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PROPOSED IMPLEMENTATION OF CONCEPTS OF ALARA (AS LOW AS REASONABLY ACHIEVABLE) AND PAMARA (PROTECTION AS MUCH AS REASONABLY ACHIEVABLE) TO REDUCE THE HEALTH RISK OF EMF RADIATION

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ABSTRACT

The advent of wireless communication technologies has led to increased exposure to EMF radiation that has enhanced risk of adverse health effects in humans. Introduction of 5G (5th Generation wireless Technology), which transmits signal at much higher frequency range (30-300 GHz) than previous Generations, has raised further concerns about its impact on human health. Most epidemiologic studies showed that EMF radiation emitted from previous Generation's frequencies increased the risk of cancer in humans. Since extensive animal and mechanistic studies confirm the conclusion of epidemiologic studies, the increased risk of cancer in human can be considered valid. However, a few epidemiologic investigations have reported no increase in cancer risk following exposure to EMF radiation. The inconsistent epidemiologic studies on cancer risk could be due to the fact that the level of frequency, dose strength (voltage per meter or V/m), intensity (milli Tesla or mT), and SAR (specific absorption rate, Watts/Kg or W/Kg of tissue) were not comparable. Supplementation with individual antioxidants reduced oxidative stress and protected against EMF radiation-induced damage. The major objectives of this review are to briefly describe (a) biological responses of 5G frequency range or less, (b) EMF radiation-induced increased risk of cancer, neurological, and non-neurological damages, (c) the role of increased oxidative stress and inflammation in such damage. The review proposes to implement the concept ALARA (as low as reasonably achievable) and PAMARA (protection as much as reasonably achievable) to reduce the health risk of EMF radiation exposure. A micronutrient mixture is suggested to implement the concept of PAMARA in the population.

KEYWORDS: EMF radiation; oxidative stress; inflammation; cancer; neurological abnormalities; protection.

1. INTRODUCTION

During the course of evolution, humans have been exposed to background ionizing, non-ionizing radiation such as ultraviolet radiation and naturally occurring non-polarized EMF radiation. In recent years, they are being exposed to increased levels of man-made polarized electromagnetic field (EMF) radiation from devices, such as mobile phones, laptops, and Wi-Fi, microwave ovens, and television sets. Humans are being exposed to EMF radiation daily at varying doses. There are substantial data to suggest that EMF radiation could induce acute and late adverse health effects, although a few epidemiologic studies revealed no harmful effects of EMF radiation in humans. It is impossible to avoid exposure to EMF radiation, because it has become the part of environment hazards. At present there are no suggested mechanism of protection against potential harmful effects of EMF radiation.

Human body has some positively and negatively charged particles all the time. Naturally occurring non-polarized EMF radiation cannot induce oscillations or vibrations in charged molecules, whereas man-made polarized EMF radiation can induce such vibration in charged molecules.[1] The magnitude of vibrations of charged molecules depends upon the frequency of EMF radiation. The vibration of charged molecules in the body can interfere with electrical communications between cells, especially in the brain and heart. Vibrated molecules become more sensitive to external and internal stressors. Therefore, Polarized EMF radiation induced vibration of charged particles in the body may represents one of the mechanisms that can increase the health risks in humans.

EMF radiation has been classified into extremely low frequency EMF (ELF-EMF), which has a frequency range up to 300 Hz, and radiofrequency EMF (RF-EMF) with a frequency range of up to KHz to 300 GHz).[2] Depending upon the frequency of EMF radiation, it can

produce thermal or non-thermal effects. EMF radiation delivered at a thermal frequency or non-thermal frequency would cause vibration of charged particles and free radicals, The health effects of EMF radiation depend upon the level of frequency, dose (strength) (voltage per meter or V/m), intensity (milli Tesla or mT), and energy absorption SAR (specific absorption rate, Watts/Kg of tissue). While determining the health risks of EMF radiation in humans, it is difficult to control all the above factors. Consequently, no human data utilizing a double-blind, placebo-controlled trials on the effects of EMF radiation on human health are available. In any epidemiologic studies, one can control frequency level and intensity, but not other factors. Therefore, results of such studies may vary from no effect to adverse health effects. All these factors can be controlled in animal or tissue culture studies; therefore, the results obtained from such would more reliable while considering the effects of EMF radiation on human health.

The introduction of 5G (5^{th} Generation), the latest wireless technology, which transmits signal at frequency range between 30-300 GHz, has alarmed many health professionals and public because of its impact on increased adverse health effects in humans. There are some major differences between 5^{th} Generation and previous generations technology. 5G utilizes millimeter waves (also called millimeter bands or extremely high frequency) and higher frequencies than the previous generations technologies. 5G EMF radiation can increase the risk of cancer, genetic damage, learning and memory deficits, and other neurological disorders.

The health effects of 5G frequency on humans have not been investigated. Most epidemiologic studies suggest that EMF radiation may increase the risk of cancer in humans.[3-6] Animal studies supported the above conclusion.[7-10] A few epidemiologic studies have reported no increase in cancer risk.[11-14]

Exposure to EMF radiation induces neurological abnormalities in some individuals, such as electromagnetic hypersensitivity, cognitive dysfunction, and abnormal electroencephalogram (EEG).[15-20] It also caused non-neurological damage such as rise in blood pressure[21], and endocrine changes, sperm and testicular damage, ocular damage, and calcium overload.[22]

Cell culture studies revealed that exposure to EMF radiation decreased the viability of cells and increased chromosomal damage and double-strand DNA breaks.[23-27] The changes in gene expression especially related to cancer, neurological and non-neurological diseases following exposure to EMF radiation have not been studied either on neuronal or non-neuronal cell culture.

Exposure to EMF radiation increased the levels of markers of oxidative damage in animals[13,28-30] and humans[31-35] suggesting that increase production of free radicals occurs during exposure to EMF radiation. In addition, it enhanced the levels of inflammation in animals[36-42] because it is known that when oxidative damage is not fully healed inflammation occurs. It appears that EMF radiation causes damage to the biological system by causing vibrations of charged molecules and by producing increased oxidative stress and inflammation. Therefore, supplementation with antioxidants which can reduce oxidative stress and inflammation and neutralize negatively charged molecules by donation an electron. Indeed, a few studies showed that administration of individual micronutrients before exposure to EMF radiation reduced the adverse health effects in animal and cell culture models[29,32,33,39,43-46] No significant studies on the effects of administration of single or multiple micronutrients administered before exposure to EMF have been performed in humans.

At present, there are no guidelines for tissue protection against EMF radiation-induced damage in humans. For protection against ionizing radiation (x-ray or gamma-ray), Each Department of Radiology in the USA has adopted the concept of ALARA (as low as reasonably achievable). This is a good physical strategy to reduce exposure to ionizing radiation among radiological workers and patients. Since of the mechanisms of injury is mediated by excessive production of free radicals, we have proposed a novel concept of PAMARA (protection as much as reasonably achievable) using a mixture micronutrients which complement the established concept of ALARA.[47] The concept of ALARA is being promoted for EMF radiation. In case of ionizing radiation, it is easy to implement; however, it is difficult to convince users of cell phone to reduce the time of use. Nevertheless, the concept of ALARA should be continue to propagate. In provide protection against EMF radiation, the concept of PAMARA proposed for ionizing radiation should be considered for EMF radiation.

The major objectives of this review are to briefly describe (a) biological responses of 5G frequency range, (b) EMF radiation-induced cancer risk, and neurological and non-neurological damage, (c) the role of increased oxidative stress and inflammation in such damage, and (d) identify gaps in the knowledge. The review proposes to extend the concept of ALARA to a novel concept of PAMARA that utilizes a mixture of micronutrients for tissue protection against EMF radiation.

2. Biological Responses to 5G Frequency Range

This 5G technology uses millimeter-wave, also known as extremely high frequency (EHF) wave, which transmits signal at frequency between 30 GHz- 300 GHz. These frequencies are called millimeter waves because they have wavelengths between 1 mm and 10 mm, whereas radio waves transmit signal at frequency between 3 KHz to 300 GHz and have longer wavelengths in centimeter.

The effects of millimeter wave on human health compared to radio wave have not been adequately

investigated. A review of several studies revealed that millimeter waves increase skin temperature, alter gene expression, promote cell proliferation and synthesis of proteins linked with oxidative stress, and inflammatory responses. These changes could damage eye and neuromuscular activity.[48] Another review analyzed 94 publications in vivo and in vitro on the health impact following exposure to frequency range between 6-100 GHZ). Eighty percent of the in vivo studies showed biological responses following exposure to EMF radiation, while 58% of the in vitro studies showed such responses. In vivo criteria of biological responses included alteration in physiological, neurological and histology parameters, whereas in vitro biological responses included changes in gene expression and protein synthesis, and enhanced cytotoxic effects, genotoxic effects, and temperature-related reactions.[49] Operating frequency ranges of currently used wireless communication devices are presented in Table 1.

3. Effects of EMF Radiation on Cancer Risk

3.1. Human studies: In 2011, an expert working group of the International Agency for Research on Cancer (IARC) defined RF-EMF radiation emitted from mobile phones or other wireless devices as Group 2B ("possible") human carcinogen.[50] Several epidemiologic studies suggest that exposure to EMF radiation enhances the risk of glioma, acoustic neuroma, and meningioma. Ipsilateral use of mobile phone showed higher risk of these brain tumors on the side used than on the contralateral side. An elevated risk of these cancers tends to enhance with increasing latency, time of use, and with first exposure at the age 20 years and younger.[3-5] Young women aged 21-39 years who were exposed to EMF radiation emitted from the Cell Phone kept in their brassieres at the rate of 10 h/day for several years developed excess incidence of multifocal invasive cancer in the area of the breast immediately adjacent to the cell phone.[6]

A few studies have reported no effect of EMF radiation emitted from mobile phones.[11,12] The use of mobile Phone by children and adolescents did not increase the incidence of brain tumors.[51] The adult users of cellular phones and cordless phones did not show enhanced the risk of glioma or meningioma.[52,53] Exposure to RF-EMF radiation did not increase the risk of brain cancer (glioma and meningioma).[14]

3.2. Animal studies: The US National Toxicology Program (NTP) has conducted comprehensive studies on the effects of EMF radiation exposure with 900 MHz in rats and with 1900 MHz in mice during pregnancy and during the entire lifespan of offspring on the incidence of cancer. These investigations showed that increased incidence of tumor, especially glioma and malignant schwannoma occur primarily in the cardiac nerves, but also in the brain. In addition, evidence of DNA damage was present in these organs.[7-9] The results of these studies were questioned by the ICNIRP (International Commission on Non-Ionizing Radiation Protection).[54] However NTP studies were supported by the Ramazzini Institute's investigations, which show that exposure to EMF radiation with1800 MHz at the highest dose of 50 V/m (volts/meter) increased the incidence of tumor of the brain and heart in rats.[10]

Some potential reasons for inconsistent epidemiologic investigations on cancer risk in humans following exposure to EMF radiation are discussed here. The health effects of EMF radiation depend upon the level of frequency, dose (strength) (voltage per meter or V/m), intensity (milli Tesla or mT), and energy absorption SAR (specific absorption rate, Watts/Kg of tissue). Higher the frequency, strength, intensity, and energy absorption greater would be the damage.[10] Among these factors, the amount of energy absorption (SAR) is most critical in determining the extent of damage. These variables can easily be controlled in animal or cell culture studies, but it is very difficult to control them in human epidemiologic investigations. This difficulty may account for the controversy regarding EMF radiation-induced increase in cancer risk. Since epidemiologic studies on EMF radiation-induced cancer risk are supported by the animal studies and by the cellular mechanisms that participate in carcinogenesis processes, EMF radiation-induced cancer in humans is a valid conclusion.

4. Effects of EMF Radiation on Neurological Abnormalities

4.1. EMF radiation-induced hypersensitivity: A review has described an early history of EMF-hypersensitivity. As early as in 1970, a study from the former Soviet Union described the "microwave syndrome" among military personnel, who were working with radio and radar equipment. This syndrome included fatigue, dizziness, headache, and inability to focus, cognitive impairment, and sleep disturbances. Similar symptoms were reported among Swedes employees, who worked in front of cathode ray tube monitors. Additional symptoms included flushing, burning, and tingling of the skin especially on the face, and photosensitivity. Similar symptoms were also reported from Finland following exposure to EMF radiation.[15] EMF radiation-induced electromagnetic hypersensitivity is now referred to as idiopathic environmental intolerance (IEI) or electro hypersensitivity (EHS). The prevalence of EMF radiation hypersensitivity was 5-30% for mild cases, 1.5% to 5% for moderate cases, and 1.5% for severe cases. The prevalence of electromagnetic hypersensitivity was 1.55% in Sweden[15] and 13.3% that decreased to 4.6% over 5 years period in Taiwan.[16]

Patients with hypersensitivity showed neurological symptoms that include headache, tinnitus, hyperacusis, dizziness, balance disorder, fibromyalgia, vegetative nerve dysfunction, and reduced cognitive capability, immediate memory loss, attention deficits, and eventually tempo-spatial confusion. These symptoms

were associated with chronic insomnia, fatigue, depressive tendency, anxiety emotional problem, and irritability.[17,18]

The International Commission of Non-Ionizing Radiation Protection Report showed that daily to RF-EMF radiation form cell phones more than 50 minutes might increase the risk of early dementia or other thermal damage.[19] Power plant workers, who were exposed to ELF-EMF radiation exhibited poor sleep quality, increased stress, depression, and anxiety.[20] Swiss adolescents exposed to RF-EMF radiation in their head area exhibited decreased memory scores (verbal memory).[55]

Exposure to mobile phone-EMF radiation for only 5-min impaired working memory, which was greater in 60 years or older individuals as well as in those who had mild cognitive impairment compared to healthy participants.[56]

EMF-radiation –induced increases in alpha band of electroencephalogram (EEG) were related to a rise in cerebral temperature in humans.[57] Short-term exposure to RF-EMF radiation reduced EEG alpha power but had no impact on cognitive function.[58] Additional human studies are needed to define EMF radiation-induced biochemical and genetic changes that leads to electromagnetic hypersensitivity, cognitive dysfunction, and depression.

Mice exposed to 835 MHz EMF radiation at absorption of energy rate SAR (specific absorption rate) of 4.0 W/Kg of tissue exhibited increased autophagy, hyperactivity, and demyelination in the cortical neurons.[59] Exposure to 900 MHz for 1 h per day for the entire adolescent period showed loss of pyramidal neurons in the hippocampus, and an increase in the levels of malondialdehyde and a decrease in catalase levels in rats. This suggests that EMF radiation-induced damage to the hippocampus was related to increased oxidative stress.[30]

Neurons are electrically charged and exchange information with other neurons electronically. This is one of the mechanisms by which neurons conduct their normal function. EMF radiation alters this mechanism of communication that could induce damage to nerve cell function. Another method of communication between neurons is mediated by biochemical compounds.

5. Effects of EMF Radiation on Non-Neoplastic and Non-Neurological Damage

A review of several studies on the effects of EMF radiation from Wi-Fi reported that such exposure caused increased oxidative stress, sperm/testicular damage, neuropsychiatric effects including EEG changes, apoptosis, DNA damage, endocrine changes, and calcium overload.[22] Exposure of reproductive system to EMF radiation emitted by GSM (global System for Mobile Communication), which has frequency range of 2G and 2.5G, increased production of free radicals by increasing the activity of reduced nicotinamide adenine dinucleotide (NADH) oxidase in the cell membrane.[60] Female rats exposed to 1800 MHz caused eye damage by upregulating the expression of caspase-2 and P38MAPK (p38 mitogen-activated protein kinase) in ocular cells.[61]

Workers using mobile phones for 60 minutes showed increased systolic blood pressure compared to those who spent less time talking on the cell phones. Occupational stress tends to enhance further the levels of systolic blood pressure. The study further revealed that men exposed EMF radiation showed an excess of blood pressure abnormalities, whereas women revealed more impairment of the ECG (electrocardiogram) profile.[21] Additional investigations with larger sample size to evaluate the effect of EMF radiation on blood pressure are needed.

6. Effects of EMF Radiation on Cellular Damage

Human peripheral blood lymphocytes were programmed to enter mitosis and then exposed to EMF radiation of 3G frequencies during the G2 phase of the cell cycle. The results showed that irradiated lymphocytes exhibited increased chromatid-type aberrations (gaps and breaks) an excess of up to 275% compared to unirradiated controls.[23] Mouse spermatocyte cells (GC-2 cell line) were exposed to ELF-EMF radiation (50 Hz) intermittently (5 min on and 10 min off) at an intensity of 1, 2, or 3 milli Tesla (mT) or RF-EMF radiation (1800 MHz) at the specific absorption rate (SAR) of 1, 2, or 4 W/kg (watts /kg of tissue) for 24 hours. The results showed that neither ELF-EMF nor RF-EMF radiation affected the viability of cells. However, ELF-EMF radiation at the highest intensity of 3 mT increased double-strand DNA breaks, but RF-EMF did not. Furthermore, RF-EMF exposure at SAR of 4 W/kg increased oxidative damage to DNA bases, but exposure to ELF-EMF did not. Thus, both ELF-EMF and RF-EMF exposures caused DNA damage, which was dependent upon intensity and energy absorption, respectively.[24] Mouse macrophages exposed to ELF-EMF with frequency of 50 Hz at the intensity of 1.0 milli Tesla (1mT) did not increase micronuclei formation, however, it enhanced the phagocytic activity of these cells.[25]

A review has reported that individuals exposed to EMF radiation exhibited enhanced chromosomal damage in their lymphocytes or exfoliated buccal cells.[26] However, one study found that mobile phone-EMF radiation exposure did not affect the levels of micronuclei in exfoliated buccal cells in humans.[62] EMF radiation emitted from the cell phone induced DNA damage in the hair follicles in the ear canal. The levels of DNA damage were increased with daily increase in exposure time.[27]

A few studies showed that EMF radiation produced no adverse effects but did not rule out completely.[63-66] The reasons for these studies showing no adverse health

effects of EMF radiations are not known. These studies have utilized different frequencies, dose (v/m), intensity (mT), and specific absorption rate in W/Kg, which may account for the above inconsistent results.

7. EMF RADIATION INCREASES OXIDATIVE STRESS

7.1. Human Studies: A review has proposed that EMF radiation enhances production of mitochondria-generated free radicals in the reproductive systems of both men and women.[31] High-voltage electricity generates ELF-EMF. Workers, who were chronically exposed to ELF-EMF, had elevated urine levels of 8-hydroxy-2-deoxy guanosine (8-OHdG) and F2-isoprostane compared to control groups.[33] Oxidative stress following exposure to either ELF-EMF or RF-EMF radiation together with impaired DNA repair processes, repair mechanism, and other cellular damages can elevate the risk of development of cancer.[34]

Exposure to ELF-EMF radiation emitted from high-voltage power lines increased oxidative stress as evidenced by elevated levels of urinary 8-isopsrostane and 8-hydroxy-deoxy guanosine in workers.[32] However, an investigation of the effects of ELF-EMF radiation did not show increased oxidative stress in workers performing tour-inspection near transformers and distribution power lines.[35]

7.2. Animal studies: Exposure of immature and mature rats with 900 MHz 2 h/day for 45 days increased oxidative damage as evidenced by decreased glutathione levels and antioxidant enzyme activity, and increased levels of lipid peroxidation and nitric oxide in lymphoid organs. Immature rats showed higher levels of oxidative stress than mature rats.[13] Acute exposure with ELF-EMF radiation increased oxidative stress in the brain as suggested by reduced activities of antioxidant enzymes catalase and superoxide dismutase in adult male rats, while it did not influence the levels of stress hormone corticosterone.[28] Exposure of rat lymphocytes with 930 MHz at a SAR (specific absorption rate) rate of 1.5 W/kg did not change basal intracellular levels of free radicals; however, it enhanced the production of free radicals generated by FeCl2 (ferrous chloride).[67] Rats exposed to 900 MHz for 30 min/day for 10 days showed increased oxidative damage in the kidney as evidenced by increased levels of MDA and decreased activities of antioxidant enzymes superoxide dismutase, catalase, and glutathione peroxidase.[29] Continuous exposure with EMF radiation of 900 MHz for 1 h throughout adolescent period increased oxidative damage in the sciatic nerve cells of male rats.[68] Male rats exposed to 1966.1 MHz at dose of 4 mV/cm^2 and SAR of 0.36 W/kg showed increased levels of oxidative stress, inflammation markers (IL-1beta, IL-6, and TNF-alpha compared to control animals. In addition, increased weight of adrenal gland and enhanced levels of stress hormones (adrenocorticotropic hormone and corticosterone were observed compared to controls.[69] Exposure to 900 MHz and 1800 MHz induced significant increase in lipid peroxidation and reduction in level of glutathione in the testis and epididymis. Although no difference was found in total sperm count, sperm motility was significantly reduced, causing impaired fertility in animals exposed to EMF radiation.[70]

8. EMF Radiation Enhances Chronic Inflammation

8.1. Animals exposed to 1800 MHz: Rats with lipopolysaccharide (LPS)-induced neuroinflammation were exposed to head only with1800 MHz EMF radiation for 2 hrs. At a specific absorption rate of 1.55 W/kg. Levels of neuroinflammation induced by LPS were further enhanced in the auditory cortex concomitant with increased growth of microglia processes and reduced firing rates. In addition, a larger proportion of auditory cortex locations had high acoustic thresholds. However, these changes were not observed in animals not treated with LPS. This suggests that 2-hour exposure to mobile cell phone operating on a frequency of 1800 MHz does not induce inflammation in normal rats but that a second stressor may be needed.[36] Experiments performed under similar experimental condition with an increased SAR (specific absorption rate) of 2.9 W/kg also aggravated LPS-induced inflammation in the cerebral cortex.[37] Exposure to EMF radiation with 900 MHz 45 min/day at an average specific absorption rate of 1.5 W/kg or 15 min/day at an average specific absorption rate of 6 W/kg emitted by mobile phones increased the levels of glial fibrillary acidic protein (GFAP), a marker of gliosis in the brain of rats.[38] EMF radiation enhanced secretion pro-inflammatory cytokines (TNF-alpha, IL-1 beta, and IL-6), and production of nitric oxide (NO), and reduced phagocytic activity of microglia cells.[39] Exposure of microglia cells in culture (N9 microglia cells) to EMF radiation activated Janus kinase 2 (JAK2) and Signal Transducer and Activator of Transcription Protein-3 (STAT3) and enhanced binding ability of STAT3 to DNA. In addition, exposure to EMF radiation markedly increased the expression of markers of inflammation (CD11b, TNF-alpha, and iNOS) and production of NO. Treatment with pyridone 6, an inhibitor of JAK2, suppressed EMF radiation induced inflammatory responses.[71]

8.2. Animals exposed to 900 MHz: A 15 minute exposure to 900 MHZ from mobile phone at a SAR (specific absorption rate) of 6 W/kg activated glia cells as evidenced by increased levels of glial fibrillary acidic protein (GFAP) in a time-dependent manner in adult rat[40]; however, it failed to produce similar effects in older rats, suggesting that the effect of EMF radiation of frequency of 900 MHz is age-dependent.[41] EMF radiation emitted from mobile phone impaired immune function in rats. But this effect was mitigated by supplementation with vitamin D.[72] Exposure to EMF radiation with 900 MHz in rats with elevated lipopolysaccharides-induced neuroinflammation during gestation or during adolescent did not influence behavior or further increase in inflammation in the brain.[42] No

studies on the levels of markers of inflammation in the blood of humans are available. Such studies should be conducted with appropriate attention to dose in V/m and specific absorption rate in W/kg).

9. HOW TO PROTECT TISSUES AGAINST EMF RADIATION

9.1. Physical Protection Suggestions

It is difficult to develop guidelines, because EMF radiation at varying levels is present all around in the environment, houses, and workplaces. US Federal Trade Commission Consumer Information report suggests that increasing distance between EMF radiation source and recipient, reducing exposure time to EMF radiation, and shielding. These principles would be effective in reducing the dose of EMF radiation, if there is a single source of EMF radiation. However, there are multiple sources of EMF radiation therefore, these principles are difficult to implement. The claims of effectiveness of shielding products made by the commercial companies are false.[73,74] In addition, Federal Trade Commission report suggests that shielding may interfere with the cell phone signal, causing it to draw even more power in order to communicate with the cell phone tower (also called base station), probably exposing individuals to more EMF radiation. Because of limitations of utilizing the principles of physical protection against EMF radiation, it is essential that a biological strategy for tissue protection should be developed.

9.2. Biological Protection with Micronutrients

Since EMF radiation increases oxidative stress and chronic inflammation, which contribute to EMF radiation-induced damage, effects of micronutrients on reducing the tissue damage were investigated. Most such studies were conducted with a single micronutrient. These studies are described here.

9.2.1. Human studies

Resveratrol and green tea: Workers, who are chronically exposed to ELF-EMF radiation from high voltage electricity exhibited increased oxidative stress. Treatment with resveratrol reduced this damage.[33] Supplementation with green tea polyphenol reduced ELF-EMF radiation-induced oxidative stress in individuals working near the high-voltage power plants.[32]

9.2.2 Animal studies

Melatonin and Omega-3-fatty acids: Melatonin treatment prevented EMF radiation (900 MHz) induced oxidative damage in the kidney of rats.[29] Prenatal exposure to 900 MHz EMF radiation together with melatonin or omega-3- fatty acids prevented EMF radiation-induced neuronal damage in the hippocampus of rats.[43]

Luteolin: Rats exposed to 900 MHz radiation showed reduced number of lending cells, primary spermatocytes, and spermatids compared to control animals. Treatment of animals with luteolin, a naturally occurring flavonoid with antioxidant and anti-inflammatory activity, enhanced the number of these cells compared to EMF irradiated animals not receiving luteolin.[44]

Garlic powder: Exposure to 900 MHz at the average specific absorption rate of 1.08 for 1h/day for 3 weeks increased the levels of MDA and advanced oxidation protein production in the brain; however, treatment with garlic powder, which exhibits antioxidant and anti-inflammation activities, reduced oxidative damage in the brain of rats.[75]

Folic acid: Exposure to RF-EMF radiation of 900 MHz 60 min/day for 21 days caused reduction in the number of total pyramidal and granular cells in the hippocampus and dentate gyres and Purkinje cell number in the cerebellum of rat. Treatment with folic acid decreased these changes in the hippocampus and cerebellum.[76]

9.2.3. Cell culture studies

Curcumin: Curcumin treatment of microglia cells in culture prevented EMF-induced elevation of pro-inflammatory cytokines and reduced phagocytic activity.[39]

Vitamin A: Exposure of porcine blood platelets to 1KHz frequency emitted from liquid-crystal-display monitors at the intensity of 220 V/m for 30 and 60 minutes increased the levels of malondialdehyde (MDA); however, treatment with vitamin A significantly attenuated such changes.[46]

Selenium: Human embryonic kidney cells (HEK293) exposed to 2.4 GHz EMF radiation for 1 h revealed increased levels of MDA and decreased activities of superoxide dismutase (SOD) and glutathione peroxidase. In addition, the levels of apoptosis and caspase-3 activity were higher and Bcl2 were lower in EMF irradiated cells compared to controls. Treatment of these cells before EMF radiation exposure with selenium reduced such EMF radiation-induced biochemical changes.[45]

The above limited studies show that micronutrients including antioxidants can reduce oxidative stress and reduce EMF radiation-induced damage mostly in animal studies. Additional studies with individual and multiple micronutrients on reducing EMF radiation-induced damage should be performed. In a meanwhile, it is unlikely that a single micronutrient would be able to provide any significant protection in humans.

10. Limitations of Using Single Antioxidant in Protecting Against EMF Radiation Damage

Although individual micronutrient has produced some benefits in experimental systems, it is unlikely that such an approach would be useful in reducing EMF radiation-induced damage in humans. The potential reasons include (a) different antioxidants are distributed differently in the sub-cellular compartments of cells;

therefore, a single antioxidant cannot protect all parts of the cell; (b) administered single antioxidant in a high internal oxidative environment of EMF radiation exposed individuals becomes oxidized and then acts as a pro-oxidant; (c) an elevation of the levels of antioxidant enzymes and dietary and endogenous antioxidants is essential for reducing oxidative stress and inflammation, a single micronutrient cannot achieve this; (d) the affinity of different antioxidant**s** for free radicals differs, depending upon their solubility; (e) both the aqueous and lipid compartments of the cell need to be protected together; a single antioxidant cannot meet this goal; (f) vitamin E is more effective in quenching free radicals in a reduced oxygenated cellular environment, whereas vitamin C and alpha-tocopherol are more effective in a higher oxygenated environment of the cells[77]; (g) vitamin C is important for recycling the oxidized form of alpha-tocopherol to the antioxidant form[78]; (h) different antioxidants alters the expression of different microRNAs each of which guides its respective mRNA to produce only protective proteins.[79] For example, some antioxidants can activate Nrf2 by upregulating miR-200a that inhibits its target protein Keap1, whereas others activate Nrf2 by downregulating miR-21 that binds with 3-UTR Nrf2 mRNA.[80]

11. Evidence for Failure of a Single Antioxidant in Human Studies

Supplementation with a single antioxidant in humans did not produce those benefits that were observed in animal models. For examples, administration of beta-carotene alone increased the risk of lung cancer in male heavy smokers.[81] Vitamin E treatment was ineffective in patients with Alzheimer's disease, but it reduced the rate of decline in cognitive function in early phase of this disease.[82,83] Vitamin E was ineffective in heart disease on primary and most secondary outcomes.[84] Thus, it is unlikely that the use of single antioxidant would significantly reduce EMF radiation-induced damage.

12. Evidence for the Usefulness of a Mixture of Micronutrient in Human Studies

Supplementation with a mixture of micronutrients produced beneficial effects in two clinical studies. For example, administration of multiple micronutrients reduced the risk of cancer in men[85] and prolonged the time period for initiating the anti-viral therapy in HIV infected patients.[86] Therefore, it is highly likelihood that proposed mixture would be effective in reducing acute and late adverse health effects following exposure to EMF radiation.

13. Proposed Concept of PAMARA (Protection as Much as Reasonably Achievable) for EMF Radiation Protection

A novel biological concept PAMARA for tissue protection against EMF radiation damage is proposed. This concept suggests that administration of a mixture of micronutrients to individuals who are likely to receive EMF radiation doses may reduce its adverse health effects. A mixture of micronutrients containing vitamin A, mixed carotenoids, vitamin C, alpha-tocopheryl acetate, alpha-tocopheryl succinate, vitamin D3, alpha-lipoic acid, n-acetyl- cysteine, coenzyme Q10, omega-3-fatty acids, curcumin, resveratrol, quercetin, green tea extract, all B-vitamins, selenomethionine, and zinc is proposed. This mixture would increase the levels of antioxidant enzymes by activating a nuclear transcriptional factor Nrf2 and the levels of dietary and endogenous antioxidant compounds. These cellular changes are essential for optimal tissue protection against EMF radiation-induced damage. Preclinical and clinical studies should be performed to test the validity the proposed concept of biological protection.

Table 1: Operating frequencies range of currently used wireless devices.

Types of devices	Frequency range
RF-EMF radiation	3 KHz - 300 GHz
EL-EMF radiation	0-300 Hz
5 G	30-300 GHz
4G	2-8 GHz
3G	1885- 2200 MHz
2G	800-1900 MHz
1G	450 MHz
WI-FI	2.4 GHz
Mobil phone models	1800 – 2200 MHz
Laptops	1000 – 3600 MHz

G = Generation

RF-EMF = Radiofrequency -Electromagnetic field. Transfer of energy by radio waves

ELF-EMF = Extremely low frequency-electromagnetic field

14. CONCLUSIONS

Humans are being exposed to increased levels of electromagnetic field (EMF) radiation from various wireless communication technologies. Adverse health effects have been reported from exposure to EMF radiation. Introduction of 5G (5th Generation technology) which transmits signal at frequency range between 30-300 GHz, has raised concerns about increased hazard to human health. No significant human studies on 5G EMF radiation have been performed.

Epidemiologic studies suggest that exposure to EMF radiation at a frequency of much lower than 5G increases the risk of certain brain cancer. Animal studies have supported the above conclusion. A few epidemiologic investigations studies have reported that EMF radiation does not increase the risk of cancer. Some potential reasons for these inconsistent results could be that the level of frequency, dose (strength) (voltage per meter or V/m), intensity (milli Tesla of mT), and energy absorption SAR (specific absorption rate, Watts/Kg of tissue) were not comparable. EMF radiation induces hypersensitivity in humans who exhibit neurological syndromes that include fatigue, dizziness, headache, lack of concentration, cognitive impairment, and sleep disturbances. Pre-treatment with individual antioxidants

reduced DNA damage, markers of oxidative damage and inflammation, and increased viability of neurons in the brain. Exposure of mammalian cells in culture to EMF radiation reduced cell viability in the brain and testis and increased chromosomal aberrations. EMF radiation increases the levels of markers of oxidative damage and inflammation, which contribute to the damage. We propose that implementation of concepts of ALARA (as low as reasonably achievable) and PAMARA (protection as much as reasonably achievable) may reduce acute and late adverse health effects of EMF radiation in humans. The concept of PAMARA can be implemented by using a proposed mixture of micronutrients.

REFERENCES

1. Panagopoulos DJ, Johansson O, Carlo GL. Polarization: A Key Difference between Man-made and Natural Electromagnetic Fields, in regard to Biological Activity. Sci Rep., 2015; 5: 14914.
2. Institute NC. Electromagnetic Fields and Cancer. In: Health NIo, editor. Bethesdam MD: National Cancer Institute, 2019.
3. Miller AB, Morgan LL, Udasin I, Davis DL. Cancer epidemiology update, following the 2011 IARC evaluation of radiofrequency electromagnetic fields (Monograph 102). Environ Res., 2018; 167: 673-83.
4. Hardell L, Carlberg M, Soderqvist F, Mild KH. Case-control study of the association between malignant brain tumours diagnosed between 2007 and 2009 and mobile and cordless phone use. Int J Oncol., 2013; 43(6): 1833-45.
5. Hardell L, Carlberg M. Mobile phone and cordless phone use and the risk for glioma - Analysis of pooled case-control studies in Sweden, 1997-2003 and 2007-2009. Pathophysiology., 2015; 22(1): 1-13.
6. West JG, Kapoor NS, Liao SY, Chen JW, Bailey L, Nagourney RA. Multifocal Breast Cancer in Young Women with Prolonged Contact between Their Breasts and Their Cellular Phones. Case Rep Med., 2013; 2013: 354682.
7. Program NT. NTP technical reporton the toxicology and catcinogenesis studies in Hsd:Sprague-Dawley SD rats exposed to whole-body radiofrequency radiation at a frequency (900 MHz) and modulations(GSM and CDMA) used by cell phones, 2018, NTP TR 595. In: Services UDoHaH, editor. Triangle Park, NC2018.
8. Program NT. NTP technical report on the toxicology and carcinogenesis studies in B6C3F1/N mice exposed to whole-body radiofrequency radiation at a frequency (1900 MGz) and modulations (GSM and CDMA) used by cell phones. NTP TR 596., 2018.
9. Melnick RL. Commentary on the utility of the National Toxicology Program study on cell phone radiofrequency radiation data for assessing human health risks despite unfounded criticisms aimed at minimizing the findings of adverse health effects. Environ Res., 2019; 168: 1-6.
10. Falcioni L, Bua L, Tibaldi E, Lauriola M, De Angelis L, Gnudi F, et al. Report of final results regarding brain and heart tumors in Sprague-Dawley rats exposed from prenatal life until natural death to mobile phone radiofrequency field representative of a 1.8GHz GSM base station environmental emission. Environ Res., 2018; 165: 496-503.
11. Karipidis K, Elwood M, Benke G, Sanagou M, Tjong L, Croft RJ. Mobile phone use and incidence of brain tumour histological types, grading or anatomical location: a population-based ecological study. BMJ Open., 2018; 8(12): e024489.
12. Nilsson J, Jaras J, Henriksson R, Holgersson G, Bergstrom S, Estenberg J, et al. No Evidence for Increased Brain Tumour Incidence in the Swedish National Cancer Register Between Years 1980-2012. Anticancer Res., 2019; 39(2): 791-6.
13. Aydin B, Akar A. Effects of a 900-MHz electromagnetic field on oxidative stress parameters in rat lymphoid organs, polymorphonuclear leukocytes and plasma. Arch Med Res., 2011; 42(4): 261-7.
14. Vila J, Turner MC, Gracia-Lavedan E, Figuerola J, Bowman JD, Kincl L, et al. Occupational exposure to high-frequency electromagnetic fields and brain tumor risk in the INTEROCC study: An individualized assessment approach. Environ Int., 2018; 119: 353-65.
15. Hedendahl L, Carlberg M, Hardell L. Electromagnetic hypersensitivity--an increasing challenge to the medical profession. Rev Environ Health., 2015; 30(4): 209-15.
16. Huang PC, Cheng MT, Guo HR. Representative survey on idiopathic environmental intolerance attributed to electromagnetic fields in Taiwan and comparison with the international literature. Environ Health, 2018; 17(1): 5.
17. Belpomme D, Irigaray P. Electrohypersensitivity as a Newly Identified and Characterized Neurologic Pathological Disorder: How to Diagnose, Treat, and Prevent It. Int J Mol Sci.., 2020; 21(6).
18. Johansson A, Nordin S, Heiden M, Sandstrom M. Symptoms, personality traits, and stress in people with mobile phone-related symptoms and electromagnetic hypersensitivity. J Psychosom Res., 2010; 68(1): 37-45.
19. Moradi M, Naghdi N, Hemmati H, Asadi-Samani M, Bahmani M. Effects of the Effect of Ultra High Frequency Mobile Phone Radiation on Human Health. Electron Physician, 2016; 8(5): 2452-7.
20. Bagheri Hosseinabadi M, Khanjani N, Ebrahimi MH, Haji B, Abdolahfard M. The effect of chronic exposure to extremely low-frequency electromagnetic fields on sleep quality, stress, depression and anxiety. Electromagn Biol Med., 2019; 38(1): 96-101.
21. Szyjkowska A, Gadzicka E, Szymczak W, Bortkiewicz A. [The reaction of the circulatory system to stress and electromagnetic fields emitted

by mobile phones - 24-h monitoring of ECG and blood pressure]. Med Pr., 2019; 70(4): 411-24.
22. Pall ML. Wi-Fi is an important threat to human health. Environ Res., 2018; 164: 405-16.
23. Panagopoulos DJ. Chromosome damage in human cells induced by UMTS mobile telephony radiation. Gen Physiol Biophys, 2019; 38(5): 445-54.
24. Duan W, Liu C, Zhang L, He M, Xu S, Chen C, et al. Comparison of the genotoxic effects induced by 50 Hz extremely low-frequency electromagnetic fields and 1800 MHz radiofrequency electromagnetic fields in GC-2 cells. Radiat Res., 2015; 183(3): 305-14.
25. Frahm J, Lantow M, Lupke M, Weiss DG, Simko M. Alteration in cellular functions in mouse macrophages after exposure to 50 Hz magnetic fields. J Cell Biochem, 2006; 99(1): 168-77.
26. Verschaeve L. Genetic damage in subjects exposed to radiofrequency radiation. Mutat Res., 2009; 681(2-3): 259-70.
27. Akdag M, Dasdag S, Canturk F, Akdag MZ. Exposure to non-ionizing electromagnetic fields emitted from mobile phones induced DNA damage in human ear canal hair follicle cells. Electromagn Biol Med., 2018; 37(2): 66-75.
28. Martinez-Samano J, Torres-Duran PV, Juarez-Oropeza MA, Verdugo-Diaz L. Effect of acute extremely low frequency electromagnetic field exposure on the antioxidant status and lipid levels in rat brain. Arch Med Res., 2012; 43(3): 183-9.
29. Oktem F, Ozguner F, Mollaoglu H, Koyu A, Uz E. Oxidative damage in the kidney induced by 900-MHz-emitted mobile phone: protection by melatonin. Arch Med Res., 2005; 36(4): 350-5.
30. Kerimoglu G, Guney C, Ersoz S, Odaci E. A histopathological and biochemical evaluation of oxidative injury in the sciatic nerves of male rats exposed to a continuous 900-megahertz electromagnetic field throughout all periods of adolescence. J Chem Neuroanat, 2018; 91: 1-7.
31. Santini SJ, Cordone V, Falone S, Mijit M, Tatone C, Amicarelli F, Di Emidio G. Role of Mitochondria in the Oxidative Stress Induced by Electromagnetic Fields: Focus on Reproductive Systems. Oxid Med Cell Longev, 2018; 2018: 5076271.
32. Zhang Y, Zhang D, Zhu B, Zhang H, Sun Y, Sun C. Effects of dietary green tea polyphenol supplementation on the health of workers exposed to high-voltage power lines. Environ Toxicol Pharmacol, 2016; 46: 183-7.
33. Zhang D, Zhang Y, Zhu B, Zhang H, Sun Y, Sun C. Resveratrol may reverse the effects of long-term occupational exposure to electromagnetic fields on workers of a power plant. Oncotarget., 2017; 8(29): 47497-506.
34. Havas M. When theory and observation collide: Can non-ionizing radiation cause cancer? Environ Pollut, 2017; 221: 501-5.
35. Li L, Xiong DF, Liu JW, Li ZX, Zeng GC, Li HL. A cross-sectional study on oxidative stress in workers exposed to extremely low frequency electromagnetic fields. Int J Radiat Biol., 2015; 91(5): 420-5.
36. Occelli F, Lameth J, Adenis V, Huetz C, Leveque P, Jay TM, et al. A Single Exposure to GSM-1800MHz Signals in the Course of an Acute Neuroinflammatory Reaction can Alter Neuronal Responses and Microglial Morphology in the Rat Primary Auditory Cortex. Neuroscience, 2018; 385: 11-24.
37. Lameth J, Gervais A, Colin C, Leveque P, Jay TM, Edeline JM, Mallat M. Acute Neuroinflammation Promotes Cell Responses to 1800 MHz GSM Electromagnetic Fields in the Rat Cerebral Cortex. Neurotox Res., 2017; 32(3): 444-59.
38. Ammari M, Gamez C, Lecomte A, Sakly M, Abdelmelek H, De Seze R. GFAP expression in the rat brain following sub-chronic exposure to a 900 MHz electromagnetic field signal. Int J Radiat Biol., 2010; 86(5): 367-75.
39. He GL, Liu Y, Li M, Chen CH, Gao P, Yu ZP, Yang XS. The amelioration of phagocytic ability in microglial cells by curcumin through the inhibition of EMF-induced pro-inflammatory responses. J Neuroinflammation, 2014; 11: 49.
40. Brillaud E, Piotrowski A, de Seze R. Effect of an acute 900MHz GSM exposure on glia in the rat brain: a time-dependent study. Toxicology, 2007; 238(1): 23-33.
41. Bouji M, Lecomte A, Hode Y, de Seze R, Villegier AS. Effects of 900 MHz radiofrequency on corticosterone, emotional memory and neuroinflammation in middle-aged rats. Exp Gerontol, 2012; 47(6): 444-51.
42. Petitdant N, Lecomte A, Robidel F, Gamez C, Blazy K, Villegier AS. Cerebral radiofrequency exposures during adolescence: Impact on astrocytes and brain functions in healthy and pathologic rat models. Bioelectromagnetics, 2016; 37(5): 338-50.
43. Erdem Koc G, Kaplan S, Altun G, Gumus H, Gulsum Deniz O, Aydin I, et al. Neuroprotective effects of melatonin and omega-3 on hippocampal cells prenatally exposed to 900 MHz electromagnetic fields. Int J Radiat Biol., 2016; 92(10): 590-5.
44. Yahyazadeh A, Altunkaynak BZ. Protective effects of luteolin on rat testis following exposure to 900 MHz electromagnetic field. Biotech Histochem, 2019; 94(4): 298-307.
45. Pastaci Ozsobaci N, Duzgun Ergun D, Durmus S, Tuncdemir M, Uzun H, Gelisgen R, Ozcelik D. Selenium supplementation ameliorates electromagnetic field-induced oxidative stress in the HEK293 cells. J Trace Elem Med Biol., 2018; 50: 572-9.
46. Lewicka M, Henrykowska G, Zawadzka M, Rutkowski M, Pacholski K, Buczynski A. Impact of electromagnetic radiation emitted by monitors on changes in the cellular membrane structure and protective antioxidant effect of vitamin A - In vitro

study. Int J Occup Med Environ Health, 2017; 30(5): 695-703.
47. Prasad KN, Cole WC, Haase GM. Radiation protection in humans: extending the concept of as low as reasonably achievable (ALARA) from dose to biological damage. Br J Radiol, 2004; 77(914): 97-9.
48. Di Ciaula A. Towards 5G communication systems: Are there health implications? Int J Hyg Environ Health, 2018; 221(3): 367-75.
49. Simko M, Mattsson MO. 5G Wireless Communication and Health Effects-A Pragmatic Review Based on Available Studies Regarding 6 to 100 GHz. Int J Environ Res Public Health, 2019; 16(18).
50. IARC. IARC Monograph on Evaluation of Carconigenic Risks to Humans. Non-ionizing Radiation, Part 2, Radiofrequency fields. In: Cancer IAfRo, editor. Lyon, France, 2013.
51. Aydin D, Feychting M, Schuz J, Tynes T, Andersen TV, Schmidt LS, et al. Mobile phone use and brain tumors in children and adolescents: a multicenter case-control study. J Natl Cancer Inst., 2011; 103(16): 1264-76.
52. Schuz J, Bohler E, Berg G, Schlehofer B, Hettinger I, Schlaefer K, et al. Cellular phones, cordless phones, and the risks of glioma and meningioma (Interphone Study Group, Germany). Am J Epidemiol, 2006; 163(6): 512-20.
53. Lonn S, Ahlbom A, Hall P, Feychting M, Swedish Interphone Study G. Long-term mobile phone use and brain tumor risk. Am J Epidemiol, 2005; 161(6): 526-35.
54. ICNIRP. ICNIRP note on recent animal carcinogenesis stuides. In: ICNIRP, editor. Munich, Germany, 2018.
55. Foerster M, Thielens A, Joseph W, Eeftens M, Roosli M. A Prospective Cohort Study of Adolescents' Memory Performance and Individual Brain Dose of Microwave Radiation from Wireless Communication. Environ Health Perspect, 2018; 126(7): 077007.
56. Kalafatakis F, Bekiaridis-Moschou D, Gkioka E, Tsolaki M. Mobile phone use for 5 minutes can cause significant memory impairment in humans. Hell J Nucl Med.., 2017; 20: 146-54.
57. Loughran SP, Verrender A, Dalecki A, Burdon CA, Tagami K, Park J, et al. Radiofrequency Electromagnetic Field Exposure and the Resting EEG: Exploring the Thermal Mechanism Hypothesis. Int J Environ Res Public Health, 2019; 16(9).
58. Vecsei Z, Knakker B, Juhasz P, Thuroczy G, Trunk A, Hernadi I. Short-term radiofrequency exposure from new generation mobile phones reduces EEG alpha power with no effects on cognitive performance. Sci Rep., 2018; 8(1): 18010.
59. Kim JH, Yu DH, Huh YH, Lee EH, Kim HG, Kim HR. Long-term exposure to 835 MHz RF-EMF induces hyperactivity, autophagy and demyelination in the cortical neurons of mice. Sci Rep., 2017; 7: 41129.
60. Yahyazadeh A, Deniz OG, Kaplan AA, Altun G, Yurt KK, Davis D. The genomic effects of cell phone exposure on the reproductive system. Environ Res., 2018; 167: 684-93.
61. Eker ED, Arslan B, Yildirim M, Akar A, Aras N. The effect of exposure to 1800 MHz radiofrequency radiation on epidermal growth factor, caspase-3, Hsp27 and p38MAPK gene expressions in the rat eye. Bratisl Lek Listy, 2018; 119(9): 588-92.
62. de Oliveira FM, Carmona AM, Ladeira C. Is mobile phone radiation genotoxic? An analysis of micronucleus frequency in exfoliated buccal cells. Mutat Res., 2017; 822: 41-6.
63. Roser K, Schoeni A, Roosli M. Mobile phone use, behavioural problems and concentration capacity in adolescents: A prospective study. Int J Hyg Environ Health, 2016; 219(8): 759-69.
64. Mortazavi G, Mortazavi SAR, Mortazavi SMJ. Comments on "Association of excessive mobile phone use during pregnancy with birth weight: an adjunct study in Kumamoto of Japan Environment and Children's Study". Environ Health Prev Med., 2017; 22(1): 67.
65. Bodewein L, Schmiedchen K, Dechent D, Stunder D, Graefrath D, Winter L, et al. Systematic review on the biological effects of electric, magnetic and electromagnetic fields in the intermediate frequency range (300Hz to 1MHz). Environ Res., 2019; 171: 247-59.
66. Kuzniar A, Laffeber C, Eppink B, Bezstarosti K, Dekkers D, Woelders H, et al. Semi-quantitative proteomics of mammalian cells upon short-term exposure to non-ionizing electromagnetic fields. PLoS One., 2017; 12(2): e0170762.
67. Zmyslony M, Politanski P, Rajkowska E, Szymczak W, Jajte J. Acute exposure to 930 MHz CW electromagnetic radiation in vitro affects reactive oxygen species level in rat lymphocytes treated by iron ions. Bioelectromagnetics, 2004; 25(5): 324-8.
68. Kerimoglu G, Hanci H, Bas O, Aslan A, Erol HS, Turgut A, et al. Pernicious effects of long-term, continuous 900-MHz electromagnetic field throughout adolescence on hippocampus morphology, biochemistry and pyramidal neuron numbers in 60-day-old Sprague Dawley male rats. J Chem Neuroanat, 2016; 77: 169-75.
69. Singh KV, Gautam R, Meena R, Nirala JP, Jha SK, Rajamani P. Effect of mobile phone radiation on oxidative stress, inflammatory response, and contextual fear memory in Wistar rat. Environ Sci Pollut Res Int., 2020; 27(16): 19340-51.
70. Mailankot M, Kunnath AP, Jayalekshmi H, Koduru B, Valsalan R. Radio frequency electromagnetic radiation (RF-EMR) from GSM (0.9/1.8GHz) mobile phones induces oxidative stress and reduces sperm motility in rats. Clinics (Sao Paulo), 2009; 64(6): 561-5.

71. Yang X, He G, Hao Y, Chen C, Li M, Wang Y, et al. The role of the JAK2-STAT3 pathway in pro-inflammatory responses of EMF-stimulated N9 microglial cells. J Neuroinflammation, 2010; 7: 54.
72. El-Gohary OA, Said MA. Effect of electromagnetic waves from mobile phone on immune status of male rats: possible protective role of vitamin D. Can J Physiol Pharmacol, 2017; 95(2): 151-6.
73. Panagopoulos DJ, Chrousos GP. Shielding methods and products against man-made Electromagnetic Fields: Protection versus risk. Sci Total Environ, 2019; 667: 255-62.
74. Leitgeb N, Cech R. Electromagnetic shielding mats: facts and fiction. Radiat Prot Dosimetry, 2007; 123(4): 450-6.
75. Bilgici B, Akar A, Avci 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.
76. Kivrak EG, Altunkaynak BZ, Alkan I, Yurt KK, Kocaman A, Onger ME. Effects of 900-MHz radiation on the hippocampus and cerebellum of adult rats and attenuation of such effects by folic acid and Boswellia sacra. J Microsc Ultrastruct, 2017; 5(4): 216-24.
77. Vile GF, Winterbourn CC. Inhibition of adriamycin-promoted microsomal lipid peroxidation by beta-carotene, alpha-tocopherol and retinol at high and low oxygen partial pressures. FEBS Lett., 1988; 238(2): 353-6.
78. Niki E. Interaction of ascorbate and alpha-tocopherol. Ann N Y Acad Sci.., 1987; 498: 186-99.
79. Prasad KN, Bondy SC. MicroRNAs in Hearing Disorders: Their Regulation by Oxidative Stress, Inflammation and Antioxidants. Front Cell Neurosci, 2017; 11: 276.
80. Wu H, Kong L, Tan Y, Epstein PN, Zeng J, Gu J, et al. C66 ameliorates diabetic nephropathy in mice by both upregulating NRF2 function via increase in miR-200a and inhibiting miR-21. Diabetologia, 2016.
81. Albanes D, Heinonen OP, Huttunen JK, Taylor PR, Virtamo J, Edwards BK, et al. Effects of alpha-tocopherol and beta-carotene supplements on cancer incidence in the Alpha-Tocopherol Beta-Carotene Cancer Prevention Study. Am J Clin Nutr., 1995; 62(6): 1427S-30S.
82. Isaac MG, Quinn R, Tabet N. Vitamin E for Alzheimer's disease and mild cognitive impairment. Cochrane Database Syst Rev., 2008; 3: CD002854.
83. Sano M, Ernesto C, Thomas RG, Klauber MR, Schafer K, Grundman M, et al. A controlled trial of selegiline, alpha-tocopherol, or both as treatment for Alzheimer's disease. The Alzheimer's Disease Cooperative Study. N Engl J Med., 1997; 336(17): 1216-22.
84. Yusuf S, Dagenais G, Pogue J, Bosch J, Sleight P. Vitamin E supplementation and cardiovascular events in high-risk patients. The Heart Outcomes Prevention Evaluation Study Investigators. N Engl J Med., 2000; 342(3): 154-60.
85. Gaziano JM, Sesso HD, Christen WG, Bubes V, Smith JP, MacFadyen J, et al. Multivitamins in the prevention of cancer in men: the Physicians' Health Study II randomized controlled trial. JAMA., 2012; 308(18): 1871-80.
86. Baum MK, Campa A, Lai S, Sales Martinez S, Tsalaile L, Burns P, et al. Effect of micronutrient supplementation on disease progression in asymptomatic, antiretroviral-naive, HIV-infected adults in Botswana: a randomized clinical trial. JAMA., 2013; 310(20): 2154-63.