Silver NanoParticles and Magnetic Fields

Summary:

1. “exposure to PMF increased the ability of AgNPs uptake”

https://pubmed.ncbi.nlm.nih.gov/39282575/

Polyvinyl Alcohol Capped Silver Nanostructures for Fortified Apoptotic Potential Against Human Laryngeal Carcinoma Cells Hep-2 Using Extremely-Low Frequency Electromagnetic Field 2024

Purpose: : Polyvinyl alcohol-capped silver nanostructures (cAgNSs) were investigated in order to enhance the cytotoxicity, pro-apoptotic, and oxidant patterns of in human laryngeal carcinoma Hep-2 cells by **employing a 50 mT electromagnetic field (LEMF) for 30 min**.

Methods: Wet chemical reduction was used to synthesize the cAgNSs, and after they had been capped with polyvinyl alcohol, they were specifically examined for particle size analysis and structural morphology. To visualize how the silver may attach to the protein targets, a molecular docking study was conducted. Estimation of cytotoxicity, cell cycle progression supported by mRNA expression of three apoptotic-promoting genes and one apoptotic-resisting.

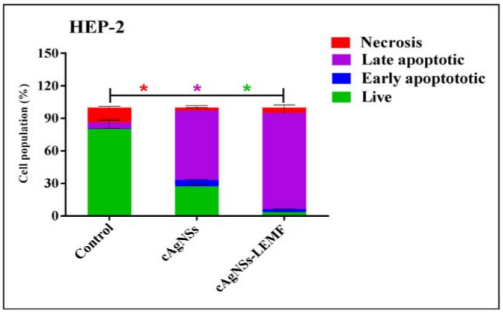
Results: Particle size analysis results were a mean particle size of 157.3±0.5 nm, zeta potential value of -29.6 mV±1.5 mV, and polydispersity index of 0.31±0.05. Significantly reduction of IC50 against Hep-2 cells by around 6-fold was concluded. Also, we obtained suppression of the proliferation of Hep-2 cells, especially in the G0/G1 and S phases. Significant enhanced mRNA expression revealed enhanced induced CASP3, p53, and Beclin-1 mediated pro-apoptosis and induced NF-κB mediated autophagy in Hep-2 cells. Augmented levels of GR, ROS and MDA as oxidative stress biomarkers were also obtained. HE staining of Hep-2 cells exposed to cAgNSs and LEMF confirmed the enhanced apoptotic potential comparatively.

Conclusion: By conclusion, the developed nano-sized structures with the aid of extremely-low frequency electromagnetic field were successful to fortify the anti-cancer profile of cAgNSs in Hep-2 cells.

It has been revealed that the cytotoxicity of metallic nanoparticles is 9 times higher in cancer cells than in normal cells, which is sufficient evidence of the particles’ ability to poison and kill cancer cells in the context of cancer treatment.

Of all the nanostructures developed utilizing nanotechnology, silver nanostructures (AgNSs) have received the greatest research and exploration.9 AgNSs have high promise as an anticancer drug, according to recent investigations.10 According to several studies, AgNSs can kill cancer cells by a number of different mechanisms, such as oxidative stress, DNA damage, cell cycle arrest, apoptosis, and necrosis.11–14

The use of therapeutic electromagnetic fields, in particular the extremely-low frequency electromagnetic field (LEMF), has been proposed for the treatment of cancer since it was found that magnetic waves interfere with many biological processes.



https://pubmed.ncbi.nlm.nih.gov/31746453/

In vitro evaluation of electroporated gold nanoparticles and extremely-low frequency electromagnetic field anticancer activity against Hep-2 laryngeal cancer cells 2019

The highest content of cells arrested in G2/M phase was observed in ELFEMF-treated cells for 30 min both at 25 or 50 mT, while the cells treated with EP AuNPs or ELFEMF 50 mT/15 min showed highest ratios of apoptotic cells. HE staining of electroporated cells and cells exposed to ELFEMF's low and higher frequencies for different times showed nuclear pleomorphic cells. Numerous apoptotic bodies were observed in the irregular cell membrane of neoplastic and necrotic cells with mixed euchromatin and heterochromatin.

Conclusions: Our observations indicate that treatment of Hep-2 laryngeal cancer cells with ELFEMF for 30 min at 25-50 mT and EP Au-NPs can cause cell damage inducing apoptosis and cell cycle arrest.

https://pubmed.ncbi.nlm.nih.gov/35120563/

Anticancer and antibacterial potentials induced post short-term exposure to electromagnetic field and silver nanoparticles and related pathological and genetic alterations: in vitro study 2022

Background: Resistance to antibiotics and anticancer therapy is a serious global health threat particularly in immunosuppressed cancer patients. Current study aimed to estimate the antibacterial and anticancer potentials of short-term exposure to extremely low frequency electromagnetic field (ELF-EMF) and silver nanoparticles (AgNPs) either in sole or combined form.

Methods: Antibacterial activity was evaluated via determination of the bacterial viable count reduction percentage following exposure, whereas their ability to induce apoptosis in breast cancer (MCF-7) cell line was detected using annexin V-fluorescein isothiocyanate and cell cycle analysis. Also, oxidative stress potential and molecular profile were investigated.

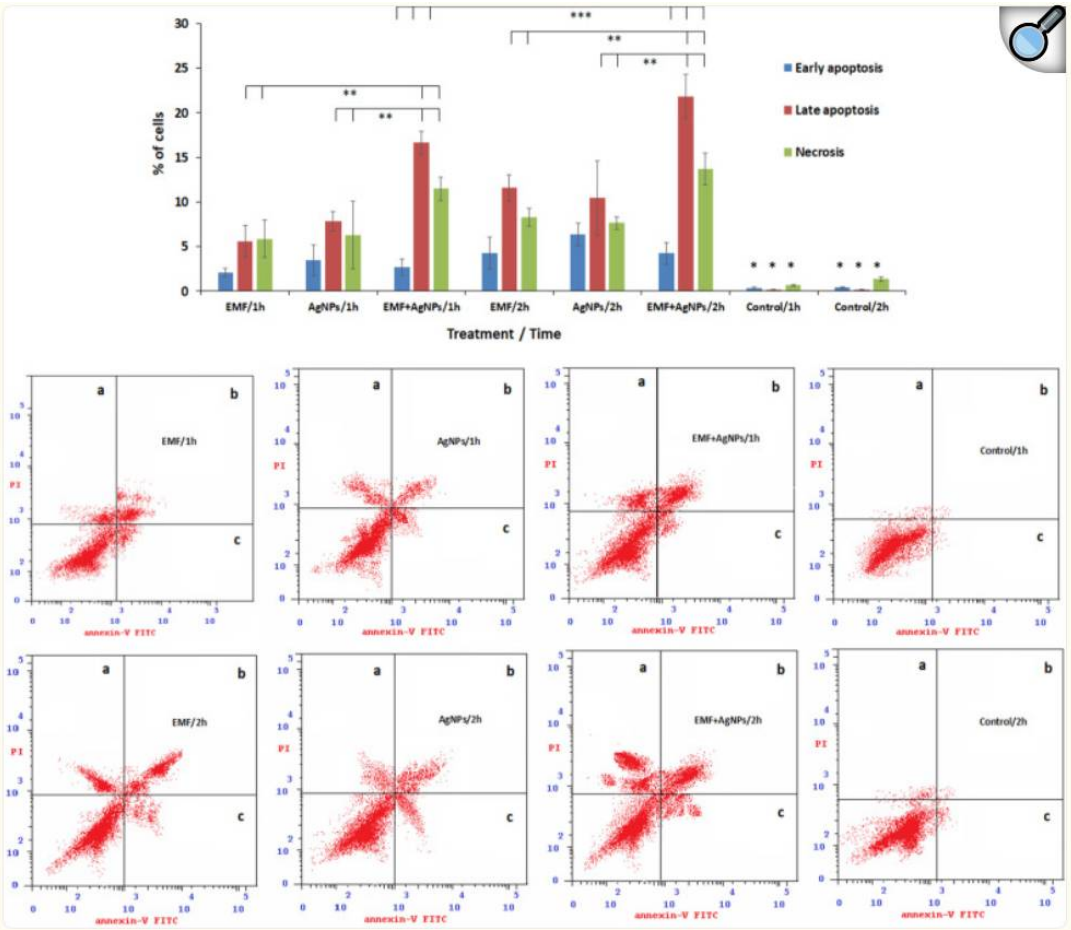
Results: ELF-EMF and AgNPs significantly ($p < 0.01$) reduced K. pneumonia viable count of compared to that of S. aureus in a time dependent manner till reaching 100% inhibition when ELF-EMF was applied in combination to 10 µM/ml AgNPs for 2 h. Apoptosis induction was obvious following exposure to either ELF-EMF or AgNPs, however their apoptotic potential was intensified when applied in combination recording significantly ($p < 0.001$) induced apoptosis as indicated by elevated level of MCF-7 cells in the Pre G1 phase compared to control. S phase arrest and accumulation of cells in G2/M phase was observed following exposure to AgNPs and EMF, respectively. Up-regulation in the expression level of p53, iNOS and NF-kB genes as well as down-regulation of Bcl-2 and miRNA-125b genes were detected post treatment.

Conclusions: The antibacterial and anticancer potentials of these agents might be related to their ability to induce oxidative stress, suggesting their potentials as novel candidates for controlling infections and triggering cancer cells towards self-destruction.

ELF-EMF generating medical devices were also applied for treatment of cancer patients in intensive care units. Consequently, during the outgoing 25 years researchers tried to investigate the impact of exposure to ELF-EMF on cellular and molecular behavior in addition to its effect on cancer cell metabolism. It was found that exposure to 50/60 Hz magnetic field promoted changes in signal transduction pathways that were directly associated to proliferative processes [8]. A study reported that electromagnetic field **(EMF) could selectively hinder the oxidation–reduction signaling in cancer cells** relying on the differential electrical

behavior between the cancer and the normal cells. This signaling plays a key role in blocking cellular functions leading to induction of programmed cell death [9]. Recently, a study reported that the tumor suppressive effects of the ELF-EMF could present a new approach for the treatment of breast cancer if this technology is clinically applied [10]. It was demonstrated that the ability of pulsed low-frequency EMF to modify the membrane integrity of cancer cells presents a new strategy in anticancer therapy. These pulsed magnetic fields (PMF) could selectively destruct the cancer cell membranes without the use of ionizing radiation or cytotoxic agents. Thus, these fields could be applied as adjuvants in cancer therapy to facilitate the delivery of anticancer agents to tumor cells [11].
The antimicrobial activities of AgNPs either alone [15] or in composites with polymer [16] have been demonstrated in addition to their anticancer [17] as well as their antiangiogenic potentials [18]. AgNPs are now considered a valuable and non-traditional alternative to antibiotics with high antimicrobial potential against multidrug-resistant (MDR) Gram-positive and Gram-negative bacterial pathogens [19]. It was also reported that AgNPs inhibited the proliferation of human glioblastoma cells [20] as well as human breast cancer (MCF-7) cells [21]. It was also found that AgNPs stimulated pro-apoptotic genes leading to interference with normal cellular functions and induction of programmed cell death. A study reported that AgNPs induced apoptosis in NIH3T3 fibroblast cells is mediated via generation of reactive oxygen species (ROS) and activation of Jun N-terminal kinases (JNK) pathway leading to mitochondrial dependent apoptosis [22].

Consequently, the present study aimed to evaluate the antibacterial and the anticancer potentials of short-term exposure to ELF-EMF and AgNPs either in sole or combined form at different time intervals.
Cells were equally aliquoted in sterile polystyrene tubes, treated with AgNPs IC_{50} value and exposed to ELF-EMF of 1 m Tesla for 1 and 2 h interval. Similar concentrations of MCF-7 cells were treated with ELF-EMF at the same conditions but in absence of AgNPs. Untreated control cells were also considered. ELF-EMF treated cells either in presence or absence of AgNPs were examined for pathological changes in addition to cell cycle and molecular analysis as well as biochemical tests.



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Evaluation of early and late apoptosis as well as necrosis post MCF-7 cells post exposure to ELF-EMF, AgNPs and ELF-EMF/AgNPs for 1 and 2 h interval using annexin V-FITC apoptosis detection kit. *$P < 0.001$, **$P < 0.01$, ***$P < 0.05$. **a** necrotic cells, **b** late apoptosis, **c** early apoptosis

Regarding the anticancer potential of AgNPs and in agreement with the present findings, it was reported that AgNPs reduced MCF-7 cellular viability in a dose dependent manner recording an IC_{50} value of 6.28 µM [45]. It was reported that excessive production of ROS in cells by direct interaction with AgNPs and/or dissolved silver ions is currently accepted as one of the main mechanisms of cellular toxicity of engineered nanoparticles in living organisms. Although ROS have many signaling and information functions, but it could also diminish the antioxidant defense system leading to damage of DNA, lipids and proteins [44]. That

was obvious in the current study, where the recorded results revealed a time dependent reduction in CAT enzyme activity, which is considered an antioxidant enzyme, post treatment with AgNPs either alone or in combination to EMF. The observed CAT enzymatic activity reduction was also in parallel to apoptosis induction following treatment with AgNPs as well as production of ROS. This might be attributed to AgNPs induced generation of oxidative stress which was intensified by reduction of CAT enzymatic activity resulting in H_2O_2 accumulation as previously explained.
Regarding investigating the mechanism of action of the EMF and AgNPs on apoptosis at the molecular level. The expression levels of two pro-apoptotic genes (p53 and iNOS) as well as two anti-apoptotic genes (Bcl-2 and miRNA-125b) in addition to the impact on the expression level of NF-kB were evaluated following exposure to different treatments. In agreement with the current findings, a recent study reported that the expression levels of pro-apoptotic genes (p53, Bax and caspase-3) were significantly up-regulated, whereas the expression of the anti-apoptotic gene Bcl-2 was significantly down-regulated in AgNPs treated MCF-7 and colon cancer (HCT-116) cells [50].
To the best of our knowledge, this is the first study that tried to explore the apoptosis induction potentials of the combination between ELF-EMF and AgNPs. Also, the mechanisms that may be involved in the antibacterial and anticancer potentials of the short-term exposure to ELF-EMF in combination to AgNPs have not been previously investigated. Current findings strongly suggest that the ability of ELF-EMF in combination to AgNPs to induce oxidative stress in bacterial and cancer cells via generation of ROS, SOD induction and catalase reduction could be responsible for their antibacterial and anticancer potentials. The significance of this study isn't only related to exploring the antibacterial and the anticancer potentials of AgNPs and ELF-EMF either alone or in combination as new therapeutic approaches, but it spotlight on the effectiveness of the combination between these agents as an essential life-saving approach if this type of treatments could be applied clinically. That might offer greater health improvement especially in the immunocompromised cancer patients who are more vulnerable to develop infections with antibiotic resistant pathogens.

Conclusions

AgNPs and ELF-EMF could be considered as potential antibacterial and anticancer agents. The activities of these agents were enhanced upon their combinations in a time dependent manner even though at short exposure time. The recorded reduction in the bacterial viable count following exposure to these agents was higher against Gram-negative bacteria as compared to Gram-positive bacterial model. These antibacterial potentials were suggested to be related to the capability of these agents to induce oxidative stress by the generation of ROS. However, their effect was magnified via enhancing the antioxidant activity of SOD and on the other side reducing the activity of catalase enzyme resulting in elevated toxicity that might be attributed to H2O2 accumulation. Consequently, the combination between the tested agents could present a novel strategy for infection control and to overcome bacterial resistance. In the meantime, a time dependent induction of apoptosis was observed following treatment of MCF-7 cells with AgNPs, ELF-EMF as well as in combination. That was proposed to the ability of the tested treatments to significantly elevated the Pre G1 apoptotic phase of MCF-7 cells. Moreover, the exposure to AgNPs induced S phase arrest, whereas the EMF treatment was accompanied by accumulation of cells in the G2/M phase. Additionally, up-regulation in the expression level of p53, iNOS and NF-kB genes was observed, however down-regulation of the anti-apoptotic genes, namely Bcl-2 and miRNA-125b was detected post treatment. Biochemical analysis also shed light on the ability of both EMF and AgNPs to induce apoptosis via generation of oxidative stress. Finally, it could be concluded that AgNPs and ELF-EMF either in sole application or in combination could be considered as potential oxidative stress generating agents that might pave the way to solve the problem of antibiotic resistance especially in immunocompromised cancer patients and could successfully direct cancer cells to death.

https://pmc.ncbi.nlm.nih.gov/articles/PMC5204255/

Synergetic effects of silver and gold nanoparticles in the presence of radiofrequency radiation on human kidney cells 2016

The aim of this study was to compare the effects of radiofrequency radiation (RF) in synergism with gold (Au) and silver (Ag) nanoparticles (NPs) on the survival fraction of human normal kidney (HNK) and human embryonic kidney (HEK) cells.
RF radiation can affect both HNK and HEK cells when irradiated for 2 h/day for 8 days. The results showed that the Ag-NPs do not increase the synergistic effects of RF compared to the Au-NPs. RF radiation at the presence of Au-NPs can be used as an efficient treatment for melanoma.
The average size of Au-NPs was 20–30 nm.
The simulator was adjusted on 1.0 W and 900 MHz frequency for the exposure. The distance between the simulator antenna and the wells was kept at 2.5 cm.

https://pubmed.ncbi.nlm.nih.gov/18334449/

In vitro analysis of cisplatin functionalized magnetic nanoparticles in combined cancer chemotherapy and electromagnetic hyperthermia 2008

A novel platform has been developed for combined cancer chemotherapy and hyperthermia based on iron oxide magnetic nanoparticles functionalized with cis-diamminedichloroplatinum(II) (cisplatin). The capabilities of this system for heating and controlled drug release were investigated, and the system was tested in vitro by the treatment of BP6 rat sarcoma cells, where we demonstrated a synergism between the effects of cisplatin-targetMAG nanoparticles and the application of electromagnetic field.

https://www.researchgate.net/publication/332321715_Therapeutic_effectiveness_of_Hydroxyapatite_Nanoparticles_and_Pulsed_Electromagnetic_Field_in_Osteoporosis_and_Cancer

Therapeutic effectiveness of Hydroxyapatite Nanoparticles and Pulsed Electromagnetic Field in Osteoporosis and Cancer 2019

In vitro study of PEMF on various human cancer cell lines like breast cancer (e.g., MCF7, MDA-MB- 231 and T47D), pheochromocytoma-derived (PC12), and colon cancer (SW-480 and HCT-116) showed blockage of the development of neovascularization required for tumor supply, ant-proliferative and mitotic spindle disruption and induced genetic instability by reducing the stringency of the late-cycle (G2) checkpoint [108-111]. Moreover, study shows that PEMF treatment is target specific [112]. It has been reported that PEMF therapy (parameters: frequency of 20 Hz, intensity of 3 mT) with exposure time of 60 min/day for up to 3 days induce apoptosis in human breast adenocarcinoma cells (MCF7), but not to normal breast epithelial cells (MCF10). Though target specific behavior of PEMF is promising, but exposure was limited to 3 days only. Hence, long-term PEMF exposure needs to be evaluated in further studies considering the fact that effectiveness of PEMF is severely linked to the signal parameters, exposure magnitude, duration, signal shape, duration of treatment as well as the type of cells exposed to the magnetic field [113, 114].

Future trends in osteoporosis and cancer research with PEMF and HApN:

Combination of Nanoparticles and Pulsed Electromagnetic Field could be used as a positive countermeasure for osteoporosis and cancer disease. Earlier, we reported that a combination of low level PEMF and Hap nanoparticles has potential to control bone loss induced by simulated microgravity [30, 31]. It can be suggested that the future prospects to treat diseases lies somewhere in the combination therapy. It should be noted that combination may lead to development toxicities, which need to be evaluated along with its potential to control the disease. Research in next decade with PEMF and Nanoparticles will definitely add information in area of medicine. Clinical studies have used PEMF therapy for both osteoporosis and cancer treatment. These studies show that PEMF therapy is safe and promising compared to other available cancer and osteoporosis therapies. On the other hand, due to its bioactive and biocompatible properties, HAp has been shown to be used as a countermeasure to prevent both osteoporosis and cancer. In the future, PEMFs with HApN could be used synergistically in the field of osteoporosis and oncology

https://pubmed.ncbi.nlm.nih.gov/29954491/

Neuroregenerative Effects of Electromagnetic Field and Magnetic Nanoparticles on Spinal Cord Injury in Rats 2018

The present study aimed to evaluate the effect of iron oxide nanoparticles (IONPs) along with electromagnetic fields (MF) exposure on spontaneous and induced axonal sprouting after spinal cord injury (SCI). Adult male Wistar rats were subjected to spinal cord transection at the T13 segment. The IONP (25 µg/mL) embedded in 3% agarose gel was implanted at the injury site and subsequently exposed to MF (50 Hz, 17.96 µT, 2 hours/day for 5 weeks). Histological analysis of spinal cord tissue showed a significant increase in the expression of the growth-associated protein GAP-43 and it was found to be co-localized with neuronal nuclei marker and neurofilaments. The results show sprouting from mature neurons and axons, significantly less demyelination and more myelinated fibers were evident at the lesion site. However, no motor or somatosensory evoked potential response was observed, suggesting lack of long-distance functional connectivity. These findings highlight the therapeutic potential of IONPs along with MF exposure in promoting neuroregeneration after SCI.

https://pubmed.ncbi.nlm.nih.gov/30409044/

Impact of electromagnetic fields on in vitro toxicity of silver and graphene nanoparticles 2019

The correlation between shape and concentration of silver nanoparticles (AgNPs), their cytotoxicity and formation of reactive oxygen species (ROS) in the presence of electromagnetic fields (EMFs) has been investigated. In addition, the bio-effects caused by the combination of EMFs and graphene nanoparticles (GrNPs) have been also assessed. The AgNPs of three shapes (triangular, spherical and colloidal) and GrNPs were added in high concentrations to the culture of human fibroblasts and exposed to EMF of three different frequencies: 900, 2400 and 7500 MHz. The results demonstrated the dependence of the EMF-induced cytotoxicity on the shape and concentration of AgNPs. The maximal cell killing effect was observed at 900 MHz frequency for NPs of all shapes and concentrations. The highest temperature elevation was observed for GrNPs solution irradiated by EMF of 900 MHz frequency. The exposure to EMF led to significant increase of ROS formation in triangular and colloidal AgNPs solutions. However, no impact of EMF on ROS production was detected for spherical AgNPs. GrNPs demonstrated ROS-protective activity that was dependent on their concentration. Our findings indicate the feasibility to control cytotoxicity of AgNPs by means of EMFs. The effect EMF on the biological activity of AgNPs and GrNPs is reported here for the first time.

https://www.researchgate.net/publication/337411782_In_vitro_evaluation_of_electroporated_gold_nanoparticles_and_extremely-low_frequency_electromagnetic_field_anticancer_activity_against_Hep-2_laryngeal_cancer_cells

In vitro evaluation of electroporated gold nanoparticles and extremely-low frequency electromagnetic field anticancer activity against Hep-2 laryngeal cancer cells 2019

The highest content of cells arrested in G2/M phase was observed in ELFEMF-treated cells for 30 min both at 25 or 50 mT, while the cells treated with EP AuNPs or ELFEMF 50 mT/15 min showed highest ratios of apoptotic cells.

Conclusions: Our observations indicate that treatment of Hep-2 laryngeal cancer cells with ELFEMF for 30 min at 25-50 mT and EP Au-NPs can cause cell damage inducing apoptosis and cell cycle arrest.

https://www.researchgate.net/publication/328942602_Synergistic_Antibacterial_Effect_of_Silver_Nanoparticles_and_Extremely_Low-Frequency_Pulsed_Magnetic_Fields_on_Klebsiella_pneumoniae

Synergistic Antibacterial Effect of Silver Nanoparticles and Extremely Low-Frequency Pulsed Magnetic Fields on Klebsiella pneumoniae 2018

This research aimed to explore the synergistic effects of the combination of exposure to ELF-PMF and supplying of AgNPs. K. Pneumonia bacterium is used as a gram-negative model to be tested undersupplying of different AgNPs concentrations and exposure to ELF-PMF at different frequencies. The best synergistic effect is determined by obtaining a most inhibitory concentration of AgNPs and resonance frequency of ELF-PMF causing maximum inhibition in bacterial growth. Kinetics of growth and MIC/MBC levels showed that exposure to 20 Hz-PMF, 30 min with a supplement of 150 ppm-AgNPs caused a highly synergistic effect by 90% enhancement of growth inhibition. It is concluded that using the benefits of exposure to electromagnetic waves with the presence of nanoparticles can limit the wide-spread of silver nano-products and give a chance of nano-antibacterial agents to be used in safe limits.

2.6. Pulsed Magnetic Field Exposure System

The power supply of direct current was used through an electronic switching device to produce an interrupted current of 50% duty cycle with different frequencies. The square-pulsed current (80 mA) then directed to a pair of Helmholtz coils (each of 445 turns and of total resistance 6.8 ohm) separated by a distance 10 cm equal to the radius of the coil to produce a homogeneous magnetic field in form of impulses. The system manufactured at the Electronics physics laboratory in the Faculty of Science, Alexandria University-Egypt. This field measured by using a Gauss/Tesla meter model 4048 at different locations, with probe T-4048.001 (USA) of accuracy ±2% in order to confirm the most homogenous zone (in the midpoint between the two coils) and field intensity found to be (0.32 mT). The tubes (5mL) of bacterial cell suspensions were set in the field point of the coils where PMF was homogeneous. The magnetic field square wave shape was also displayed using the Linear Hall-effect IC sensor on the oscilloscope.

5. CONCLUSION

The exposure to PMF increased the ability of AgNPs uptake and hence moved its effect to the higher level of bacterial inhibition. Accordingly, a lower concentration of AgNPs is needed and wide-spread of products containing silver nano-forms will be limited. Moreover, the benefits of electromagnetic waves give chance to safe use of different nanoparticles at low permissible concentrations and decrease the possible bio-toxicity

https://www.researchgate.net/publication/329195944_The_Combined_Effects_of_Multi-Sized_Silver_Nanoparticles_by_Arc_Discharge_and_Pulsed_Magnetic_Fields_Exposure_on_K_pneumoniae

The Combined Effects of Multi-Sized Silver Nanoparticles by Arc Discharge and Pulsed Magnetic Fields Exposure on K. Pneumoniae 2018

The combination of 30 min exposure to 0·32 mT, 20 Hz pulsed magnetic field and treatment with silver nanoparticles with serial concentrations (10:500 parts per million) and different sizes (94, 38 and 17 nm) was used to study the antibacterial effects against K. pneumoniae. Confirmation of silver nanoparticles by using an ultraviolet–visible spectrometer, a particle size analyzer and a high-resolution transmission electron microscope depicted three sizes (~94, ~38 and ~17 nm) at rotational speeds (0, 350 and 950 revolutions/min, respectively). The antibacterial results indicated serially more inhibition of bacterial growth with increase in silver nanoparticle concentration, with the maximum effect of more than 70% inhibition produced by 17 nm silver nanoparticles. Particularly, the combination of pulsed magnetic field and silver nanoparticles (17 nm) indicated significant enhancement in growth inhibition by 56·7% compared to each alone. The study presents a new trend for water disinfection with significant impact of such combination effects on K. pneumoniae with low silver nanoparticle concentrations and less toxicity.