

Extremely low frequency electromagnetic field (ELF-EMF) as a promising tool for treatment against multi-drug resistant bacteria

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ABSTRACT

Electromagnetic fields of extremely low frequencies are present in all aspects of everyday life which include (electrical transmission and power cables, common household appliances, and communication gadgets) influence various biological processes and their potential effects on bacteria have been a subject of debate. The effect of ELF-EMF on bacterial growth, cellular function, antibiotic susceptibility, and bacterial DNA in addition to the possible uses of ELF-EMF in improving the treatment of infectious diseases, sterilization, and other medical/industrial applications increased interest in studying ELF-EMF. Different studies showed that the effect of ELF-EMFs using short/long term exposure durations can reduce bacterial cell activity, and growth and even induce mutations in bacterial genome, therefore, extremely low-frequency electromagnetic field has attracted attention to be used as a promising alternative or adjuvant in combating multi-drug resistant pathogens. Accordingly, the present review will concentrate on the effects of the waves of electromagnetic field with extremely low frequency on different bacterial organisms to highlight the promising application of ELF-EMF as an alternative/adjuvant against pathogenic bacteria.

Keywords: Frequency; Hz; Genome; DNA; Cell; Growth.

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1. Introduction

Our modern world is filled with electromagnetic fields (EMFs) and they have become one of the most prevalent and quickly expanding environmental factors. Nearly all living interact with and are submerged in a wide range of electromagnetic fields (EMFs). Bacteria are among the many different living that exhibit varying degrees of responsiveness to electromagnetic fields (EMFs) [1]. The electromagnetic spectrum extends from

extremely low frequencies (ELF) to radio frequencies (RF), infrared radiation, visible light, ultraviolet (UV), X-rays, and gamma-ray frequencies [2].

The impact of electromagnetic fields (EMFs) on biological systems has been a topic of discussion for a long time. Some studies found no noticeable biological impact [1], while others found that electromagnetic field (EMF), has a substantial impact.

In previous publications on radiation and

field hazards, the extremely low-frequency electromagnetic field (ELF-EMF) was given a range of 3 Hz to 3,000 Hz [2]. Later on, entities such as World Health Organization (WHO), referred to the term extremely low frequency (ELF) as the frequency range of 0-300 Hz [4]. Nowadays, the ELF range is defined by the International Telecommunication Union (ITU) as the frequency range between 3 and 30 Hz only [5].

Despite the nonionizing character of extremely low-frequency electromagnetic field (Insufficient energy to break bonds on an exposed organism), The generated electromagnetic amount in the environment has increased significantly due to the rapid expansion of electrical applications, resulting in modifications in the biological systems of nearly all livings [6].

Recently, an extremely low electromagnetic field has been used clinically as an intervention to enhance the healing of chronic ulcers and the healing of chronic infected wounds [7]. Several

studies have also shown that ELF-EMF accelerated wound closure, bone healing, neurogenesis, reduced wound pain, and promoted circulation, especially in diabetic patients [8, 9]. These findings highlight the potential uses of ELF-EMF on biological systems, including the potential to control bacterial infections *in vivo*.

The effect of ELF-EMF exposure on bacterial growth, antibiotic susceptibility, and bacterial genome has been of considerable interest; in healthcare settings and in food sterilization techniques for maintaining the food's quality [10]. It was recently discovered that magnetic and electric fields of particular frequencies can have an influence on bacterial cells and this effect could be either stimulatory or inhibitory [11]. The impact of ELF-EMF on the behavior of biological systems especially pathogenic bacteria makes ELF-EMF a topic for academic research to examine that effect as a novel potential strategy in combating multiple drug-resistant bacterial infections.

2. Cellular response to ELF-EMF

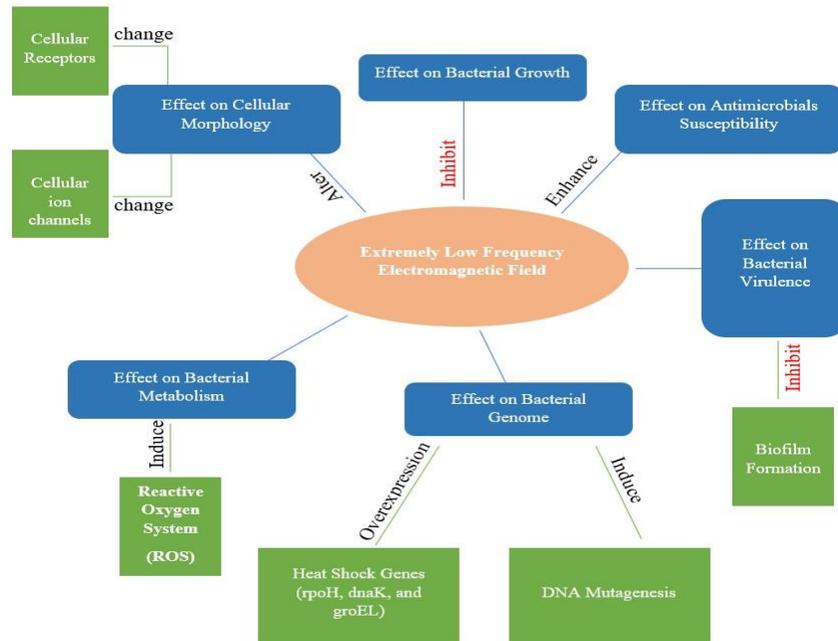


Fig. 1. Schematic representation of the possible mechanism of extremely low electromagnetic field (ELF-EMF) on bacteria.

Many studies have investigated whether there are effects of electromagnetic field (EMF) or not *in vitro*. The reasons for the various results might be attributed to the fact that there are many uncontrolled experimental variables along the mechanism of interaction between cells and the electromagnetic field is not fully understood. Although there are many hypotheses, it remains unclear how the effect of EMF on cells occurs; certain investigations indicate that the interaction occurs at the membrane of the cell or inside the cell. It has been acknowledged that ELF-EMF has insufficient energy for breaking molecules suggests that the interaction may occur at the gene level, where it either initiates gene or protein activation or repression, which then induces a series of processes leading to various biological processes (such as cell-cycle regulation, apoptosis, and immune cell reactions), or it may occur via developing heat caused by the provoked electromagnetic fields that alter the structure of particles like receptors and ion channels or stimulating the respiratory chain, which raises the level of ROS [12].

The schematic representation of the possible mechanism of extremely low electromagnetic field (ELF-EMF) on bacteria is shown in (Fig. 1).

3. Extremely low-frequency electromagnetic field affects bacterial growth

Sale and Hamilton 1967 conducted the initial research on the impact of electrical pulses on microorganisms [13], which examined the impact of electromagnetic pulse irradiation on the viability of the exposed bacterial cells as well as the fatal outcome and also found that different species had varying degrees of sensitivity to the field. In the last years, several studies have been done to investigate the effect of ELF-EMF on bacterial growth, and the implications of that effect in medical applications as an alternative to combat pathogenic infections or in industrial settings as a sterilization technique.

Electromagnetic field affects the growth pattern of bacteria in diverse ways; depending on the bacterial strain, frequency of field, and duration of exposure and could affect the growth rate irreversibly. According to *Inhan-Garip et al.*, [3] who used six bacterial strains, three Gram-negative (*Klebsiella pneumoniae*, *Escherichia coli*, and *Pseudomonas aeruginosa*) and three Gram-positive (*Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Enterococcus fecal*) and were subjected to 50 Hz extremely low-frequency electromagnetic field for six hours, it was noticed that (in comparison to control), all exposed strains to ELF-EMF had a significant decrease in growth rate and the decrease in growth-rate continued when exposed bacteria were cultured without field application suggesting that a mutation in a bacterial genome is induced and irreversible. Also following *Oncul et al.*, [8] observed a decrease in the growth of *S. aureus* & *E. coli* bacteria after exposure to 50 Hz ELF-EMF for 2 h when compared to the unexposed controls. Interestingly what was found by *Chen et al.*, [1] the growth rate was noticeably enhanced after *E. coli* exposure to 50 Hz ELF-EMF for 1 h, while a decrease in growth was observed for groups with an exposure time of more than 1 h (4 h, 8 h, and 16 h) relative to the untreated group, recommending (after examining different frequencies 40-60 Hz and 60-80) that the effect was frequency and time-dependent, and the ELF-EMF of 50 Hz was the most effective in inhibiting growth of the *E. coli* with exposure duration longer than 1 h time. Along with the findings by *Martirosyan*, 2012 [14] which showed after *E. coli* exposure for 30 min to ELF-EMF of frequencies (2, 4, 6, 8, 10 Hz), the effect on growth is the frequency-dependent effect, exposure to 2, 4, 6 Hz of ELF-EMF stimulated the growth while exposure to 8 and 10 Hz inhibited the growth in comparison with untreated bacterial cells. In 2013, *Aslanimehr et al.* [15] Concluded that exposure of *S. aureus*

and *E. coli* to ELF-EMF affects the growth rate and viability of bacteria in case of using different exposure times and it seems that the selection of proper exposure time would have a higher inhibition effect on growth. The investigations of Fojt *et al.*, Strasak *et al.*, El-Sayed *et al.*, and Segatore *et al.*, [16-19] showed that ELF-EMF exposure has an inhibitory effect on the growth of different bacterial species in a time-dependent manner and it is clear that proper selection of frequency and exposure duration plays a significant role in the effect of extremely low-frequency electromagnetic field on bacterial growth. The ideal circumstances for ELF-EMF to inhibit bacterial growth have been investigated and discussed in several studies; however, the literature has not yet resolved the mechanism of action regarding the interaction between ELF-EMF and the bacterial cell, which plays a significant role and might alter the application of EMF treatment as well as the selection of proper conditions.

4. Extremely low-frequency electromagnetic field affects cell morphology

Bacterial cell morphological alterations that are triggered by ELF-EMF have been investigated in many studies, suggesting ELF-EMF effect on bacterial morphology is induced through changes in metabolic activity or electrostatic properties of the cell surface and EMF controls cellular activities by using waves frequencies that resonate the bacterial bioelectric signals which generated during metabolic activity. According to Fang *et al.*, [10] who observed the difference between *Pseudomonas aeruginosa* bacteria before and after exposure to ELF-EMF by using the transmission electron microscopes (TEM), it was found that the cell walls of the treated bacteria were broken forming irreversible perforations on the cell membrane; the cell inclusions and cell components were leaked and the cytoplasm and nucleolus

substances flowed away leading to cell death. Based on several recent studies Garip *et al.*, Fadel *et al.*, Volpe *et al.*, Cellini *et al.*, [3, 20], [21, 22] documented that after exposure to ELF-EMF, bacterial membrane hyperpolarization was induced and electron transport system was impaired that lead to cell damage, stating that the utilization of extremely low-frequency electromagnetic waves (ELF-EMW) to treat infections *in vivo* could be a promising approach; as it can suppress pathogenic microorganisms. Furthermore, ELF-EMF may work with other disinfectant agents, making it a viable choice for use in industrial settings. Del Re *et al.* suggested that these fields induce changes in bacterial surface charge because bacteria interpret the fields as stressors [23]; charge alteration affects the membrane potential causing changes in ions conduction which affect directly bacterial viability [8]. The membrane potential has significance because it affects many other vital functions. Strahl and Hamoen [24], showed that the presence of membrane potential is necessary for the proliferation and survival of bacteria, as well as it was concluded that exposure to an electromagnetic field would alter the activity of bacteria since cell surface charge is crucial for bacterial adhesion and defense mechanisms in host settings, and also alter the physicochemical properties of bacteria and consequently will affect survival, virulence, viability and growth.

5. Effect of ELF-EMF on antibiotic sensitivity

The fact that bacteria have become more resistant to nearly all of the antimicrobials that are now on the market turns this matter into a major global issue. These factors reinforce studying the effects of extremely low-frequency electromagnetic fields on bacteria not only to study the effects of environmental stress on biological systems but also to discover novel methods to control the sensitivity of bacteria to antibiotics in clinical

settings as well as in the environment. Depending on the physical characteristics of the electromagnetic field (frequency, duration of exposure, as well as the type of bacteria employed), ELF-EMF could affect antimicrobial sensitivity and biological functions (cell growth and survival). The potential for a synergistic and/or additive impact induced by the combination of suitable ELF waves and particular antibiotics has warranted particular consideration concerning the threat that antimicrobial resistance represents to public health. According to Segatore *et al.*, [19] who used *Escherichia coli* and *Pseudomonas aeruginosa* to evaluate the effect of ELF-EMF on antibiotics susceptibility and concluded that by interfering with the surface charges on bacterial membrane, the rate at which antimicrobials penetrate is altered, in particular, at 4, 6, and 8 h, the number of bacterial cells was significantly decreased in bacteria exposed to electromagnetic field when compared with the control. The effect of ELF-EMF on antibiotic susceptibility is dependent on the drug's mode of action on bacterial cells and that was confirmed by Ibrahim and Darwish [24] who found that increasing in inhibition zone diameter of the *Bacillus Subtilis* towards amikacin, ceftriaxone, rifampicin while no increasing in the zone of norfloxacin and ciprofloxacin. Along with Kamel *et al.*, [25], increasing the zone of inhibition of gentamycin and tobramycin after exposure of *P. aeruginosa* to 6 h ELF-EMF was aligned with the results of Ahmed Hamdy *et al.*, [25] who found an increase in *P. aeruginosa* susceptibility to the meropenem and ciprofloxacin after short-term exposure of 3 h to ELF-EMF. Interestingly some studies [19, 26] showed that the long-term exposure of periods of (24 and 36 h) to ELF-EMF could induce a reversible defensive mechanism to repair the provoked damage, allowing an adaptive response with no remarkable change or even causing a

decrease in the susceptibility.

Overall, It is proven that electromagnetic fields affect the susceptibility of bacteria to antibiotics. However, it is crucial to determine the mechanism of action of ELF-EMF and physical parameters of the EMF (frequency applied, exposing duration, and antibiotics mode of action) to fulfill optimum results and to be considered as a new non-invasive technique that is promising to control resistant bacteria.

6. Effect of ELF-EMF on biofilm formation

Biofilm formation is considered as one of bacteria virulence that is used to adapt themselves in different environments [27] and to survive in stressed conditions. Bacteria form biofilm during infection, to withstand more effectively the host's immune responses and antimicrobial penetration. Additionally, biofilms in the natural environment can shield against harmful substances and aid in the spread and infection of pathogenic bacteria. [28].

Only a few investigations have examined how exposure to electromagnetic fields of extremely low frequency affects biofilms in bacteria. Many studies suggest that exposure to ELF results in stress responses that alter cell phenotype and transcription, as well as surface adherence in biofilm-forming cells [23]. Karaguler *et al.*, [29] examined the impact of EMF by exposing Gram -ve *P. aeruginosa* and Gram +ve *S. epidermidis* for 24 h to 50 Hz frequency of the field and were comparable with the corresponding controls who hadn't been exposed. As a result, it was observed that implementing EMF at 50 Hz resulted in a 50% reduction in biofilm formation, indicating that ELF-EMF has direct effects on biofilm formation. These effects may be caused by their impact on the electrical charges embedded in the cell membrane, which alters the behavior of the cells by affecting exopolymeric matrix structure

formation. Along with the findings by Haagenen *et al.*, [30] who found that (after exposure of *P. aeruginosa* to 3.9 Hz ELF-EMF) specific MFs can interfere with microbial biofilm formation, leading to a 27% reduction in biofilm formation compared to non-exposed. As a result, EMF presents a non-chemical approach for combating resistant bacteria. Although the literature has not yet answered the question regarding the mechanism behind the effect of ELF-EMF on biofilm, the hypothesis is, that the effect is due to the ability of ELF-EMF to reduce cell biomass, cell adhesion, and change morphology. This hypothesis was suggested by Di Campi *et al.*, who found [28] (after exposure of *H. pylori* to 50 Hz electromagnetic field) undetectable differences in DNA fingerprinting regarding biofilm in exposed samples, however, according to the results of the study, exposing bacteria to magnetic field changed the morphology and cell adhesion of *H. pylori*. The bacteria were also unable to progress in their viable, stable morphology, which also decreased their ability to protect themselves and their cell viability. The extremely low-frequency electromagnetic field is promising a novel approach against bacterial biofilm and consequently bacterial antimicrobial resistance.

7. Effect of ELF-EMF on reactive oxygen species

Reactive oxygen species (ROS) are molecules that contain free radicals, which makes them extremely chemically reactive. As part of normal cell metabolism, ROS formation occurs naturally, and the amount is often regulated by particular enzymes. In the natural cellular metabolism, there is an equilibrium between reactive radical production and the activity of the antioxidant system.

Bacteria may be protected by their antioxidant-mediated response from both the human immune system and antibiotic therapy.

This makes bacteria more feasible to cause chronic infections [31]. Excessive amounts of reactive oxygen species (ROS) can result in lethal modifications in bacteria through the formation of lipid peroxides, degrading cellular proteins, deactivation of enzymatic activity, DNA damage, and breakage. Since free Radicals destroy DNA directly they are unable to differentiate between bacterium and human cells. As a result, they can cause modifications in particular targets of antimicrobials, which lead to resistance to the antimicrobials and the development of unresolving bacterial infections [32, 33].

Researchers have studied the direct and indirect relation between magnetic field (MF) exposure and the generation of reactive oxygen species by assessing DNA injury after various exposure conditions. They observed that MF triggered the oxidative processes that contribute to magnetic field potency [34]. Recently the study by Mattsson and Simkó 2014, [35] analyzed 41 relevant scientific papers to investigate that the bacterial oxidative state alterations are the result of in vitro exposure to ELF-EMF. The authors suggested that ELF-EMF exposure can strongly influence the oxidative status at 50 Hz frequency and the effects are not dependent on exposure duration. In addition, several various studies have examined how exposure to magnetic fields can induce the formation of reactive oxygen species. Zeng *et al.*, [36] was repeatedly exposing bacteria to 50 Hz EMF to investigate oxidative stress induction after exposure to ELF-EMF and detected increased ROS levels. Although several studies have investigated the effect of ROS, the correlation between ROS (which is specifically induced by ELF-EMF exposure) and cellular viability has not yet been explored in the literature.

8. Effect on bacterial genome

Several researchers have examined the

hypothesis that ELF-EMFs have an impact on the gene expression of mRNA transcription and protein translation levels. These researches have primarily concentrated on the function of individual genes and their expressed proteins. Recent research used new analytical methods, where large segments of the mRNAs and proteins are examined. Those novel strategies, which are called "high inputs" or "high content screening," make use of cutting-edge molecular biology methods that can identify minimum quantities of biomolecules. Through the use of such techniques, researchers can concurrently study the expression levels of hundreds of genes, mRNAs, proteins, or metabolic byproducts. This is a remarkable method that, when paired with practical ELF-EMF research, can yield novel and insightful conclusions. While those techniques have significant usage in several fields of biological science, they have not been used to the full extent in examining the biochemical effects of electromagnetic fields.

It is still unclear how ELF-EMF affects the bacterial genome and how it affects expression. It is well-proven that stress conditions can affect gene expression, and several studies have considered magnetic waves as a stress factor. According to Ali *et al.*, [37] they noticed the appearance of new bands in the DNA pattern of exposed bacteria after exposure of *P. aeruginosa* to 0.7 Hz ELF-EMF indicating that genetic sequences of bacterial DNA were modified. This finding was also supported in another study by Fadel *et al.*, [21] which revealed genetic fingerprinting variation observed in the electrophoresis patterns between exposed and unexposed cells of *S. aureus* after exposure to 0.8 Hz EMF. In addition, other studies connected between ELF-EMF effect on bacterial genome and subsequently modification in protein and enzyme synthesis expression. Cairo *et al.*, and Del Re *et al.*, [23, 38], reported that following exposing *E. coli* to an extremely low-frequency

electromagnetic field, caused increased levels of mRNA and protein for the heat shock genes (rpoH, dnaK, and groEL), which had an impact on the survival of the bacterial cells. El May *et al.*, [39] have shown molecular changes in *Salmonella* after exposure to ELF-EMF and reported overexpression of the genes rpoA, katN, and dnaK and corresponding proteins which in correlation affected *Salmonella* growth and viability. Ahmed Hamdy Badr *et al.*, [25] stated that due to ELF-EMF's inactivating impact on *Pseudomonas aeruginosa*'s antibiotic-resistance genes, it may be possible to apply this approach to combat bacterial resistance in future applications. Selecting the appropriate frequency and exposure duration are significant in determining the extremely low-frequency electromagnetic field effect on bacteria. To reduce the damaging effects of magnetic waves, several bacterial species have shown adaptation to the field and altered expression after long-term exposure to ELF-EMFs. That was supported by Baraúna *et al.*, Huwiler *et al.*, and Cellini *et al.*, [20, 40, 41] who observed minor damage in DNA after exposure of different bacterial species to 50 Hz ELF-EMF, suggesting that bacteria enhanced expression of some genes to prevent or repair physical damage to DNA. Moreover, this helped the bacteria to adapt to the stress generated by the electromagnetic field.

Magnetic fields induce a variety of effects in cells and tissues. The literature frequently presents contradicting results, and our understanding of the mechanisms by which magnetic fields affect biological material is still limited. Research has indicated that exposure to a magnetic field can result in DNA mutagenesis, degradation, or instability of the genome, which alters DNA replication, transcription, and translation Potenza *et al.*, [42]. Electromagnetic field has a genotoxic effect on bacteria, therefore,

investigations are required to confirm the safety when applying the magnetic field *in vivo* and to protect humans from its genotoxic effect.

Different mutagenic effect on the bacterial and resistance genes after exposure to the ELF-EMF is shown in (Fig. 2).

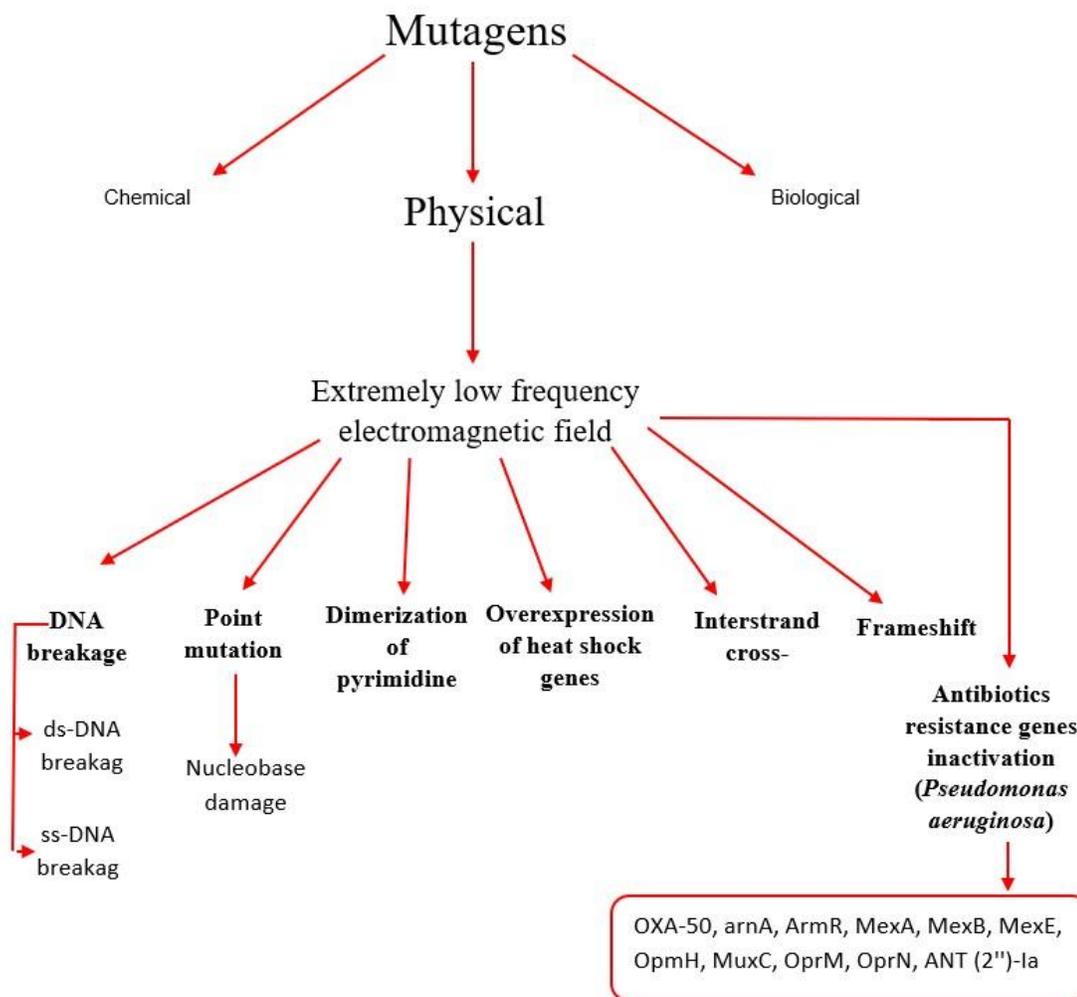


Fig. 2. Different mutagenic effects on the bacterial and resistance genes after exposure to the ELF-EMF.

9. Safety of ELF-EMF

9.1. Possible effect of ELF-EMF on human genes

Kuzniar *et al.*, [43] (using three different cell lines), investigated the effects of exposure to a 50 Hz magnetic field using proteome analysis. It involved 15 h of alternating exposure, with 5-minute on and 15 min off intervals. The findings from all three cell lines suggested that the DNA

mismatch protein MLH1 was increased, and the results showed that less than 1% of the proteome in the cell lines responded to exposure and had moderate alterations in expression (typically <1.5 fold). In two studies, the human neuroblastoma SH-SY5Y cell line was exposed to ELF-EMF for three hours, and the results showed that exposure to ELF-EMF has significant impacts on the cells. Hasanzadeh *et al.*, Rezaie-Tavirani *et al.*, [44,

[45], 189 proteins were identified to have modifications in comparison to the control cells using 2D gel electrophoresis to detect changes in protein expression.

Frahm *et al.* [46] utilized gene expression profiling (whole-genome cDNA array) after exposing human monocytes to the magnetic field for 45 minutes. It was found that 986 genes related to metabolism, intracellular physiological processes, signal transduction, and immunological activity were modified.

Reale *et al.* [47] reviewed a reanalysis of transcriptomics data from multiple investigations on human cell lines. The analysis evaluated results from 5 researches with complete microarray data and 3 researches with a list of substantially altered mRNAs from the perspectives of signal transduction and metabolic pathways. The analysis additionally examined whether the data could suggest that electromagnetic field has an impact on the development of any particular diseases, but the data did not demonstrate that magnetic fields can result in any particular disease.

Being exposed to EMF in the environment has lately been directly linked to the epigenetic regulation of gene expression; with suggestions reason for EMF causes genomic instability resulting from alterations in DNA methylation patterns Miousse *et al.*, [48]. Research revealed that exposure to EMF radiation from the environment resulted in both general hypomethylation and particular hypermethylation of different tumor suppressor genes. This makes it harder for the tumor suppressor genes to be transcribed, which allows tumor development [48]. It's interesting to note that regular cellular metabolism can directly affect epigenetic signaling when it produces redox intermediates as a result of exposure to direct or indirect magnetic fields. [49]. The pathophysiology of

cardiovascular, Alzheimer's diseases, and several types of cancer have been significantly linked to the correlation between metabolism and epigenetics. The transposable portions that are found in the genome should also be taken into account. These portions are DNA sequences that repeat frequently and are thought to be important regulators of gene expression Miousse *et al.*, [50]. They are regulated by epigenetic mechanisms, such as DNA methylation and histone modifications, stress factors from the environment, for instance, may reduce the inhibitory effects of these modifications, which will allow the transposable elements to be activated, potentially be transcribed, and produce a variety of defective proteins. Cancer is one of the many disease conditions that might result from this [50].

Several researches have been conducted to investigate the impact of ELF-EMF on markers for epigenetic processes of gene expression in recent years. In two researches, [51, 52], Liu *et al.* used the mouse spermatocyte-derived GC-2 cell line to conduct trials with 50 Hz of electromagnetic field (for 72 h of exposing duration). The first research has discovered that exposure affected the expression of the DNA methyltransferases DNMT1 and DNMT3b, which catalyze the methylation of the CpG dinucleotides in the genome, as well as DNA methylation in a flux density-dependent manner. The second research concentrated on microRNAs (miRNAs), which are noncoding RNAs that bind to the 3' untranslated regions of mRNAs to control gene expression at the post-transcriptional stage. This binding is thought to be a significant part of the epigenetic regulation of gene expression, leading to enhanced mRNA degradation and/or suppression of translation. Aberrant mRNA expression has been linked to some disease conditions, including cancer. The findings indicated that several mRNAs expressed differently following exposure.

Exposure changed a greater number of mRNAs, but no changes in growth, apoptosis, or cell cycle divisions were observed.

Nevertheless, still limited data are known about how cells respond to extremely low-frequency electromagnetic fields. Other studies have examined the utilization of ELF-EMF as a possible method for inhibition of tumor cells. In Sun *et al.*, 2023 study [53], they assessed the direct effects of magnetic fields as well as the indirect effects on cultivated cells. An extremely low-frequency magnetic field of 20 Hz has been applied to Hepg2 cells and A549 cells. The tumor cells were susceptible to the magnetic field with an estimated 18% and 30% inhibition rate for Hepg2 and A549, respectively. According to the study's findings, exposure to magnetic fields may be used as a cutting-edge cancer management technique, and tumor growth is significantly inhibited by ELF-EMF. The cells were hyperpolarized, as evidenced by the intracellular ion fluorescence (IIF), which revealed that the magnetic field dramatically changed the membrane potential and the ROS that these cells

release seems to be responsible for inhibiting the growth of tumors. Koh *et al.*, [54], (after studying the effect of an extremely low-frequency magnetic field on prostate cancer cells) have found that prostate cancer cell growth was suppressed by using a 60-Hz magnetic field. The suppression of cell growth induced by MF was primarily caused by apoptosis and cell cycle arrest, which were mediated by ROS generated by MF, and concluded that a magnetic field would be employed in the treatment of prostate cancer. Furthermore, research that was conducted by El-Bialy and Rageh [55], showed that ELF-EMF increased the cytotoxic activity of cisplatin in the therapeutic management of Ehrlich carcinoma and demonstrated that ELF-EMF had a strong anticancer effect and also found that exposure to the normal cells to MF, displayed no abnormal structural aberrations, suggesting that ELF-EMF is not harmful.

The potential effect of extremely low-frequency electromagnetic fields on human DNA is shown in (Fig. 3).

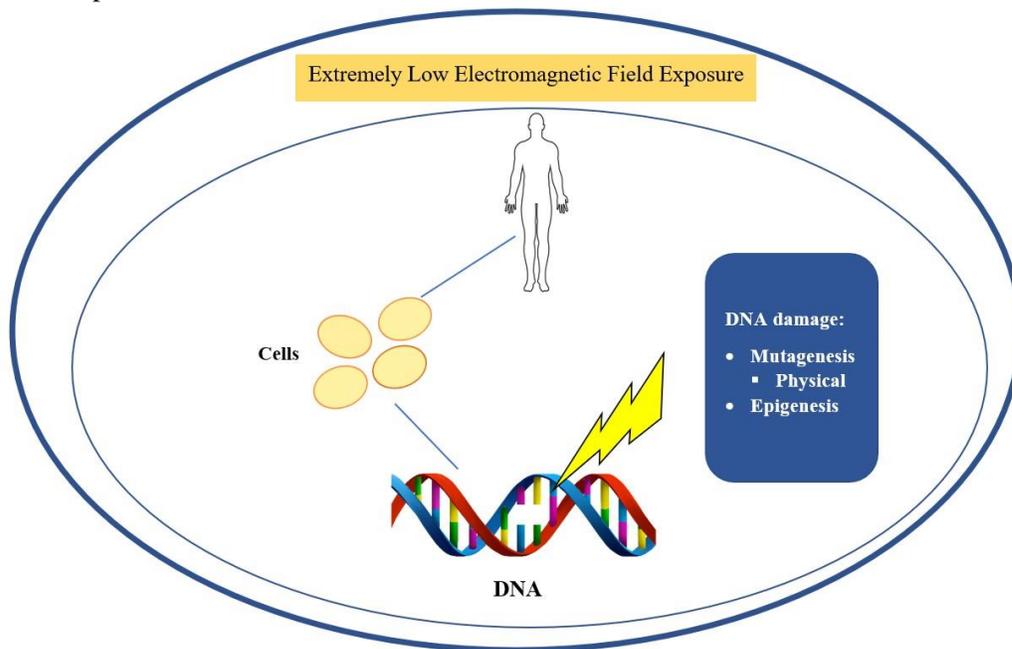


Fig. 3. Potential effect of extremely low-frequency electromagnetic field on human DNA.

9.2. The genetic toxicity

Nowadays, it has been proven that DNA injury during cell division plays a role in the development of cancer. That damage can occur naturally, but also exposure to environmental stressful factors can lead this to occur. Such environmental stressful factors can either directly or indirectly cause genotoxicity; they can also function as co-factors with another directly gene-toxic factor or cause conditions (radicals production) that compromise DNA integrity.

Although it is unlikely that ELF-EMF will have a direct genotoxicity impact, exposure to ELF-EMF may have an impact indirectly. This hypothesis has been studied in various researches. DNA from different organisms, such as humans (mainly occupational exposure), animals (*in vivo* exposure), and cell culture (primary cells and cell lines) have all been the subject of several investigations; examining DNA strand breaks, micronucleus formation, DNA repair, and gene mutations.

Vijayalaxmi and Obe [56], conducted a review of the effects of extremely low-frequency electromagnetic fields on mammalian cells. They studied related research from 1990 to 2003 and classified the results based on whether exposure induces DNA injury or has no impact at all. In conclusion, the research stated that 14 of the 63 examined studies discovered greater injuries in exposed cells when compared to controls whereas, 49 studies revealed no impacts. According to the investigations, they concluded that there was limited evidence of indirect effects and no direct gene-toxic consequences from ELF-EMF exposure.

10. Applications of ELF-EMF

Applications of electromagnetic fields in clinical, environmental, or industrial settings are expanding vastly. The electromagnetic field

(EMF) could represent an alternative/additive to conventional treatment for chronic non-healing wounds or as an intervention to enhance the healing of chronically infected wounds, bone healing, neurodegeneration, reduced wound pain, and promote circulation, especially in diabetic patients. Mostafa Elnakib, 2023 [7] utilized EMF therapy to assess treatment and closure of the wounds associated with infection. The study achieved interesting and innovative results which showed that the EFM had achieved a high success rate in the treatment of patients with chronic, resistant, wounds with complete symptomatic relief.

Piyadasa *et al.* [57] reviewed several studies conducted and summarized the experiences while managing precipitation and fouling in inverse-osmosis membrane systems, specifically for desalination. Under regulated conditions, exposure to electromagnetic fields produced a reduction in cellular viability and cultivability, and the application of EMFs aided in accelerating the accumulation of suspended particulates and their precipitation. Yavuz and Çelebi [58] describe the impacts of an electromagnetic field in the field of wastewater treatment. They show that the microorganisms' growth in free condition, (acquired from samples of activated sludge), is reduced and that their substrate removal efficiency is increased.

Zhou *et al.* [59], administrated EMF to a bioelectrochemical system which resulted in alterations in the microbial community at the anode: comparatively more *Geobacter* spp. (4-8%) were discovered than in the control. By altering species evenness rather than species richness, the EMF considerably reduced the bacterial and archaeal diversities of the anode biofilms. Additionally, it enabled the selective enrichment of exoelectrogenic bacteria (*Geobacter*) on the anode surface, which promoted microbial electrochemical activities.

According to Sudarti *et al.*, [60] Utilizing extremely low frequency (ELF) was successful in preventing the growth of pathogenic bacteria, increasing the physical resilience of Vannamei shrimp (a type of fish that rots easily, only able to survive for 6 h at room temperature).

In terms of sterilization, a study by Liu *et al.*, [61] was conducted to examine the sterilizing treatment with ELF-EMF on heterotrophic bacteria in manufacturing cooling water circulation. The findings indicated that the inhibition effect of the EMF on bacteria was 7.22%~to 20.35% greater than that of the chemical treatment. The study conducted by Zhaowen Zhang [62], showed interesting outcomes regarding sterilization in an industrial setting and verified that in contrast to high-temperature sterilization, MF has a bactericidal effect on fruit juice and should be utilized as a new, non-thermal technique for food manufacturers to handle the sterilization of fruit juice products. This technique is effective in sterilizing the fruit juice from bacteria and fungi while preserving its nutritional value.

In the livestock industry, antibiotic-resistance genes are retained in poultry manure. This study showed that an external magnetic field reduced antibiotic resistance genes during the composting of swine manure. A total of 12 antibiotic-resistance genes were found, according to the results. Antibiotic resistance gene quantity was more effectively reduced by a magnetic field, with a clearance rate of 20.66–100%. These results show that applying an external static magnetic field can significantly increase the reduction in antibiotic resistance genes and they offer a useful strategy for managing the possible antibiotic resistance genes danger associated with composting organic waste. Ma *et al.*, 2023 [63]. In terms of antiseptic use which has been increased recently in the treatment and prevention of topical, biofilm-related infections,

particularly those affecting the skin and wounds. Ciecholewska-Juško *et al.*, 2022 [64], have used a magnetic field of two frequencies, 5 and 50 Hz. in potentiating the effect of octenidine dihydrochloride-based antiseptic (OCT) against *Staphylococcus aureus* biofilms in skin wounds, and the results showed that combination of MF and OCT has increased the eradication of biofilms by more than 40%.

Declarations

Consent to publish

All authors have read and agreed to the published version of the manuscript

Ethics approval and consent to participate

Not applicable.

Availability of data and material

All data generated or analyzed during this study are included in this published article in the main manuscript.

Conflict of Interest

The authors assert that there are no conflicts of interest.

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Authors Contribution

Mostafa Elnakib, Mohammad M Aboulwafa, Sarra E Saleh: conceptualization, supervision, manuscript writing and revision. M. Hosny: data collection, writing the original draft of the manuscript. All authors have read and approved the final manuscript.

11. References

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