Positive correlation between ELF and RFelectromagnetic fieldon cancer risk

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ABSTRACT

Extremely low frequency (ELF) and Radio frequency (RF) electromagnetic field may affect biological systems by raising generation free radicals by decline activities of glutathione peroxidase dismutase or increase in the lifetime of free radicals with inhibited pretreatment of cells antioxidant like that alpha tocopherol. ELF and RF electromagnetic field maycan damaged DNA with raising level hydroxyl radicals in cells and it is can interact DNA and form mainly 8-hydroxy-2′–deoxyguanosine(8-OHdG) adducts. Many study showed Electromagnetic field radiation(EMF) can change gene expression and conformation of protein. It may declineexpression of some genes such as superoxide dismutase orraise expressionof certain genes such as Hsps (heat shock proteins). ELF and RFelectromagnetic field can effects on homeostasis Ca^{2+} and alteration in important cellular and molecular processes such as differentiation, proliferation, gene expression, cytoskeletal reorganization and metabolism. Use of radio frequency electromagneticfield onsatellite jamming in Iran and some country may can harmful to human health and it could be a risk factor for cancer.

Keywords: Extremely low frequency; Radio frequency; Cancer; Heat shock proteins (Hsps).

INTRODUCTION

Extremely low frequency electromagnetic field (ELF-EMF) is non-ionizing radiation with frequencies 30-300 Hz. ELF -EMF was generally present in daily life all over the world and has raised consider electromagnetic radiation significantly in parallel with growing technology such as ordinary household appliances and power lines and electrically powered devices andelectrical transmission lines. somestudies suggested that there is a probable relation between ELF-MFs and malignancies in childhood and adulthood such as nervous system tumors and leukemia[1]. International Agency for Research on Cancer has classified RF-EMF and ELF-EMF as 'probably carcinogenic to humans' in group 2B [2, 3]. Howeversome candidate mechanisms have been suggested; it has been suggested that the interaction between living organisms and ELF-MFs could intervene with reactive oxygen species (ROS) generation and their half-life extension [4-6]. Several in vivo and in vitro studies showed that ELF-EMF could act as a promoter or co-promoter of cancer [7] . Radio frequency electromagnetic field (RF-EMF) is non-ionizing radiation with frequencies with frequencies 100 kHz to 300 GHz and usetelevision, cell phone and radio transmitters and radar produce RF fields. These fields are used to transmit information over long distances and form the basis of telecommunications as well as television and radio broadcasting all over the world. Microwaves are RF fields at high frequencies in the GHz range and generally use in mobile communication (800 MHz – 2.45 GHz),etc. The widespread use of cell phonecommunication devices has increased concerns about raised cancer risks [3]. The biological effects of radiofrequency (RF) radiation emitted from wireless devices such as cell phones induce oxidative stress in cells and raising free radicals [8]. These fieldslead to induction of histopathologic changes in tissue such ascell proliferation, proteins conformation, capillary proliferation, [9, 10] as well as change in gene expression such as heat shock protein 70 (Hsp70)[11, 12].ELF-EMF and RF-EMF can effect on biological system but five specific variables

factor dependent to RF and ELF exposure influence cells: (1) frequency, (2) specific absorption rate, (3) exposure as continuing wave, pulsed wave and occupationally exposed/mobile phone users, (4) duration of exposure, (5) different cell types [13]. Each of these factors can determine effect of RF and ELF on cells or biological system.

EFFECT ELF AND RF ELECTROMAGNETICFIELD ONOXIDATIVE STRESSRESPONE CELLS

Oxidative stress is a cellular or physiological condition of increased concentrations of reactive oxygen species that cause molecular damage to fundamental structures and functions[8] Several factors effect on oxidative stress divided exogenous (such as alcohol, food, cigarette smoke, environmental pollutants and radiation) and endogenous (such as psychological stress and exercise) origin[14]. The exposure microwave electromagnetic fields produced by mobile phones can influence NADH oxidase of HeLa cells and mediated rapidly production and raising the concentration of ROS (reactive oxygen species). These ROS then straightly stimulate MMPs (matrix metalloproteinases) and permit them to cleave and release Hb-EGF [heparin-binding EGF (epidermal growth factor)].

This secreted factor activates the EGF receptor, which in turn further activates the ERK (extracellular-signal regulated kinase) cascade (Figure 1)[15]. The ERK cascade is a central pathway that transmits signals from many extracellular agents to regulate cellular processes such as differentiation, proliferation and cell cycle progression [16].So, Radiofrequency fields canaffect biological systems by increasing free radicals.

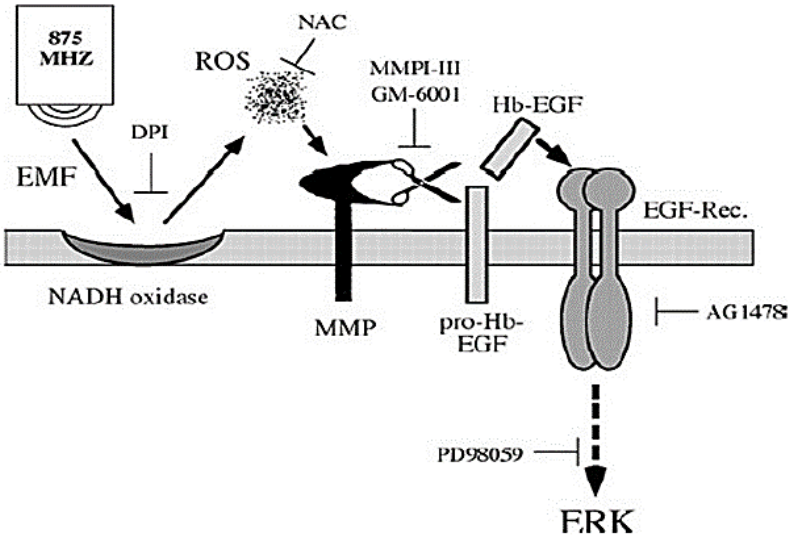

Figure 1. This pathway is mediated by irradiation-induced activation of NADH oxidase which produces ROS in the plasma membrane. ROS then straightly activate MMPs to cleave and release Hb-EGF, which binds to EGF receptor (EGFR) and activates the ERK cascade[15].

Microwave electromagnetic fields increase lipid peroxidation in the plasma membrane and decline activity of the glutathione peroxidase (GSH-Px) and superoxide dismutase (SOD) in human erythrocytes while the activity of catalase did not considerably decrease. As a result it can cause raising the free radicals [17][8]. Human skin fibroblast activity and morphological alteration have been reported after an hour exposure to mobile phone radiation[18]Another study also showed that exposure to mobile phone-induced radiation at 900 MHz lead to considerably higher exocytose in Merkel cells [19].Irradiation microwave electromagnetic increases the generation of reactive oxygen species in skin fibroblast. It can cause histopathologic alteration

in skin such as basal cell proliferation raising granular cell layer(Figure 2)[9].The Cells exposed to ELF-EMF revealed the modifications of NFnB-related proteins (p65-p50 and InBa) with raised formation of p65-p65 or p65- p50 active forms, a process generally attributed to redox reactions[6, 20]. These results suggest that ELF-EMF affect DNA damage and proliferation in cells through the action of free radical species [6]. The effects of ELF-EMF on cell DNA damage and proliferation were inhibited by pretreatment of cells with an antioxidant like α-tocopherol. The EMF can be a stimulus to induce an ‘‘activated state’’ of the cell such as phagocytosis and direct activation macrophages leads to free radical generation[21]. In addition cause raise in the lifetime of free radicals with inhibited pretreatment of cells antioxidant[9].Mobile phones microwave irradiation reason oxidative damage by raising the levels of NO, MDA as well as XO and ADA activities in brain tissue.It can cause histopathological alteration[9, 22]. The Effect of Ginkgo biloba (Gb) treatment inhibited EMR-induced histopathological alteration in the rat brain with protect oxidative stress[22].Melatonin has free-radical scavenging and antioxidant properties and protects DNA, cytosolic proteins and membrane lipids from oxidative damage induced by ROS [23, 24]. Melatonin at low doses (10 mg/kg) was even more efficient in reducing oxidative stress [8, 13,25]. The ELF-EMF decline melatonin stimulates in mammary cancer formation induced with Nitrosomethyl urea (NMU) [26].

ELF AND RF ELECTROMAGNETICFIELD ON GENE EXPRESSION AND CONFORMATION PROTEIN

Many study showed that RF Electromagnetic field can change geneexpression and alter conformation of proteins. Exposure of human HL-60 cells on 2.45 GHz RF electromagnetic field (generally used in telecommunication) can change in expression of 221 genes after 2h exposure.

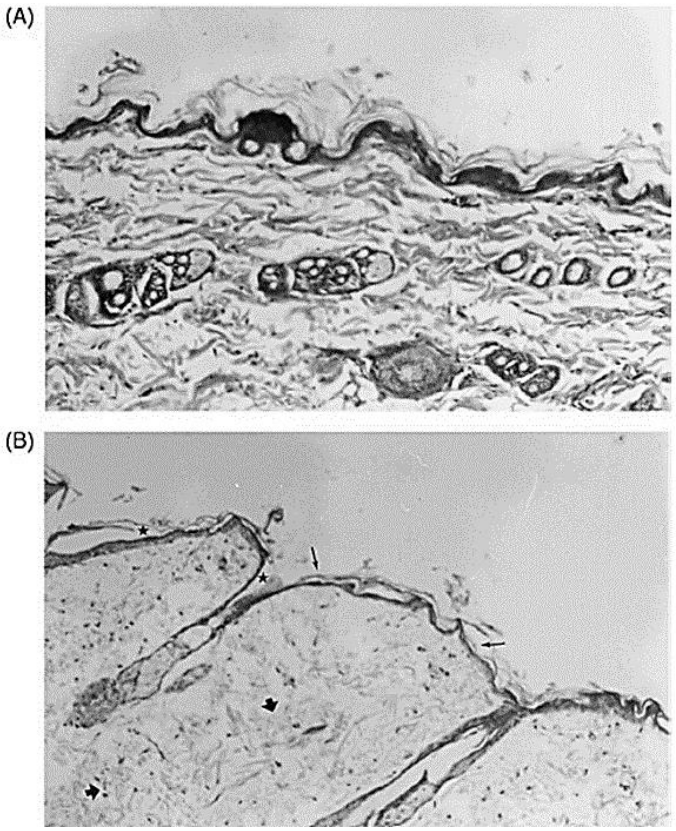

Figure 2. (A) Histological exhibition of rat epidermis and dermis from the control group. Normal structure is seen (hematoxylin-eosin). (B) Focal atrophy of epidermis (thick arrows), papillamatosis (stars) and orientation losses of dermal collagen (arrowheads) are seen in 900 MHz exposed rat (hematoxylin-eosin) [9].

The number of affected genes increased to 759 after 6h exposure. Functional classification of the affected genes reveals that apoptosis-related genes and cell cycle genes [12].The RF electromagnetic fields induce change in gene expression heat shock proteins, such as Hsp70 and Hsp27/p38MAPK [27-29].Heat shock proteins (Hsps) are highly conserved proteins working as molecular chaperones for some cellular proteins important in normal cell viability and growth. Cancer cells experience high levels of proteotoxic stress and rely upon stress-response pathways for survival and proliferation, so becoming related on proteins such as stress-inducible Hsps[30]. Microwave radiation limited denaturation of cellular proteins such as Hsps and may speed up rates of folding and unfolding for globular proteins leading to irreversible aggregation.

It can cause activationof Hsps and raising the expression of Hsps[10, 31-33].Also microwave radiation can influencesthe refolding kinetics of eukaryotic proteins[34].Studies evaluating the effects of RF radiation on proto-oncogenes showed that RF radiation may change expression of c-fos, c-myc and c-jun genes [31] and increase c-fos expression in tissue such as murine brains [35]. These genes are constitutively expressed at low levels but are quickly and transiently induced in response to stressful external stimulation. Each of these genes encodes for a transcription factor that regulates expression of genes through binding on enhancer box sequences (E-boxes) and recruiting histone acetyltransferases. Given their ability to regulate cellular growth, differentiation and proliferation [31]. Extremely Low Frequency (ELF)-Electromagnetic Fields (EMF) can change the cell morphology and protein expression in human SH-SY5Y cell line (Figure 3)[7].

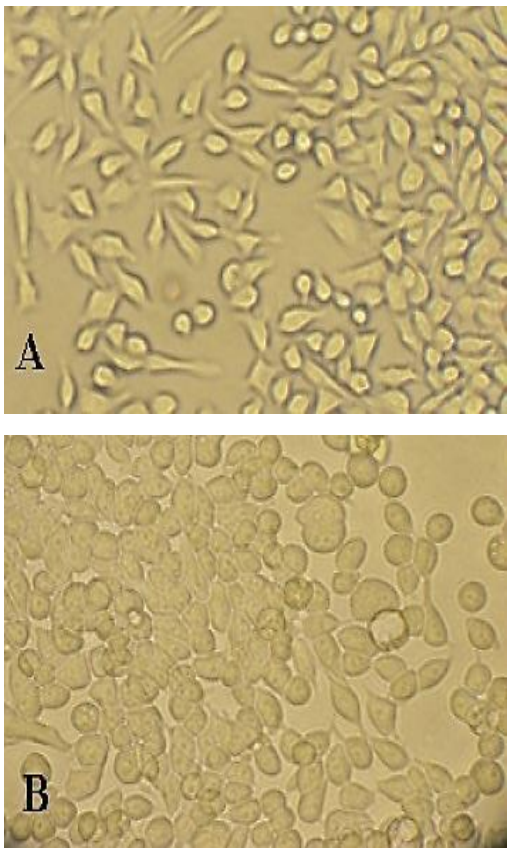

Figure 3. It has shown morphology of SH-SY5Y human neuroblastoma cell in the control (A) and exposed (B) condition[7].

The ELF-EMF excitation increase activity of the Protein Kinase C (PKC), which plays a key role in transferring external signals to the cells internal in order to regulation of differentiation and proliferation, as well as other processes[5]. Enhance in ornithine decarboxylase (ODC) activity in cultured mammalian cells after exposure to EMF were reported by some authors [36, 37]. This enzyme is the first and rate-limiting step in the synthesis of polyamines. The increase in cell cycle progression of human lymphocytes exposed to 50 Hz were determined [38] the EMF persuasible overexpression of Ets1 in Jurkat T-lymphoblastoid and Leydig TM3 cell lines [39]. Ets1 is a member of the Ets family of genes and is functionally involved in cell tumorigenesis, differentiation and apoptosis.

EFFECTS RF-EMF AND ELF-EMF ON DNA OR CHROMATIN

Many study exhibited considerably increase in genetic damage in human cells exposed to RF-EMF and ELF-EMF supplies a potential mechanism for its carcinogenic potential. The mechanism capacity ELF-EMF and RF-EMF in damage or change DNA can with raise in heterochromatin granule quantity (HGQ) leads to condensation of chromatin in cell such as buccal cell nuclei. The effect of chromatin condensation alter chromatin functional [40, 41]and formation of heterochromatin is related with a decrease of transcriptional activity of chromatin(Figure 4)[41].

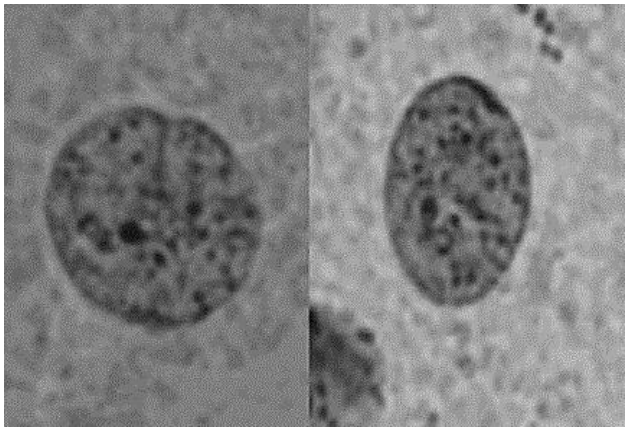

Figure 4. The nucleus human buccal epithelium cell before (left) and after (right) irradiation [41].

The ELF-EMF and RF-EMF raising level of free radicals including hydroxyl radicalsin cells, so it can interact with DNA and form mainly 8-hydroxy-2′ –deoxyguanosine(8-OHdG) adducts, may causing in single strand breaks [6, 42, 43]. The ELF-EMF have negative influenceson repair mechanisms innormal cells[4],so it is a cancer risk.

SATELLITE JAMMING AND CANCER

Satellite jamming is a tool used to censor and inhibit access to information. The term satellite jamming' refers to instances of deliberate interference for the express purpose of preventing access to specific content. Satellite jamming has two forms orbital and terrestrial. Orbital jamming involves the perpetrator beamingcontradictory signals directly towards a satellite via a rogue uplink station and terrestrial jamming involves transmitting rogue frequencies in the direction of local consumer-level satellite dishes.

Many reported say Iran use both of technique to prevent access to specific channels broadcast on satellite radio and television from abroad (A Small Media Report.,2012).Terrestrial jammers covered have a range of 3-5 kilometers in urban and in rural areas, their range can increase to up to 20 kilometers. Five specific variables factor related to RF–EMF exposure effect on cells: (1) frequency, (2) specific absorption rate, (3) exposure as continuing wave (4) duration of exposure, and (5) different cell types [13].

Table 1. Ten most common malignancies in Iran (2009-2010 data)

Males	Frequency	Females	Frequency
Skin (non-melanoma)	**14%**	Breast	**23%**
Stomach	**11.9%**	Skin (non-melanoma)	**10.1%**
Prostate	**9.4%**	Colorectal	**8.5%**
Bladder	**9.1%**	Stomach	**6.1%**
Colorectal	**8.3%**	Esophagus	**4.4%**
Leukemia	**5.2%**	Thyroid	**4.1%**
Lung, bronchus, trachea	**5.2%**	Leukemia	**4%**
Esophagus	**4.5%**	Ovary	**3.3%**
Non-Hodgkin lymphoma	**3.6%**	Brain, nervous system	**2.9%**
Brain, nervous system	**3%**	Corpus Uteri	**2.8%**
Other	**25.8%**	Other	**30.8%**

We have any data about what frequencies Iran use for satellite jamming but exposure as continuous RF-EMF and longtime duration it may can a risk factor for cancer. Iranian Society of Clinical Oncology (ISCO) (http://isco.ir) reported cancer is the third main cause of death in Iran and evaluated that more than 90 thousands of new cancer cases occur annually in Iran but it is postulated this figure will double by the year 2020. The occurrence of approximately all types of malignancies has alarmingly increased in the past two decades. Ten most common malignancies in Iran (2009-2010 data) is showed in Table 1.

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