



Evidence of Radioprotective Effect of Resveratrol against Clastogenic Effect of Extremely Low-Frequency Electromagnetic Fields

J. Antonio Heredia-Rojas¹, Michaela Beltcheva², Abraham O. Rodríguez-De la Fuente¹, Ricardo Gomez-Flores¹, Roumiana Metcheva², Pedro C. Cantú-Martínez¹ & Omar Heredia-Rodríguez¹*

¹ Facultad de Ciencias Biológicas, Universidad Autónoma de Nuevo León, México

² Institute of Biodiversity and Ecosystem Research, Bulgarian Academy of Sciences, 1 Tsar Osvoboditel Blvd., 1000 Sofia, Bulgaria

Abstract: The living organisms have never before in its evolutionary history been exposed to electromagnetic radiation, especially to extremely low-frequency electromagnetic fields (ELF-EMFs) that are ubiquitous in the modern environment. There are some investigations that suggest that such fields have detrimental effects on cells. On the other hand, there have been many attempts to develop radioprotective agents. In the present study, BALB/c mice were exposed to 2.0 mT ELF-EMFs at 60 Hz frequency for 72 h, in the presence or absence of resveratrol (15 mg/kg), using sham-exposed mice and saline solution as negative controls, after which clastogenic effects were assessed by the micronucleus (MN) test. Resveratrol was shown to significantly ($p < 0.05$) reduce ELF-EMFs-induced clastogenic effect on mice bone marrow MN. These findings suggest a potential use of resveratrol for radioprotection.

Key words: Extremely low-frequency electromagnetic fields, clastogenic effect, radiation protection, micronucleus, resveratrol.

Introduction

The hazards of non-ionizing radiation, i.e. 50 to 60-hertz frequencies, which fall in the extremely low-frequency range, usually defined as running from zero to 300 hertz became apparent since several years ago when some works were published indicating a potential risk associated with an exposure to extremely low-frequency electromagnetic fields (ELF-EMFs) (WHO 2007). Nowadays, the ELF-EMFs are very common in the modern environment.

ELF-EMFs potential to induce genotoxic effects has been demonstrated in a number of bio-

logical systems, under several exposure conditions (WINKER et al. 2005, ERDAL et al. 2007, CELIKLER et al. 2009, RAGEH et al. 2012, UDROIU et al. 2015, HEREDIA-ROJAS et al. 2018 a,b). Furthermore, chemical substances have been reported to significantly decrease radiation effects in biological systems (SINGH & KRISHNAN 2015, FARHOOD et al. 2019); such molecules are known as “chemical protectors” or “chemical radioprotectors”. Several chemical compounds that act as radioprotectors are also antioxidant agents. Resveratrol (3,5,4'-trihydroxy-trans-stilbene) is a natural antioxidant compound mainly found in grapes and it has been shown

*Corresponding author: jose.heredia@uanl.edu.mx

that possesses *in vivo* free radicals scavenging properties, probably due to its effects as a gene regulator (XIA et al. 2017).

Antigenotoxic potential of resveratrol, alone or in combination with other phytochemicals (ABRAHAM et al., 2012), in addition to its effects on reducing DNA oxidative damage (ATTIA 2012), bone marrow chromosomal aberrations (BINGÖL et al. 2014), and genotoxins activity (ABRAHAM et al. 2016) have been reported. Most of the researchers in this field, agreed that resveratrol possesses a multiplicity of effects related to health benefits (KURŠVIETIENĖ et al. 2016).

In the extant literature, there are no works trying to evaluate the antigenotoxic activity of resveratrol against the clastogenic or mutagenic effects induced by ELF-EMFs. However, a recent report indicated that resveratrol may reverse the effects of ELF-EMFs on oxidative stress and immune response among workers exposed to a long-term occupational exposure (ZHANG et al. 2017). Also, resveratrol is capable to alleviate physiopathological or morphological changes in testis of rats exposed to alternating electric fields (ASLANKOC et al. 2017).

In view of this interesting issue involving radioprotection strategies, the current study was undertaken to further evaluate the radioprotective effect of *in vivo* administration of resveratrol on preventing ELF-EMFs-induced clastogenicity on murine bone marrow cells.

Materials and Methods

Animals

Twelve-week-old male Balb/c mice (27 ± 2.1 g) were provided by the Bioterium of Facultad de Ciencias Biológicas at Universidad Autónoma de Nuevo León, México. They were kept in a pathogen- and stress-free environment at 24 °C, under a light-dark cycle (light phase, 06:00-18:00 h), and given water and food *ad libitum*. All animal treatments and surgical procedures were performed in accordance with the University's Animal Care and Use for Research Protocol, which is based on the National Guidelines for Ethics and Biosafety under the General Law of Health for issues regarding Health Research (Ministry of Health, Mexico City).

In vivo experimental procedure

To determine the effect of resveratrol on ELF-EMF-treated animals, the following groups (6 mice per group) were considered: (a) 72 h of continuous 2.0 mT ELF-EMF exposure plus intraperitoneal (i.p.) administration of resveratrol (Sigma-Aldrich, St.

Louis, MO) in saline isotonic solution (15 mg/kg) before radiating, (b) 72 h of continuous 2.0 mT ELF-EMF exposure plus i.p. administration of saline isotonic solution before radiating, (c) sham-exposed mice treated with resveratrol, and (d) sham-exposed animals treated with saline alone. In spite of the low solubility of resveratrol in water, it was diluted in saline solution based on the rapid liver polyphenol metabolism and plasma binding to lipoproteins and albumin, which facilitates its entry to cells (JANNIN et al. 2004).

ELF-EMF exposure

A standardized and characterized home-made magnetic field exposure facility, as previously reported (HEREDIA-ROJAS et al. 2004, HEREDIA-ROJAS et al. 2010, HEREDIA-ROJAS et al. 2017) was used. In brief, a coil was prepared by winding 552 turns of enamel-insulated copper wire (1.3 mm diameter), which produced a 13.5-cm radius and 71-cm length cylindrical solenoid. It was connected to step-down and variable transformers and plugged to a 110 V AC source. Animals were then placed in the middle of this structure in a homogeneous magnetic field, and kept at $25 \pm 0.2^\circ\text{C}$ and 45% humidity. Sham-treated animals were used as negative controls, which were placed in the same room, but with the magnetic field device turned off.

Magnetic flux density was determined using a gaussmeter (Bell FW 6010, Orlando, FL) and an attached oscilloscope (BK-Precision model 2120, Dynascan Corp., Chicago, IL), which was required to monitor the resulting field. A 60-Hz alternating sinusoidal magnetic field was then generated. Frequency content was almost pure 60 Hz (<2% total harmonic distortion) and 0.3 μT and 20 μT values were observed for respective background magnetic field and local geomagnetic field. To maintain the exposure geometry, a plastic separator was inserted in the solenoid to allow placing mice in predetermined zones where the oscillating magnetic field rms value was 2.0 mT, providing food and water *ad libitum*.

Micronucleus (MN) test

At the end of the exposure time, mice were sacrificed by cervical dislocation and bone marrow micronucleated erythrocytes frequency was evaluated as reported by SCHMID (1976). For this, femurs bone marrow was flushed into a microfuge tube with 2.0 ml foetal calf serum (FCS, Sigma-Aldrich), using a 22 G needle and 1.0 ml syringe. Cells were then obtained by centrifugation at 500g for 10 min and supernatant fluid discarded. Next, pellet was suspended in 100 μl FCS and spread on microscope

coded slides. Air-dried smears were then stained with 5% May-Grünwald-Giemsa for 12-15 min and evaluated using a Leica DM2500 microscope (Leica Microsystems, Milton Keynes, UK) at 1000x. To determine MN frequency, 2000 consecutive polychromatic erythrocytes (PCE) were scored for each animal, 3 smears per animal, giving a total of 18 smears per studied group, after which slides were decoded. The used criteria for MN and PCE scoring were based in those established by HAYASHI et al. (1983) and MACGREGOR et al. (1990), who standardized and validated the original test developed by SCHMID (1976). In rodents, MN remains in the cell after the main nucleus has been pushed out; these micronuclei are easy to observe under the microscope as small DNA-staining bodies in the cytoplasm. Similarly, PCEs are easily identified; polychromatic cells that uniformly stain positive for RNA or do not stain are referred to as PCEs or normochromatic erythrocytes (NCEs), respectively.

Statistical analysis

Statistical differences among groups were determined by analysis of variance for normal distributions and the correspondent Tukey test for establishing individual differences. Data normality was calculated by the Kolmogorov-Smirnov test ($p < 0.05$). Results were expressed as mean \pm SEM of the response of 6 animals per treatment group. Analyses were carried out by using SPSS v.15.0 package.

Results

The aim of the present study was to evaluate the potential of resveratrol to protect mice against ELF-EMFs clastogenic effect, which was assessed by determining bone marrow MN frequency. As shown in Fig. 1, a higher MN frequency was observed in ELF-EMF exposed group without resveratrol ($p < 0.05$), as compared with resveratrol-treated group and controls, as expected, based in our previous reports (HEREDIA-ROJAS et al. 2017, HEREDIA-ROJAS et al. 2018a, 2018b). Moreover, in order to test if resveratrol itself could be an influence in MN frequency, unexposed ELF-EMFs animals and treated with resveratrol were compared with unexposed and injected with the vehicle only. Non-significant MN frequency between resveratrol-treated sham-exposed animals and untreated control (sham-exposed) was observed (Fig.1).

Discussion

Discovery of chemical protection for organisms has caused considerable interest among radiation biologists, especially in view of its possible practical applications. A large number of chemicals have been screened worldwide for possible radioprotective activity, however only a limited number of substances have been found to possess a considerable radioprotective action (YASHUNSKII and KOVTUN 1985, SHI-

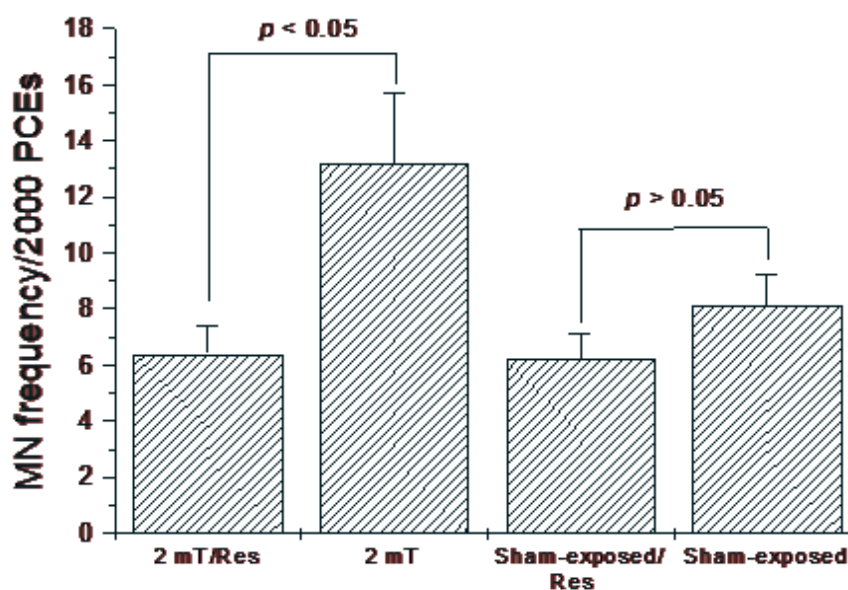


Fig. 1. Effect of resveratrol (Res) on murine bone marrow cells MN frequency. Cells were exposed to ELM-EMFs or untreated (sham-exposed), in the presence or absence of Res, and MN frequency measured as explained in the text. MN = micronucleus; PCEs = polychromatic erythrocytes; mT = miliTesla. Bars represent mean \pm SEM. Different letters on the bars indicate significant ($p < 0.05$) difference between groups.

RAZI et al. 2007, VASIN 2014, SZEJK et al. 2016).

In the present study, protective effect of resveratrol on the clastogenic effect induced by a critical exposure to ELF-EMFs was observed. However, the problem of how chemical protectors operate in diminishing the effects of irradiation has been the object of much discussion. Suggestions and theories are still controversial and debatable at present. On the other hand, there is no valid reason to believe that all radioprotectors must act by the same mechanism. Furthermore, the same substance may quite possibly protect with different mechanisms in different systems. Resveratrol antioxidant activity is well known (Gülçin 2010, SINGH et al. 2016, NAWAZ et al. 2017, XIA et al. 2017). Since the 1970s, oxidative stress has been evoked as a contributor to pathogenesis, including genotoxicity, and thousands of studies have reported protective benefits of antioxidants (SCHMIDT et al. 2015, XU et al. 2017).

In addition, a number of reports have shown the antigenotoxic effects of resveratrol; antimutagenic activity against the heterocyclic amine MeIQx and the well-known mutagen ethyl methanesulfonate in Chinese hamster V79 cell line was observed (BOYCE et al. 2004). Furthermore, *in vitro* experiments using HL-60 cells showed an inhibitory effect of resveratrol on chromosomal damage induced by diepoxybutane, mitomycin-C, and patulin (ABRAHAM et al. 2012). A pre-treatment with resveratrol has also been showed to protect against aflatoxin-induced chromosome aberrations and sister chromatid exchanges in cultured human lymphocytes (Türkez and ŞİŞMAN 2012). Regarding radioprotective effects, resveratrol has shown protection against chromosomal damage induced by gamma radiation (CARSTEN et al. 2008). Moreover, resveratrol pretreatment of cultured human lymphocytes, significantly reduced the genotoxicity induced by subsequent exposure to radioiodine-131 (HEDAYATI et al. 2013).

On the other hand, in the current study, direct resveratrol genotoxic effects were not observed (Fig. 1). In this regard, there are some reports that claim for genotoxic effects of this compound. MATSUOKA et al. (2001), observed an increased frequency of sister chromatid exchanges in CHL cells treated with resveratrol. In addition, MN frequency increase was also observed in CHO-K1 cells (BASSO et al. 2013). However, most scientists agree that resveratrol has low toxicity as it is well-tolerated in several short-term experiments (ALMEIDA et al. 2009, LA PORTE et al. 2010, WONG et al. 2011). Moreover, recent clinical trials demonstrated that resveratrol is pharmacologically safe (PATEL et al. 2011). Data on toxicity of resveratrol in long-term bioassays are scarce

(ZAMORA-ROS et al. 2006, CHOW et al. 2010).

In the present study, > 99% resveratrol was selected instead of natural extracts from plants, fruits or commercial products, because its concentration is lower compared with the purified reagent. Furthermore, resveratrol treatment at 15 mg/kg was chosen from a previous reports indicating effective doses of 6.25 to 30 mg/kg in exerting antigenotoxic effects (ABRAHAM et al. 2016). On the other hand, it is necessary to consider that electromagnetic field radiation induces stand-alone and combined effects on biological systems (KOSTOFF and LAU 2013), and for this reason several factors could be involved in the radioprotective response. In a recent report by KIM et al. (2017), it was shown that an exposure of a macrophage cell-line (RAW 264.7) at 0.8µT of ELF-EMFs can decrease the effectiveness of resveratrol against inflammatory responses through enhanced macrophage activation. In the present study, as we exposed the animals simultaneously to both, ELF-EMFs and resveratrol, an inhibition of the resveratrol action as antigenotoxic agent caused by magnetic fields exposure was not observed.

In summary, it was demonstrated that *in vivo* resveratrol treatment significantly reduce ELF-EMFs murine bone marrow MN genotoxicity.

References

- ABRAHAM S.K., ECKHARDT A., OLI R.G. & STOPPER H. 2012. Analysis of *in vitro* chemoprevention of genotoxic damage by phytochemicals, as single agents or as combinations. *Mutation Research – Genetic Toxicology and Environmental Mutagenesis* 744(2): 117–124. DOI:10.1016/j.mrgentox.2012.01.011.
- ABRAHAM S.K., KHANDELWAL N., HINTZSCHE H. & STOPPER H. 2016. Antigenotoxic effects of resveratrol: Assessment of *in vitro* and *in vivo* response. *Mutagenesis* 31(1): 27–33. DOI:10.1093/mutage/gev048.
- ALMEIDA L., VAZ-DA-SILVA M., FALCÃO A., SOARES E., COSTA R., LOUREIRO A.I., FERNANDES-LOPES C., ROCHA J.F., NUNES T., WRIGHT L. & SOARES-DA-SILVA P. 2009. Pharmacokinetic and safety profile of trans-resveratrol in a rising multiple-dose study in healthy volunteers. *Molecular Nutrition and Food Research* 53(1): S7–S15. DOI:10.1002/mnfr.200800177.
- ASLANKOC R., GUMRAL N., SAYGIN M., SENOL N., ASCI H., CANKARA F.N. & COMLEKCI S. 2018. The impact of electric fields on testis physiopathology, sperm parameters and DNA integrity – The role of resveratrol. *Andrologia* 50: e12971. doi.org/10.1111/and.12971.
- ATTIA S.M. 2012. Influence of resveratrol on oxidative damage in genomic DNA and apoptosis induced by cisplatin. *Mutation Research – Genetic Toxicology and Environmental Mutagenesis* 741(1): 22–31. DOI:10.1016/j.mrgentox.2011.10.008.
- BASSO E., FIORE M., LEONE S., DEGRASSI F. & COZZI R. 2013.

- Effects of resveratrol on topoisomerase II- α activity: Induction of micronuclei and inhibition of chromosome segregation in CHO-K1 cells. *Mutagenesis* 28(3): 243–248. DOI:10.1093/mutage/ges067.
- BINGÖL G., Gülkaç M.D., DILLIOĞLUGİL M.Ö., POLAT F. & KANLI A.Ö. 2014. Effect of resveratrol on chromosomal aberrations induced by doxorubicin in rat bone marrow cells. *Mutation Research – Genetic Toxicology and Environmental Mutagenesis* 766: 1–4. DOI:10.1016/j.mrgentox.2014.03.008.
- BOYCE A., DOEHMER J. & GOODERHAM N.J. 2004. Phytoalexin resveratrol attenuates the mutagenicity of the heterocyclic amines 2-amino-1-methyl-6-phenylimidazo[4,5- b] pyridine and 2-amino-3,8-dimethylimidazo[4,5- f]quinoxaline. *Journal of Chromatography B* 802(1): 217–223. DOI:10.1016/j.jchromb.2003.10.057.
- CARSTEN R.E., BACHAND A.M., BAILEY S.M. & ULLRICH R.L. 2008. Resveratrol reduces radiation-induced chromosome aberration frequencies in mouse bone marrow cells. *Radiation Research* 169(6): 633–638. DOI:10.1667/RR1190.1.
- CELIKLER S., AYDEMİR N., VATAN O., KURTULDU S. & BILALOGLU R. 2009. A biomonitoring study of genotoxic risk to workers of transformers and distribution line stations. *International Journal of Environmental Health Research* 19(6): 421–430.
- CHOW H.H., GARLAND L.L., HSU C.H., VINING D.R., CHEW W.M., MILLER J.A., PERLOFF M., CROWELL J.A. & ALBERTS D.S. 2010. Resveratrol modulates drug- and carcinogen-metabolizing enzymes in a healthy volunteer study. *Cancer Prevention Research* 3(9): 1168–1175. DOI:10.1158/1940-6207.CAPR-09-0155.
- ERDAL N., Gürgül S. & CELİK A. 2007. Cytogenetic effects of extremely low frequency magnetic field on Wistar rat bone marrow. *Mutation Research* 630(1-2): 69–77.
- FARHOOD B., GORADEL N.H., MORTEZAEI K., KHANLARKHANI N., SALEHI E., NASHTAEI M.S., MIRTAVOOS-MAHYARI H., MOTEVASELI E., SHABEB D., MUSA A. & NAJAFI M. 2019. Melatonin as an adjuvant in radiotherapy for radioprotection and radiosensitization. *Clinical and Translational Oncology* 21: 268. doi.org/10.1007/s12094-018-1934-1940.
- Gülçin İ. 2010. Antioxidant properties of resveratrol: A structure–activity insight. *Innovative Food Science and Emerging Technologies* 11(1): 210–218. DOI:10.1016/j.ifset.2009.07.002.
- HAYASHI M., SOFUNI T. & ISHIDATE JR M. 1983. An application of acridine orange fluorescent staining to the micronucleus test. *Mutation Research Letters* 120(4): 241–247.
- HEDAYATI M., SHAFAGHATI N. & HOSSEINIMEHR S.J. 2013. Resveratrol mitigates genotoxicity induced by iodine-131 in primary human lymphocytes. *Radiation and Environmental Biophysics* 52: 287. doi.org/10.1007/s00411-013-0461-1.
- HEREDIA-ROJAS J.A., CABALLERO-HERNÁNDEZ D.E., RODRÍGUEZ-DE LA FUENTE A.O., RAMOS-ALFANO G. & RODRÍGUEZ-FLORES L.E. 2004. Lack of alterations on meiotic chromosomes and morphological characteristics of male germ cells in mice exposed to a 60 Hz and 2.0 mT magnetic field. *Bioelectromagnetics* 25: 63–68.
- HEREDIA-ROJAS J.A., RODRÍGUEZ-DE LA FUENTE A.O., ALCOCER-GONZÁLEZ J.M., RODRÍGUEZ-FLORES L.E., RODRÍGUEZ-PADILLA C., SANTOYO-STEPHANO M.A., CASTAÑEDA-GARZA E. & TAMÉZ-GUERRA R.S. 2010. Effect of 60 Hz magnetic fields on the activation of hsp70 promoter in cultured INER-37 and RMA E7 cells. *In Vitro Cellular and Developmental Biology – Animal* 46: 758–63.
- HEREDIA-ROJAS J.A., BELTCHEVA M., RODRÍGUEZ-DE LA FUENTE A.O., HEREDIA-RODRÍGUEZ O., METCHEVA R., RODRÍGUEZ-FLORES L.E., SANTOYO-STEPHANO M.A. & CASTAÑEDA-GARZA E. 2017. Evidence of genotoxicity induced by 60 Hz magnetic fields on mice bone marrow as assessed by *in vivo* micronucleus test. *Acta Zoologica Bulgarica, Supplement* 8: 69–75.
- HEREDIA-ROJAS J.A., RODRÍGUEZ-DE LA FUENTE A.O., GÓMEZ-FLORES R., HEREDIA-RODRÍGUEZ O., RODRÍGUEZ-FLORES L.E., BELTCHEVA M. & CASTAÑEDA-GARZA E. 2018a. *In vivo* cytotoxicity induced by 60 Hz electromagnetic fields under a high-voltage substation environment. *Sustainability* 10(8): 2789. doi.org/10.3390/su10082789.
- HEREDIA-ROJAS J.A., BELTCHEVA M., METCHEVA R., GÓMEZ-FLORES R., RODRÍGUEZ-DE LA FUENTE A.O., HEREDIA-RODRÍGUEZ O., RODRÍGUEZ-FLORES L.E. & CASTAÑEDA-GARZA E. 2018b. Evidence of *in vivo* genotoxicity induced by extremely-low frequency electromagnetic fields compared with ionizing radiation and a chemical mutagen. *Journal of Environmental Protection and Ecology* 19 (3): 1261–1269.
- JANNIN B., MENZEL M., BERLOT J., DELMAS D., LANÇON A. & LATRUFFE N. 2004. Transport of resveratrol, a cancer chemopreventive agent, to cellular targets: Plasmatic protein binding and cell uptake. *Biochemical Pharmacology* 68(6): 1113–1118. DOI:10.1016/j.bcp.2004.04.028.
- KIM S.J., JANG Y. W., HYUNG K. E., LEE D. K., HYUN K. H., JEONG S. H., MIN K. H., KANG W., JEONG J. H., PARK S. & HWANG K. W. 2017. Extremely low-frequency electromagnetic field exposure enhances inflammatory response and inhibits effect of antioxidant in RAW 264.7 cells. *Bioelectromagnetics* 38: 374–385. DOI:10.1002/bem.22049.
- KOSTOFF R.M. & LAU C.G.Y. 2013. Combined biological and health effects of electromagnetic fields and other agents in the published literature. *Technological Forecasting and Social Change* 80: 1331–1349.
- KURŠVIETIENĖ L., STANEVIČIENĖ I., MONGIRDIENĖ A. & BERNATONIENĖ J. 2016. Multiplicity of effects and health benefits of resveratrol. *Medicina* 52(3): 148–155. DOI:10.1016/j.medic.2016.03.003.
- LA PORTE C., VODUC N., ZHANG G., SEGUIN I., TARDIFF D., SINGHAL N. & CAMERON D.W. 2010. Steady-state pharmacokinetics and tolerability of trans-resveratrol 2000 mg twice daily with food, quercetin and alcohol (ethanol) in healthy human subjects. *Clinical Pharmacokinetics* 49: 449. doi.org/10.2165/11531820-000000000-00000.
- MATSUOKA A., FURUTA A., OZAKI M., FUKUHARA K., & MIYATA N. 2001. Resveratrol, a naturally occurring polyphenol, induces sister chromatid exchanges in a Chinese hamster lung (CHL) cell line. *Mutation Research – Genetic Toxicology and Environmental Mutagenesis* 494(1): 107–113. DOI:10.1016/S1383-5718(01)00184-X.
- MACGREGOR J.T., WEHR C.M., HENIKA P.R. & SHELBY M.D. 1990. The *in vivo* erythrocyte micronucleus test: measurement at steady state increases assay efficiency and permits integration with toxicity studies. *Toxicological Sciences* 14(3): 513–522.
- NAWAZ W., ZHOU Z., DENG S., MA X., MA X., LI C. & SHU X. 2017. Therapeutic versatility of resveratrol derivatives. *Nutrients* 9(11): 1188. DOI:10.3390/nu9111188.

- PATEL K.R., SCOTT E., BROWN V.A., GESCHER A.J., STEWARD W.P. & BROWN K. 2011. Clinical trials of resveratrol: Clinical trials. *Annals of the New York Academy of Sciences* 1215(1): 161–169. DOI:10.1111/j.1749-6632.2010.05853.x.
- RAGEH M.M., EL-GEHALY R.H. & EL-BIALY N.S. 2012. Assessment of genotoxic and cytotoxic hazards in brain and bone marrow cells of newborn rats exposed to extremely low-frequency magnetic field. *Journal of Biomedicine and Biotechnology* 2012: 1–7.
- SCHMID W. 1976. The micronucleus test for cytogenetic analysis. In: HOLLAENDER A. (Ed.): *Chemical mutagens. Principles and Methods for their Detection*. New York: Plenum Press, pp. 31–35.
- SCHMIDT H.H., STOCKER R., VOLLBRACHT C., PAULSEN G., RILEY D., DAIBER A. & CUADRADO A. 2015. Antioxidants in translational medicine. *Antioxidants and Redox Signaling* 23(14): 1130–1143. DOI:10.1089/ars.2015.6393.
- SHIRAZI A., GHOBADI G. & GHAZI-KHANSARI M. 2007. A radiobiological review on melatonin: a novel radioprotector. *Journal of Radiation Research* 48(4): 263–272. doi.org/10.1269/jrr.06070.
- SINGH C.K., SIDDIQUI I.A., EL-ABD S., MUKHTAR H. & AHMAD N. 2016. Combination chemoprevention with grape antioxidants. *Molecular Nutrition and Food Research* 60(6): 1406–1415. DOI:10.1002/mnfr.201500945.
- SINGH P.K. & KRISHNAN S. 2015. Vitamin E analogs as radiation response modifiers. Evidence-based complementary and alternative medicine. 2015: 741301. DOI:10.1155/2015/741301.
- SZEJK M., KOŁODZIEJCZYK-CZEPAS J. & ZBIKOWSKA H. 2016. Radioprotectors in radiotherapy – advances in the potential application of phytochemicals. *Postepy Higieny i Medycyny Doswiadczalnej* 70: 722–734.
- Türkez H. & ŞIŞMAN T. 2012. The genoprotective activity of resveratrol on aflatoxin B1-induced DNA damage in human lymphocytes *in vitro*. *Toxicology and Industrial Health* 28(5): 474–480. DOI:10.1177/0748233711414614.
- UDROIU I., ANTOCCIA A., TANZARELLA C., GIULIANI L., PACCHIEROTTI F., CORDELLI E. & ELEUTERI P. 2015. Genotoxicity induced by foetal and infant exposure to magnetic fields and modulation of ionising radiation effects. *PLoS One* 10(11): e0142259.
- VASIN M.V. 2014. Comments on the mechanisms of action of radiation protective agents: basis components and their polyvalence. *SpringerPlus* 3: 414. DOI:10.1186/2193-1801-3-414.
- WHO 2007. Extremely low-frequency fields, *Environmental Health Criteria Monograph no. 238*. Geneva: World Health Organization (WHO), 121 p.
- WINKER R., IVANCSITS S., PILGER A., ADLKOEFER F. & Rüdiger H.W. 2005. Chromosomal damage in human diploid fibroblasts by intermittent exposure to extremely low-frequency electromagnetic fields. *Mutation Research* 585(1-2): 43–49.
- WONG R.H.X., HOWE P.R.C., BUCKLEY J.D., COATES A.M., KUNZ I. & BERRY N.M. 2011. Acute resveratrol supplementation improves flow-mediated dilatation in overweight/obese individuals with mildly elevated blood pressure. *Nutrition, Metabolism and Cardiovascular Diseases* 21(11): 851–856. DOI:10.1016/j.numecd.2010.03.003.
- XIA N., DAIBER A., Förstermann U. & LI H. 2017. Antioxidant effects of resveratrol in the cardiovascular system. *British Journal of Pharmacology* 174: 1633–1646. DOI:10.1111/bph.13492.
- XU D.P., LI Y., MENG X., ZHOU T., ZHOU Y., ZHENG J., ZHANG J.J. & LI H.B. 2017. Natural antioxidants in foods and medicinal plants: Extraction, assessment and resources. *International Journal of Molecular Sciences* 18(1): 96. DOI:10.3390/ijms18010096.
- YASHUNSKII V.G. & KOVTUN V.Y. 1985. New chemical agents for protection against ionising radiation. *Russian Chemical Reviews* 54(1): 76–97. DOI: 10.1070/RC1985v054n01A-BEH002968.
- ZAMORA-ROS R., URPI-SARDÀ M., LAMUELA-RAVENTÓS R.M., ESTRUCH R., Vázquez-AGELL M., SERRANO-MARTÍNEZ M., JAEGER W. & ANDRES-LACUEVA C. 2006. Diagnostic performance of urinary resveratrol metabolites as a biomarker of moderate wine consumption. *Clinical Chemistry* 52(7): 1373–1380; DOI: 10.1373/clinchem.2005.065870.
- ZHANG D., ZHANG Y., ZHU B., ZHANG H., SUN Y. & SUN C. 2017. Resveratrol may reverse the effects of long-term occupational exposure to electromagnetic fields on workers of a power plant. *Oncotarget* 8(29): 47497–47506. DOI:10.18632/oncotarget.17668.