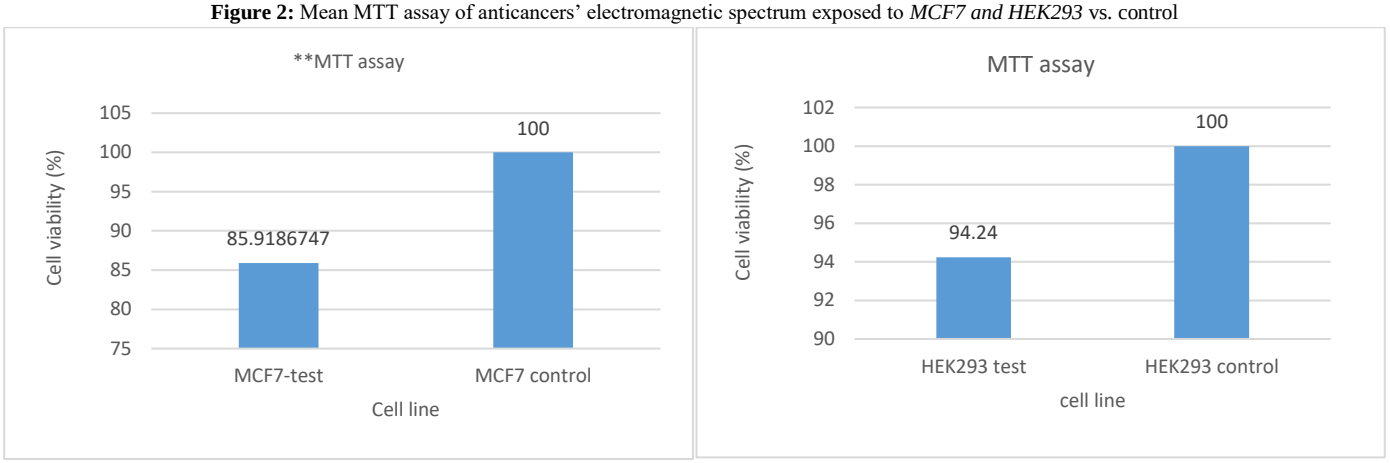
	Paired Sample Test							
	Paired Differences					t	Df	Sig. (2-tailed)
	95% Confidence Interval of the Difference							
	Mean	Std. Deviation	Std. Error Mean	Lower	Upper			
Pair 1 MCF7T – MCF7C	-.10986	.12019	.03005	-.17391	-.04582	-3.656	15	.002**
Pair 2 HEK293T - EK293C	-.08961	.24130	.06033	-.21819	.03897	-1.485	15	.158

**$p < 0.01$ is statistically very significant

The difference between the survival of anticancers' electromagnetic spectrums-exposed cells and control cells, as well as the difference between different cell types, was observed. The percentages of cell viability after exposure to anticancer' electromagnetic spectrums are given in [Figure 2], respectively. The anticancer' electromagnetic spectrums inhibited cell growth in each of the two investigated cell lines. However, the breast cancer cell line MCF-7 was more sensitive to anticancer' electromagnetic spectrums after exposure times

(inhibition = 14.09% of MCF-7 cell growth). While the HEK 293 cell line after exposure times (inhibition = 5 .76% of HEK 293 cell growth). The inhibition of the cell growth of treated HEK 293 was not statistically significant in comparison to control HEK 293 cells. While the inhibition of the cell growth of treated MCF-7 was statistically very significant. The effects of anticancer' electromagnetic spectrums on MCF-7 cells were measured and *the p*-value was ($p = 0.02$) compared to the control. The effects of anticancer' electromagnetic spectrums on HEK 293 cells were measured and the *p*-value was ($p = 0.158$) as compared to the control [Table 2].

Figure 2: Mean MTT assay of anticancers' electromagnetic spectrum exposed to *MCF7 and HEK293* vs. control



A: Mean MTT assay, MCF7 test Vs MCF7 control B: Mean MTT assay, HEK293 test Vs HEK 293 control

**$p < 0.01$ is statistically very significant

Effects anticancer' electromagnetic spectrums on the cancer cell line after 3 days exposure. (A) MCF7 cell line after 3 days of exposure. (B) HEK293 after 3 days of exposure. The histogram illustrate the effects of anticancer' electromagnetic spectrums on human breast cancer cell line MCF7 and human embryonic kidney cell line HEK293. The antiproliferative effect was measured by MTT assay after 3 days of exposure. All values are mean ± SEM, n = 16, **$p < 0.01$ as compared with control (100%) [Table 2].

DISCUSSION

Many studies have assessed the effect of different electromagnetic frequencies on cancer cell growth [5, 14, and 15]. However, our study is unique as it is the first study that assesses antcancers' electromagnetic spectrums effect on cancer cell line growth. Filipovic, et al. evaluated investigated *in vitro*, and with computer simulation, the influence of a 50 Hz EMF on three cancer cell lines: MDA-MB-231(breast cancer), SW-480 (colon cancer), and HCT-116 (colon cancer). After 24 h pre-incubation, cells were exposed to 50 Hz extremely low frequency (ELF) radiofrequency EMF using *in vitro* exposure systems for 24 h and 72 h. A computer reaction-diffusion model with the net rate of cell proliferation and the effect of EMF in time was developed [20].

Sun et al, evaluate the effect of the magnetic field directly on cultured cells and the indirect effect mediated by the cell environment (conditioned medium). 293T cells (kidney cell), HepG2 cells (liver cancer), and A549 cells (lung cancer) have been cultured at 37 ± 0.18 °C in the presence of an ELF magnetic field of 20 Hz. The adherent tumor cells were more sensitive to magnetic field inhibition in the original environment (conditioned medium) with adherence inhibition rates for HepG2 and A549 estimated at 18% and 30% respectively [21].

Crocetti et al, Investigated the effect of ultra-low intensity and frequency pulsed electromagnetic fields (PEMFs) to kill or inhibit the growth of breast cancer cells. MCF7 breast cancer cells and their normal counterparts, MCF10 cells, were exposed to PEMFs, and cytotoxic indices were measured to design PEMF paradigms that best kill or inhibit the growth of breast cancer cells. They observed a vulnerability of MCF7 cells to PEMFs of 20 Hz frequency, and Exposure duration of 60 minutes per day. The cell damage accrued in response to PEMFs increased with time and gained significance after Three days of consecutive daily exposure. By contrast, the PEMFs parameters determined to be most cytotoxic to breast cancer MCF-7 cells were showed not statistically significant damaging to normal MCF-10 cells [22].

The promising results of our study furnish a new concept of treatment that the anticancers' electromagnetic spectrums of the medications may have the same effect as the chemical compound, and the mechanism of drug action can be explained beyond the simple chemical-receptor interaction [23].

CONCLUSION

Anticancers' electromagnetic spectrums showed promising and very significant results in reducing cancer growth rates in MCF-7 breast cancer cells while not statistically significant in comparison to HEK 293 cells. However, the study needs more specific cellular assay tests to identify the exact cytotoxic mechanism of action.

ACKNOWLEDGMENTS

We acknowledge that we used KAIMRC and IRMC facilities to perform this study.

KAIMRC is King Abdullah International Medical Research Center,

Riyadh 11481, and Kingdom of Saudi Arabia.

IRMC is Institute for Research and Medical Consultations (IRMC), Imam Abdulrahman Bin Faisal University, Dammam, Saudi Arabia.

Conflict of Interests

The authors declare that they do not have any commercial or associative interest that represents a conflict of interest in connection with the work submitted.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

REFERENCES

1. Yu, C., Peng, RY, 2017. Biological effects and mechanisms of shortwave radiation: a review. Military Med Res. 4(1), Pages - 1-6. Doi: https://doi.org/10.1186/s40779-017-0133-6.

2. Mumtaz, Sohail, Juie Nahushkumar Rana, et al, 2022. Microwave Radiation and the Brain: Mechanisms, Current Status, and Future Prospects. International Journal of Molecular Sciences. 23(16), Pages 9288. Doi: https://doi.org/10.3390/ijms23169288.

3. Cifra M, Fields JZ, Farhadi A, 2011. Electromagnetic cellular interactions. Progress in Biophysics and Molecular Biology. 105(3), Pages 223- 246. Doi: 10.1016/j.pbiomolbio.2010.07.003.

4. Inhan-Garip A, Aksu B, Akan Z, et al, 2011. Effect of extremely low frequency electromagnetic fields on growth rate and morphology of bacteria. International Journal of Radiation Biology. 87(12), Pages 1155-1161. Doi: 10.3109/ 09553002.2011.560992.

5. Moulder JE, Foster KR, 1999. Is there a link between exposure to power frequency electric fields and cancer? IEEE Engineering in Medicine and Biology Magazine. 18(2), Pages 109-116. Doi: https://doi.org/10.1109/51.752996.

6. Bodewein L, Schmiedchen K, Dechent D, et al, 2019. Systematic review on the biological effects of electric, magnetic and electromagnetic fields in the intermediate frequency range (300 Hz to 1 MHz). Environ Res. 171, Pages 247-259. Doi: https://doi.org/10.1016/j.envres.2019.01.015.

7. Kirson ED, Gurvich Z, Schneiderman R, et al, 2004. Disruption of cancer cell replication by alternating electric fields. Cancer Res. 64(9), Pages 3288-3295. Doi: https://doi.org/10.1158/0008-5472.CAN-04-0083.

8. Kirson ED, Dbaly V, Tovarys F, et al, 2007. Alternating electric fields arrest cell proliferation in animal tumor models and human brain tumors. Proc Natl Acad Sci. 104(24), Pages 10152-10157. Doi: https://doi.org/10.1073/pnas.0702916104.

9. Zimmerman, J., Pennison, M., Brezovich, I. et al, 2012. Cancer cell proliferation is inhibited by specific modulation frequencies. Br J Cancer. 106(2), Pages 307–313. Doi: https://doi.org/10.1038/bjc.2011.523.

10. Barbault, A., Costa, F.P., Bottger, B. et al, 2009. Amplitude-modulated electromagnetic fields for the treatment of cancer: Discovery of tumor-specific frequencies and assessment of a novel therapeutic approach. J Exp Clin Cancer Res. 28(1), Pages 51. Doi: https://doi.org/10.1186/1756-9966-28-51.

11. Tsai S-R, Hamblin MR, 2017. Biological effects and medical applications of infrared radiation. Journal of Photochemistry and Photobiology B: Biology. 170, Pages 197-207. Doi: https://doi.org/10.1016/j.jphotobiol.2017.04.014.

12. Pickering SA, Bayston R, Scammell BE, 2003. Electromagnetic augmentation of antibiotic efficacy in infection of orthopaedic implants. The Journal of Bone & Joint Surgery British 85(4), Pages 588-593. Doi: 10.1302/0301-620x.85b4.12644.

13. Bayır E, Bilgi E, Şendemir-Ürkmez A, et al, 2015. The effects of different intensities, frequencies and exposure times of extremely low-frequency electromagnetic fields on the growth of Staphylococcus aureus and Escherichia coli O157:H7. Electromagnetic Biology and Medicine. 34(1), Pages 14- 18. Doi: https://doi.org/10.3109/15368378.2013.853671.

14. Fang, M., Zhang, H. & Xue, S., 1998. Role of calcium in apoptosis of HL-60 cells induced by harringtonine. Sci. China Ser. C.-Life Sci. 41, Pages 600–607. Doi: https://doi.org/10.1007/BF02882901

15. Da Silva CP, de Oliveira CR, da Conceição M, et al, 1996. Apoptosis as a mechanism of cell death induced by different chemotherapeutic drugs in human leukemic T-lymphocytes. Biochem Pharmacol. 51(10), Pages 1331-1340. Doi: 10.1016/0006-2952(96)00041-x.

16. Mosmann T, 1983. Rapid colorimetric assay for cellular growth and survival: application to proliferation and cytotoxicity assays. J Immunol Meth. 65(1-2), Pages 55-63. Doi: https://doi.org/10.1016/0022-1759 (83)90303-4.

17. Baskić D, Popović S, Ristić P, et al, 2006. Analysis of cycloheximide-induced apoptosis in human leukocytes: fluorescence microscopy using annexin V/propidium iodide versus acridin orange/ethidium bromide. Cell Biol Int. 30(11), Pages 924-932. Doi: https://doi.org/10.1016/j.cellbi.2006.06.016.

18. Yu Q, Liu Y, Wang C, et al, 2012. Chiral Ruthenium (II) polypyridyl complexes: stabilization of g-quadruplex DNA, inhibition of telomerase activity and cellular uptake. PLoS One. 7(12), Pages 50902. Doi:10.1371/journal.pone.0050902.

19. Filipovic, N., Djukic, T., Radovic, M. et al, 2014. Electromagnetic field investigation on different cancer cell lines. Cancer Cell Int. 14, Pages 84. Doi: https://doi.org/10.1186/s12935-014-0084-x.

20. Sun, J., Tong, Y., Jia, Y. et al, 2023. Effects of extremely low frequency electromagnetic fields on the tumor cell inhibition and the possible mechanism. Sci Rep. 13, Pages 6989. Doi: https://doi.org/10.1038/s41598-023-34144-5.

21. Mrunmayi Kakde, 2023. Drug resistance and current challenges to overcome. International journal of therapeutic innovation, V 1 - I 1, Pages 0031 – 0037. Doi: https://doi.org/10.55522/ijti.V1I1.0011.

22. Crocetti S, Beyer C, Schade G, et al, 2013. Low intensity and frequency pulsed electromagnetic fields selectively impair breast cancer cell viability. PLoS One. 8(9), Pages e72944. Doi: 10.1371/journal.pone.0072944.