RESEARCH ARTICLE

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In vitro Evaluation of the Combined Effects of a Static Magnetic Field and Curcumin on MCF7 and HeLa Cell Lines

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Abstract

Objective: This study examined how varying levels of curcumin and static magnetic fields (SMF) affected three cell types, with outcomes influenced by field strength and curcumin concentration in normal and cancerous cells. **Methods:** The effects of static magnetic fields on cell proliferation and death rates were evaluated using the MTT assay and flow cytometry. The efficacy of the magnetic field, with or without curcumin (10–40 µg/ml), was assessed. Cells were treated with curcumin at the optimal concentration from the MTT assay and simultaneously exposed to a static magnetic field (7, 10, or 25 mT) for 48 hours. **Result:** Our study demonstrated that SMF (7 mT) exposure significantly increased the proportion of HeLa and MCF-7 cells in the early apoptotic phase. Curcumin application markedly elevated necrosis rates in both cell lines. Additionally, curcumin (5 µg/ml) significantly affected apoptosis rates in HeLa and MCF-7 cells ($p < 0.05$). **Conclusion:** This study demonstrated that SMF exposure significantly increased necrotic cell death in HeLa cells and accelerated apoptosis in both cancer cell types. The minimum effective dose of curcumin combined with SMF caused a four-fold increase in apoptosis in HeLa cells compared to curcumin alone.

Keywords: Cancer cell line- Static magnetic field- Curcumin- *In vitro*

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Introduction

In vitro studies and animal experiments have shown promising results using nonionizing static magnetic fields (SMFs) or electromagnetic fields (ELFs) [1]. Exposure to SMFs has been associated with a reduced number of living cells compared to control groups [2].

Unlike static electric fields, SMFs can penetrate living systems and directly interact with moving electric charges (e.g., ions) through various mechanisms [3]. Since nothing in a living organism is static [3, 4], studies have investigated SMFs effects on cell survival, differentiation [5], apoptosis [6, 7], gene expression [8], phenotypic abnormalities in mouse embryos [9], the concentration of sodium ions [10] , calcium distribution across membranes [11], protein synthesis stimulation [12], and enzyme activity [13] Gurhan and Barnes, [11]reported that SMFs alter the hyperfine coupling between chemically active electrons and nuclear spins. Research also suggests that magnetic fields can penetrate living tissues and potentially affect cell membranes [11].

SMF has been reported to disrupt the distribution of proteins and glycoproteins in the membrane and cytoskeleton. It also affects ion flux and transport across the membrane, particularly calcium (Ca^{2+}), potentially interfering with various physiological activities [14]. Calcium influx into the mitochondria is one of the initial steps in the corresponding changes. If matrix calcium increases beyond physiological demands, it can help open the mitochondrial permeability transition pore (mPTP), and as a result, trigger apoptotic or necrotic cell death. Studies have shown that the magnetic field affects the function of ion channels [15, 16]. The genotoxic effects of static magnetic field (SMF) exposure have been primarily studied in cell culture [17, 18]. By altering membrane receptor distribution, transmembrane ion fluxes, and increasing ROS and P53 levels, MFs significantly impact cancer cell viability [8, 19, 20].

Reactive oxygen species [21] and oxidative stress play crucial roles in various cellular functions [22]. Radical pairs are short-lived intermediates. Studies have shown that magnetic fields (MF) can increase radical oxygen production in tumor cell membranes and enhance the uptake of chemotherapeutic drugs [5, 23]. The concurrent use of SMFs and conventional anticancer drugs has been explored to improve therapeutic outcomes. A study assessed the synergistic cytotoxic effects of an extremely low-frequency electromagnetic field with doxorubicin on the MCF-7 cell line, indicating that electromagnetic fields can enhance the efficacy of chemotherapeutic agents

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[24]. In cells treated with four anticancer drugs cisplatin, Taxol, doxorubicin, and cyclophosphamide along with exposure to a static magnetic field, membrane permeability changes, increasing the penetration of the drugs [25].

The integration of static magnetic fields (SMFs) with herbal extracts or anticancer drugs has garnered significant attention in recent years, particularly concerning their combined effects on apoptosis in cancer cells. Studies have demonstrated that SMFs can modulate cellular functions, and when used in conjunction with certain herbal compounds or chemotherapeutic agents, they may enhance anticancer efficacy. For instance, research has shown that the application of SMFs can intensify the cytotoxic effects of herbal extracts on cancer cells. A study by Namvar et al. [26] investigated the cytotoxic effect of magnetic iron oxide nanoparticles synthesized via seaweed aqueous extract on cancer cells, revealing significant anticancer activity.

Similarly, the combination of SMFs and Ferula gummosa extract exhibited enhanced cytotoxicity in the HeLa cell line, suggesting a potential synergistic effect [27].

Herbal medicines and their derivatives are widely used today to treat various diseases. Many cytotoxic natural products are derived from medicinal plants. Curcumin exhibits anti-arthritic, anti-amyloid, anti-ischemic, anti-inflammatory properties, and improving diseases caused by immunodeficiency [28-30]. This substance has antidiabetic and antioxidant effects, positively influencing oxidative stress indicators [31, 32, 17]. Curcumin affects various biological processes and exhibits antitumor properties both in vitro and in vivo. Curcumin, a polyphenol derived from the turmeric plant (Curcuma longa), exhibits significant anticancer properties. It suppresses cancer cell proliferation across various types, including prostate, colorectal, breast, pancreatic, brain, head, and neck cancers [33]. Additionally, curcumin enhances the efficacy of radiation therapy by increasing the radio sensitivity of cancer cells, thereby improving treatment outcomes [34].

These findings underscore the potential of combining SMFs with herbal extracts or anticancer drugs to induce apoptosis more effectively in cancer cells. However, the exact mechanisms underlying these synergistic effects remain to be fully elucidated. Further research is essential to determine optimal conditions, such as field intensity, exposure duration, and appropriate herbal or drug concentrations, to maximize therapeutic benefits while minimizing adverse effects.

The aim of this study to investigate the combined effects of static magnetic fields (SMF) and varying curcumin concentrations on the proliferation, apoptosis, and necrosis rates of normal and cancerous cells, with a focus on identifying optimal conditions for enhancing anticancer activity while minimizing effects on normal cells.

Materials and Methods

Cell culture

Curcumin was purchased from Sigma-Aldrich. The cell culture reagents RPMI-1640 and fetal bovine serum (FBS) were obtained from Gibco (UK). MTT salt was purchased from Sigma-Aldrich, and dimethylsulfoxide (DMSO) was obtained from Merck (Darmstadt, Germany). Normal skin fibroblast cells (Hu02, mesenchymal, C10309-HU-3) were obtained from the Iranian National Center for Genetic and Biological Resources, while human breast carcinoma cells (MCF-7, C135) and cervical cancer cells (HeLa, C115) were obtained from the National Cell Bank of Iran (NCBI), Pasteur Institute. The cells were cultured in RPMI-1640 medium (Gibco, UK) supplemented with 100 µg/mL streptomycin, 100 U/mL penicillin (Gibco, UK), and 10% FBS (Gibco) at 37°C, 5% CO2, and 95% humidity.

Static magnetic field application

SMF exposure was conducted via a device that included an incubator, a power supply, and a field generator (Figure 1). The incubator was placed between two Helmholtz coils with average radius of 25 cm. The distance between the centers of two coils is 25 cm. Each coil contained 400 turns of a lacquered copper wire. A single-phase autotransformer (50 Hz, 15 kVA, 50 A, 300 V) was connected to the power supply, allowing voltage and current to be adjusted by changing the volume. The samples cultured in the incubator were exposed to the magnetic field from the coil. These coils can produce static and alternating fields with intensities ranging from 0 to 17 mT. The exposure time was 48 hours. Before each exposure, the SMF intensity was checked using a tesla meter to ensure the appropriate intensity. The system was equipped to measure and control temperature, humidity, and CO2 levels. The humidity system (model SHT11) had a measurement range of 10-100% and an accuracy of ± 4.25%. The temperature sensor (model SMT172) had a range of -45 °C to 130 °C, with a control accuracy of 0.25% and sensitivity of ± 0.1°C. Calibration and testing of the static magnetic field's accuracy and uniformity were carried out using a Teslameter (516 62 Teslameter, Leybold company,German) (Figure 1).

Three fixed magnetic field intensities (7, 10, and 15 mT) [23] were used to irradiate the samples (HeLa, MCF-7, and Hu02). The optimal field strength was determined based on a significant reduction in cancer cells and minimal impact on normal cells after 24 hours of exposure (Table 1).

Table 1. Comparison of the Effects of Different Static Magnetic Field (SMF) Intensities on the Average Percentage ± SD of Cell Viability in Three Cell Lines after 24 hours of Exposure.

	SMF exposure (24h)		
Groups	7 (mT)	10 (mT)	15 (mT)
MCF-7	88.89 ± 6.54	79.18 ± 13.69	135.92 ± 8.14
HeLa	90.71 ± 4.10	79.36 ± 6.64	105.95 ± 15.62
Huo 2	92.72±6.52	83.11±5.21	114.99±14.14

MTT assay

The impact of curcumin on cell viability was investigated by incubating HeLa, MCF-7, and Hu02 cells with various concentrations ranging from 10 µg/ml [35] to 80 µg/ml [36]. The inhibitory concentration of curcumin was determined for the three cell lines based on survival curves obtained from the MTT assay. The assay showed that different curcumin concentrations had varying effects on cell viability percentages. The cells (HeLa, MCF-7 and Hu02) which were obtained directly from National Cell Bank of Iran (NCBI) had a passage in our laboratory. Then the cells (each separately) were classified into sub-groups according to treatment direction:

The first group (sham) consisted of cells placed undergoes all aspects of the experimental setup except the active treatment (placed in the incubator for 48 hours without radiation or curcumin). The second group included cells treated with different concentrations of curcumin (determined to produce the most favorable outcome in the MTT test) for 48 hours. The third group was exposed to static magnetic fields (7, 10, and 15 mT) for 48 hours. The fourth group (SMF+CUR) received curcumin treatment (at the concentration showing the optimum effectiveness in the MTT test) and was subjected to a static magnetic field (at the optimal strength) for 48 hours.

Based on the results from the fourth group, the treatment subgroup that received curcumin (10 µg/ml) and the optimal field strength (7 mT) was selected for flow cytometry analysis

All conditions (e.g., temperature, humidity, and CO2 levels) were consistent across all groups. All experiments were conducted within six months of receiving the cell lines.

Statistical analysis

Data were analyzed statistically using one-way ANOVA followed by Tukey's post-hoc test. Experiments were independently repeated three times, and results are presented as mean ± standard deviation (M ± SD). Differences were considered statistically significant at $P < 0.05$.

Results

The effect of various curcumin concentrations (10-80 µg/ml) was investigated in three cell lines after 48 hours (Table 2). We aimed to identify concentrations that would minimally impact healthy cells while being effective on both cell lines (IC50). Ultimately, we chose the lowest dose that remained gentle on normal cells. Therefore, we determined the minimum doses (10-40 µg/ml) that would have the least effect on normal cells. Table 1&3 shows the impact of different static magnetic field intensities (7, 10, and 15 mT) on the average cell viability percentage of the three cell lines after 24 and 48 hours.

The viability percentage of the cells in the third group, which were administered curcumin (with the most advantageous results in the MTT assay for cancer cells and displaying the highest value based on the MTT assay of normal Cells, (10-40 µg/ml) and were exposed to a static magnetic field (7mT, at the best intensity) for a duration of 24 and 48 h, is shown in Figures 3-5. Investigating the influence of different curcumin concentrations under static magnetic fields on three cell lines revealed that the effect varied based on the intensity of field and the curcumin concentration in both healthy and cancer cells.

Based on the results, the optimal conditions (minimal effect on normal cells and maximal effect on cancer cells) were selected to study apoptosis.

Table 2. Comparative Effects of Administering Different Concentrations of Curcumin on the Average cell Viability (%) ± SD of Three Cell Lines after 48 hours

Curcumin Group	10 (µg/ml)	20 (µg/ml)	30 (µg/ml)	40 (µg/ml)	50 (µg/ml)	60 (µg/ml)	70 (µg/ml)	80 (µg/ml)
MCF-7	77.72±4.36	83.29±4.40	84.89±2.14	76.88±3.57	71.135±2.78	68.39±1.30	72.04±2.67	77.91±1.37
HeLa	93.05±10.46	89.43±6.77	84.73±6.51	86.9±11.30	68.02± 7.14	68.46± 4.19	68.93±6.96	69.35±8.92
Hu02	92.8±6.47	82.32±4.48	78.49±4.48	74.14±6.94	71.41±1.85	65.62±4.73	63.71±3.18	60.71±3.18

Figure 1. Magnetic Field Generating Device. The generator was built and calibrated at Arak University of Medical Sciences by authors Fathi Y. and Soleimani H. (Grant no: 2409)

Table 3. Comparison of the Effects of Different Static Magnetic Field (SMF) Intensities on the Average Percentage ± SD of Cell Viability in Three Cell Lines after 48 hours of Exposure.

	SMF exposure (48 h)		
Groups	7 (mT)	10 (mT)	15 (mT)
MCF-7	71.2 ± 4.62	124.2 ± 7.74	103.6 ± 5.03
HeLa	95.67 ± 7.40	135.56 ± 12.09	114.22 ± 11.16
Hu02	90.2 ± 5.02	103.79 ±15.58	96.32 ± 9.64

Apoptosis/necrosis measurements

Flow cytometry analysis was performed on harvested single cells tagged with annexin V/FITC to measure the variations in apoptosis/necrosis [17]. Tables 4-6 present the findings of this evaluation for the three specific cell types, indicating the percentage of cells in both the living and death phases. The results revealed insignificant differences between Hu02 and HeLa cells in the sham groups. The percentage of necrotic and apoptotic cells were calculated to better explain the behavior of cells exposed to SMF and curcumin. Figure 6 shows the comparison results of normal fibroblast (Hu02) and HeLa cell line apoptosis analysis by flow cytometry.

Discussion

The control and application of external static magnetic fields (SMFs) in combination with anticancer agents hold significant clinical potential [37]. Our study corroborates prior findings that the effects of SMF depend on exposure duration, field intensity, and cell type. The variability in cellular response arises due to distinct chemical and physical properties intrinsic to different cell types. Interestingly, reactive oxygen species (ROS) levels demonstrate a complex relationship with SMF intensities. Specifically, studies have shown that ROS levels increase at lower intensities (100 and 200 μT), decrease at moderate levels (300 and 400 μT), and rise again at higher intensities (500 and 600 μT) [11]. This modulation suggests that weak SMFs can fine-tune oxidative stress, potentially leading to differential cellular responses depending on the intensity of the magnetic field.

Results from our investigation revealed that varying SMF intensities have unpredictable effects on cell survival rates. This phenomenon indicates that different field

Table 4. The Distribution Percentage of Apoptosis and Necrosis Rate (% Mean ± SD) of Hu02 Cells at 48 hours by Flow cytometry

Groups	Live cells	Early apoptotic cells	Late apoptotic cells	Necrotic cells
Control (Sham)	99±0.2 a	0.53±0.23 a	0.44±0.39 a	0.08±0.07a
SMF	96.02±2.66 ab	1.51±0.79 b	2.13±1.64 a	0.02±0.02a
Curcumin	91.10±6.43 b	1.29±0.22 ab	1.51±1.43 a	5.51±4.88b
Curcumin+SMF	95.61±4.26 a	3.57±0.41 c	0.11±0.01 a	0.03±0.02a

Hu02 cells were treated with curcumin (10 μg/ml) individually and in combinations (SMF+Curcumin) for 48 h. Different letters "a, b, c" refer to significant differences according to Tukey's test ($P < 0.05$). "a" letter means, there was a significant difference between "a" group with "b" group and "c" group, but there was no significant difference between groups with the same letter. " ab" letter means, there was no significant difference between "ab" group with "a" and "b" group. "bc" letter means, there was no significant difference between Bbc^ group with "b" group and "c" group.

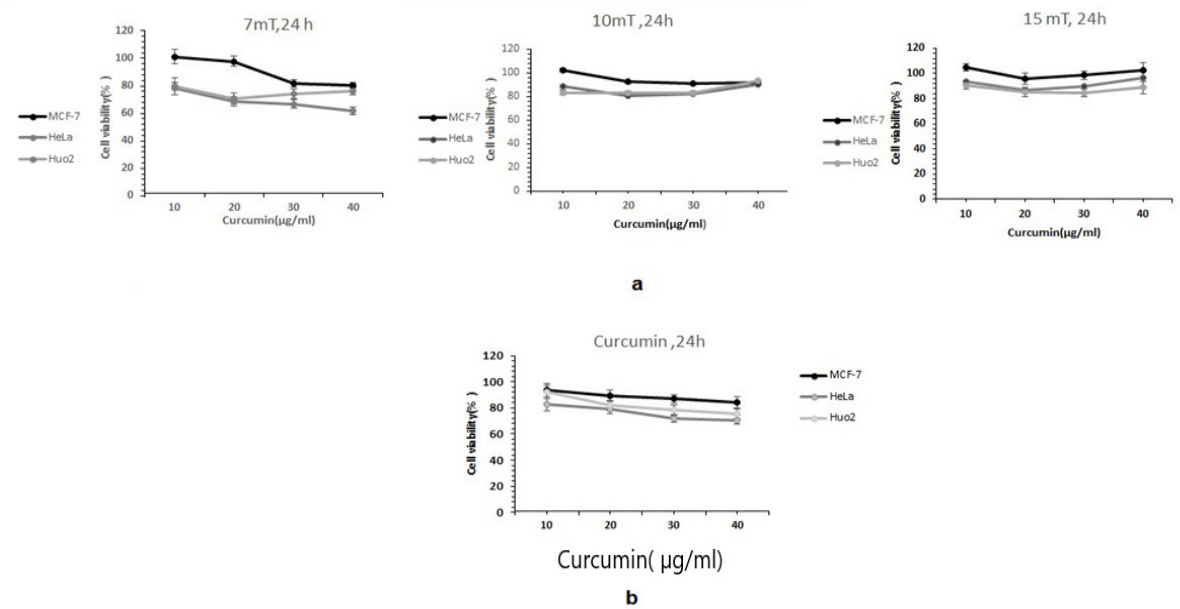

Figure 2. a. Comparison of the combined effects of different concentrations of curcumin and exposure to a static magnetic field (7,10, 15 mT) on three cell lines after 24 hours.b. Effects of different concentrations of curcumin on three cell lines after 24 hours

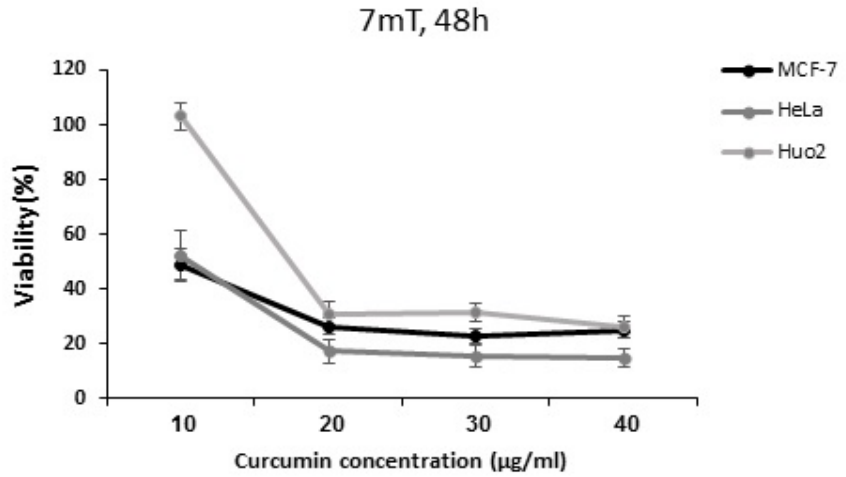

Figure 3. Comparison of the Combined Effects of Different Concentrations of Curcumin and Exposure to a Static Magnetic Field (7 mT, at the optimal level) on Three Cell Lines after 24 hours.

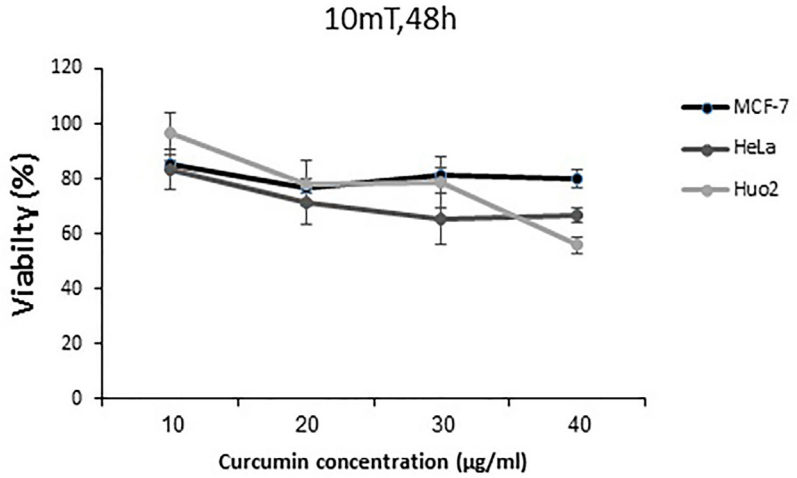

Figure 4. Effect of Electromagnetic Field (10 mT) Exposure Combined with Different Concentrations of Curcumin on Cell Lines after 48 hours

intensities may function as specific biological thresholds. Literature supports that moderate-intensity SMFs (1 mT to 1 T) initiate a spectrum of biological effects that span from cellular responses to systemic alterations [38, 39]. In our research, exposure to SMFs at 7, 10, and 15 mT produced inconsistent effects on the survival rates of HeLa and MCF-7 cancer cells. For example, we noted a decrease in MCF-7 cell viability at 7 mT, which increased to 70% at 10 mT, affirming findings reported by Dini et al. [38] that prolonged SMF exposure can lead to complex outcomes, such as reduced spontaneous apoptosis in some cells while inducing apoptosis in others by approximately 20%.

SMFs combined with apoptogenic drugs profoundly influence apoptosis rates and cellular morphology. Notably, a study demonstrated that aloe vera augments apoptosis rates in HeLa cells synergistically when paired

Table 5. The Distribution Percentage of Apoptosis and Necrosis Rate (% Mean ± SD) of HeLa Cells at 48 hours by Flow Cytometry

Groups	Live cells	Early apoptotic cells	Late apoptotic cells	Necrotic cells
Control (Sham)	97.48±2.99 a	0.22±0.02 a	0.49±0.25 a	0.10±0.08a
SMF	68.16±2.00 b	7.06±0.48 b	4.75±1.11 c	19.78±1.86c
Curcumin	73.77±1.87a	0.66±0.10 a	6.11±2.16 bd	25.91±1.25b
Curcumin+SMF	39.05±3.70 c	4.83±1.31 c	19.69±1.46 d	41.22±2.87d

HeLa cells were treated with curcumin (10 μg/ml) individually and in combinations (SMF+Curcumin) for 48 h. Different letters "a, b, c" refer to significant differences according to Tukey's test ($P < 0.05$). "a" letter means, there was a significant difference between "a" group with "b" group and "c" group, but there was no significant difference between groups with the same letter. "bd" letter means, there was no significant difference between "bd" group with "b" group and "d" group. "bc" letter means, there was no significant difference between Bbc^ group with "b" group and "c" group.

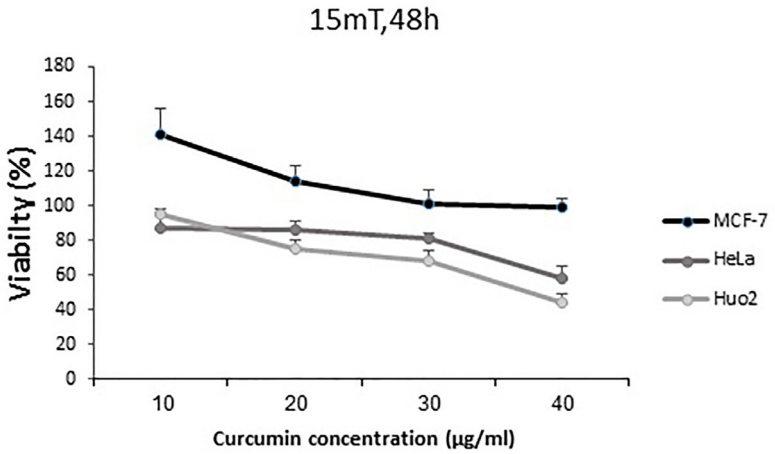

Figure 5. Effect of Electromagnetic Field (15 mT) Exposure Combined with Different Concentrations of Curcumin on Cell Lines after 48 hours

Table 6. The Distribution Percentage of Apoptosis and Necrosis Rate (% Mean ± SD) of MCF-7 Cells at 48 hours by Flow Cytometry

Groups	Live cells	Early apoptotic cells	Late apoptotic cells	Necrotic cells
Control (Sham)	61.7±1.58a	0.87±0.69a	36.75±2.47a	0.90±0.15a
SMF(7mT)	53.68±4.13b	7.00±1.96b	39.21±2.15b	0.11±0.0.04a
Curcumin	36.3±3.85c	1.55±0.19a	49.99±2.22c	12.21±1.82b

MCF-7 cells were treated with curcumin (10 µg/ml) individually and in combinations (SMF+Curcumin) for 48 h. Different letters "a, b, c" refer to significant differences according to Tukey's test ($P < 0.05$). "a" letter means, there was a significant difference between "a" group with "b" group and "c" group, but there was no significant difference between groups with the same letter.

with SMFs. This combination resulted in a nearly fourfold increase in apoptosis compared to aloe vera treatment alone [17]. The increased apoptotic rate is possibly due to enhanced mitochondrial membrane permeability induced by the magnetic field [40], allowing curcumin to exert its pro-apoptotic effects more effectively.

In our study, treating cancer cells with curcumin revealed its selective cytotoxicity, differentiating between cancerous and normal cells [10]. Curcumin modulates various molecular targets, including oncogenic Raf-1, TNF-α, IL-8 genes, and telomerase, highlighting its multitarget anticancer activity, especially in MCF-7 cells

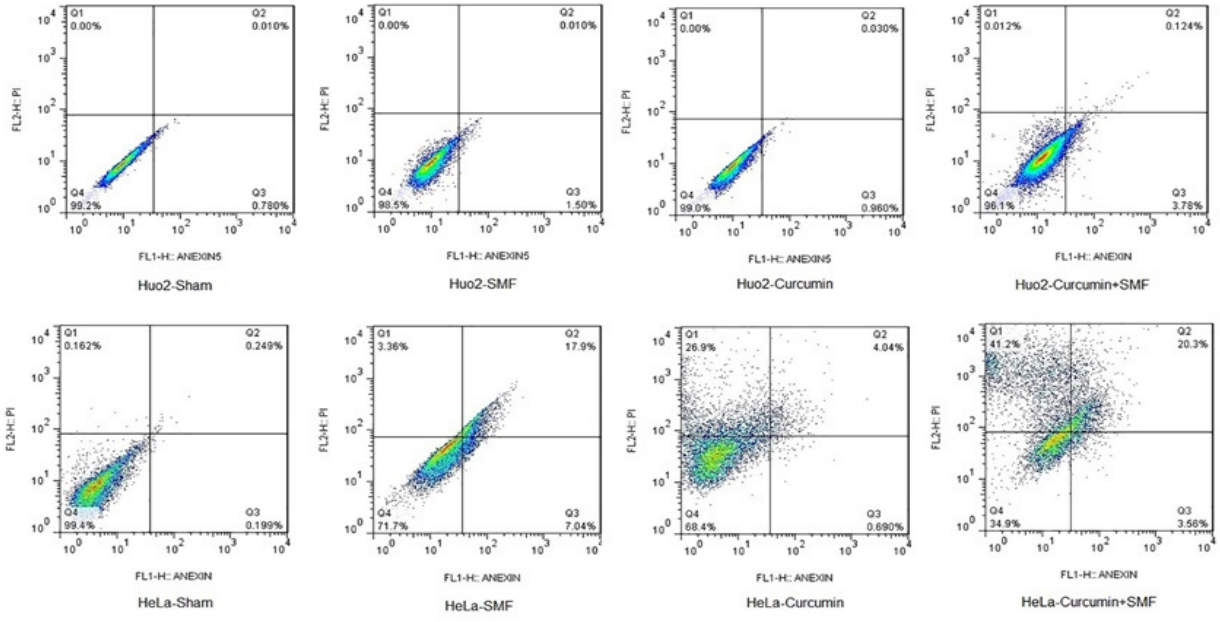

Figure 6. Flow Cytometric Analysis of Early and Late Apoptosis in HeLa Cells Line and Fibroblast Cells (Hu02) Following Treatment with SMF(7mT), Curcumin (10 µg/ml), and Curcumin(10 µg/ml) under Static Magnetic Field(SMF, 7mT) in Comparison with Sham after 48h. Annexin V and PI quadrant gating: (left bottom) viable, (left top) necrotic, (right top) late apoptotic and (right bottom) early apoptotic cells.

[41]. Our findings indicated that curcumin and SMF synergistically enhanced apoptosis rates in both HeLa and MCF-7 cells, reaching 61% and 26%, respectively. Notably, SMF exposure resulted in an increased percentage of early apoptotic HeLa and MCF-7 cells, and curcumin treatment significantly raised the proportion of necrotic cells. Specifically, the lowest effective doses of SMF (7 mT) and curcumin (10 μg/ml) impacted HeLa cells substantially, evidenced by 24% of cells entering apoptosis and approximately 41% undergoing necrosis. Recent evidence indicates that the combined pro-apoptotic effects of SMF and curcumin on cancer cells are mediated through multiple interrelated pathways, primarily centered around oxidative stress and mitochondrial dysfunction. Curcumin's ability to elevate ROS levels leads to mitochondrial membrane permeabilization, releasing pro-apoptotic factors like cytochrome c, and activating caspases such as caspase-9, thereby triggering intrinsic apoptosis [42-44]. Simultaneously, SMFs have been shown to influence ROS production possibly via modulating mitochondrial electron transport chains and NADPH oxidases, amplifying oxidative damage and promoting apoptosis [45, 46]. This oxidative stress further downregulates anti-apoptotic proteins such as Bcl-2 while upregulating pro-apoptotic factors like Bax, facilitating mitochondrial pathway activation [47]. Moreover, both agents affect cell cycle regulation, with curcumin inducing G2/M arrest through downregulation of cyclins and CDKs, rendering cells more susceptible to apoptotic stimuli [48, 49]. SMFs may bolster this effect via modulation of p53 and p21 pathways, enhancing cell cycle arrest and apoptotic readiness [39]. Additionally, the suppression of NF-κB signaling by both curcumin and SMF contributes to decreased expression of survival genes, again tipping the balance toward apoptosis [50-52]. Altogether, these pathways underpin the observed increase in apoptosis and necrosis in treated cancer cells, highlighting the multifaceted mechanisms involved.

The differential response of cancer versus normal cells to treatment is critical for developing effective therapeutic strategies. This variability stems from inherent differences in cellular metabolism, signaling pathways, and apoptosis regulation. For instance, cancer cells often exhibit dysregulated apoptosis pathways and altered cell cycle control, leading to enhanced survival compared to healthy cells [53, 17, 37]. Supporting this notion, recent investigations into Pseudocerastes persicus venom highlighted differential cytotoxic effects on Hu02 normal cells versus A549 lung cancer cells, demonstrating that while toxicity was evident in both lines, Hu02 cells displayed greater resilience [54]. Additionally, the effects of extremely low-frequency magnetic fields on NOTCH1 expression in Hu02 cells and gastric adenocarcinoma cells underscore the importance of including normal cell lines in these studies. This distinct regulatory response indicates that normal fibroblasts and cancer cells demonstrate contrasting molecular reactions to magnetic field exposure [55].

Moreover, bioeffects of SMFs on cellular behavior are influenced by cell type. Notably, MCF-7 cells exhibited significant changes in biomechanical properties, including membrane ultrastructure and F-actin distribution, which are crucial for maintaining cellular integrity and function [56, 10]. The reduction in F-actin content and altered elasticity observed in these cells 49.35% decrease in breast cancer compared to a 32.47% decrease in cervical cancer cells may be attributed to the reorganization of cytoskeletal components in response to SMF exposure. This highlights the potential of SMFs to not only alter cell viability but also modify cellular structure and mechanics, potentially leading to enhanced therapeutic efficacy against cancer [57, 40].

Further exploration into the mechanistic pathways involved could include examining the activation of specific signaling cascades initiated by curcumin and the synergistic effects of SMF exposure. For instance, curcumin has been shown to inhibit key survival pathways, such as PI3K/Akt and NF-κB, which are often hyperactivated in cancer cells [58, 51]. Understanding how SMF exposure may influence these pathways can provide greater clarity on the mechanisms underpinning the observed synergistic effects.

In summary, our study reinforces the clinical potential of combining SMFs with curcumin in cancer therapy. By unraveling the complex interactions at the cellular and molecular levels, we can better harness the therapeutic properties of this combination, ultimately leading to more effective cancer treatment strategies.

In conclusion, our study provides compelling evidence that the combined application of SMFs and curcumin exhibits significant anticancer effects, with minimal impact on normal cells. These findings suggest a promising therapeutic strategy for enhancing cancer treatment efficacy while minimizing side effects. However, further research is needed to elucidate the long-term safety and mechanisms of these combined therapies and their potential protective role in normal cells. Future studies should focus on optimizing treatment parameters, including SMF intensity, curcumin concentration, and exposure duration, to achieve the most effective and safe therapeutic outcomes.

Recommendation

To strengthen the findings, it is essential to explore potential mechanisms, such as the generation of reactive oxygen species (ROS), modulation of ion channels, or alterations in cellular signaling pathways induced by SMFs. Providing such insights, supported by references to prior research, would not only validate the observed effects but also enhance the scientific rigor and applicability of the study.

Author Contribution Statement

Y. Fathi and H. Soleimani made electromagnetic device. M. Shojapour and YF carried out the experiments. Both authors, G. Mosayebi and H.S, contributed equally in developing the theory, performing the computations, contributing to the interpretation of the results and H.S wrote the final manuscript. All authors read and approved the final manuscript.

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Approval

It is not part of an approved student thesis.

Consent for publication

The author read and approved the final manuscript for publication.

Ethical Declaration

All experiments were approved by ethical committee of the Arak University of Medical Sciences in this research (The ethic committee no: IR.ARAKMU.REC.1396.85).

Data Availability

The datasets are available from the corresponding author on reasonable request.

Conflict of Interest

The authors declare that they have no competing interests.

References

1. Atak Ç, Çelik Ö, Olgun A, Alikamanoğlu S, Rzakoulieva A. Effect of magnetic field on peroxidase activities of soybean tissue culture. Biotechnol Biotechnol Equip. 2007;21(2):166-71. https://doi.org/10.1080/13102818.2007.10817438.
2. Tofani S, Barone D, Berardelli M, Berno E, Cintorino M, Foglia L, et al. Static and elf magnetic fields enhance the in vivo anti-tumor efficacy of cis-platin against lewis lung carcinoma, but not of cyclophosphamide against b16 melanotic melanoma. Pharmacol Res. 2003;48(1):83-90.
3. Driessen S, Bodewein L, Dechent D, Graefrath D, Schmiedchen K, Stunder D, et al. Biological and health-related effects of weak static magnetic fields (≤ 1 mt) in humans and vertebrates: A systematic review. PLoS One. 2020;15(6):e0230038. https://doi.org/10.1371/journal.pone.0230038.
4. Funk RHW, Monsees TK. Effects of electromagnetic fields on cells: Physiological and therapeutical approaches and molecular mechanisms of interaction: A review. Cells Tissues Organs. 2006;182(2):59-78. https://doi.org/10.1159/000093061.
5. Yuge L, Okubo A, Miyashita T, Kumagai T, Nikawa T, Takeda S, et al. Physical stress by magnetic force accelerates differentiation of human osteoblasts. Biochem Biophys Res Commun. 2003;311(1):32-8. https://doi.org/10.1016/j.bbrc.2003.09.156.
6. Tofani S, Barone D, Cintorino M, de Santi MM, Ferrara A, Orlassino R, et al. Static and elf magnetic fields induce tumor growth inhibition and apoptosis. Bioelectromagnetics. 2001;22(6):419-28. https://doi.org/10.1002/bem.69.
7. Zafari J, Rastegar-Pouyani N, Javani Jouni F, Najjar N, Azarshin SZ, Jafarzadeh E, et al. Static magnetic field reduces cisplatin resistance via increasing apoptosis pathways and genotoxicity in cancer cell lines. Scientific Reports. 2024;14(1):5792. https://doi.org/10.1038/s41598-024-56605-1.
8. Rosen AD. Mechanism of action of moderate-intensity static magnetic fields on biological systems. Cell Biochem Biophys. 2003;39(2):163-73. https://doi.org/10.1385/cbb:39:2:163.
9. Miyakoshi J. Effects of static magnetic fields at the cellular level. Prog Biophys Mol Biol. 2005;87(2-3):213-23. https://doi.org/10.1016/j.pbiomolbio.2004.08.008.
10. Kotani H, Iwasaka M, Ueno S, Curtis A. Magnetic orientation of collagen and bone mixture. Journal of Applied Physics. 2000;87(9):6191-3. https://doi.org/10.1063/1.372652.
11. Gurhan H, Bruzon R, Kandala S, Greenebaum B, Barnes F. Effects induced by a weak static magnetic field of different intensities on ht-1080 fibrosarcoma cells. Bioelectromagnetics. 2021;42(3):212-23. https://doi.org/10.1002/bem.22332.
12. Zadeh-Haghighi H, Simon C. Magnetic field effects in biology from the perspective of the radical pair mechanism. J R Soc Interface. 2022;19(193):20220325. https://doi.org/10.1098/rsif.2022.0325.
13. Frachini ECG, Silva JB, Fornaciari B, Baptista MS, Ulrich H, Petri DFS. Static magnetic field reduces intracellular ros levels and protects cells against peroxide-induced damage: Suggested roles for catalase. Neurotox Res. 2023;42(1):2. https://doi.org/10.1007/s12640-023-00679-8.
14. Rosen AD. Inhibition of calcium channel activation in gh3 cells by static magnetic fields. Biochim Biophys Acta. 1996;1282(1):149-55. https://doi.org/10.1016/0005-2736(96)00053-3.
15. Panagopoulos DJ, Karabarbounis A, Yakymenko I, Chrousos GP. Human-made electromagnetic fields: Ion forced-oscillation and voltage-gated ion channel dysfunction, oxidative stress and DNA damage. Int J Oncol. 2021;59(5):1-16. https://doi.org/10.3892/ijo.2021.5272.
16. Wu H, Li C, Masood M, Zhang Z, González-Almela E, Castells-Garcia A, et al. Static magnetic fields regulate t-type calcium ion channels and mediate mesenchymal stem cells proliferation. Cells. 2022;11(15):2460. https://doi.org/10.3390/cells11152460.
17. Satari M, Javani Jouni F, Abolmaleki P, Soleimani H. Influence of static magnetic field on hela and huo2 cells in the presence of aloe vera extract. Asian Pac J Cancer Prev. 2021;22(S1):9-15. https://doi.org/10.31557/apjcp.2021.22.s1.9.
18. Rekena A, Livkisa D, Kamolins E, Vanags J, Loca D. Biopharmaceutical-type chinese hamster ovary cell cultivation under static magnetic field exposure: A study of genotoxic effect. Front bioeng biotechnol. 2021;9:751538. https://doi.org/10.3389/fbioe.2021.751538.
19. Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394-424. https://doi.org/10.3322/caac.21492.
20. Novikov V, Yablokova E, Fesenko E. A decrease of the respiratory burst in neutrophils after exposure to weak combined magnetic fields of a certain duration. Biophysics. 2020;65(1):84-9. https://doi.org/10.1134/S0006350920010157.
21. Tavasoli Z, Abdolmaleki P, Mowla SJ, Ghanati F, Sarvestani AS. Investigation of the effects of static magnetic field on apoptosis in bone marrow stem cells of rat. Environmentalist. 2009;29(2):220-4. https://doi.org/10.1007/s10669-008-9210-4.
22. Jomova K, Raptova R, Alomar SY, Alwasel SH, Nepovimova E, Kuca K, et al. Reactive oxygen species, toxicity, oxidative stress, and antioxidants: Chronic diseases and aging. Arch

Toxicol. 2023;97(10):2499-574. https://doi.org/10.1007/s00204-023-03562-9.
23. Kamalipooya S, Abdolmaleki P, Salemi Z, Javani Jouni F, Zafari J, Soleimani H. Simultaneous application of cisplatin and static magnetic field enhances oxidative stress in hela cell line. In Vitro Cell Dev Biol Anim. 2017;53(9):783-90. https://doi.org/10.1007/s11626-017-0148-z.
24. Ramazi S, Salimian M, Allahverdi A, Kianamiri S, Abdolmaleki P. Synergistic cytotoxic effects of an extremely low-frequency electromagnetic field with doxorubicin on mcf-7 cell line. Sci Rep. 2023;13(1):8844. https://doi.org/10.1038/s41598-023-35767-4.
25. Liu Y, Qi H, Sun RG, Chen WF. An investigation into the combined effect of static magnetic fields and different anticancer drugs on k562 cell membranes. Tumori. 2011;97(3):386-92. https://doi.org/10.1177/030089161109700322.
26. Namvar F, Rahman HS, Mohamad R, Baharara J, Mahdavi M, Amini E, et al. Cytotoxic effect of magnetic iron oxide nanoparticles synthesized via seaweed aqueous extract. Int J Nanomedicine. 2014;9:2479-88. https://doi.org/10.2147/ijn.S59661.
27. Forouzmand SH, Mousavi SH, Vazifedan V, Nourbakhsh M, Chamani J, Hoseini A, et al. Synergistic effects of ferula gummosa and radiotherapy on induction of cytotoxicity in hela cell line. Avicenna J Phytomed. 2018;8(5):439-77.
28. El-Saadony MT, Yang T, Korma SA, Sitohy M, Abd El-Mageed TA, Selim S, et al. Impacts of turmeric and its principal bioactive curcumin on human health: Pharmaceutical, medicinal, and food applications: A comprehensive review. Front Nutr. 2022;9:1040259. https://doi.org/10.3389/fnut.2022.1040259.
29. Tantry IQ, Ali A, Mahmood R. Curcumin from curcuma longa linn. (family: Zingiberaceae) attenuates hypochlorous acid-induced cytotoxicity and oxidative damage to human red blood cells. Toxicol In Vitro. 2023;89:105583. https://doi.org/https://doi.org/10.1016/j.tiv.2023.105583.
30. Sharma RA, Euden SA, Platton SL, Cooke DN, Shafayat A, Hewitt HR, et al. Phase i clinical trial of oral curcumin: Biomarkers of systemic activity and compliance. Clin Cancer Res. 2004;10(20):6847-54. https://doi.org/10.1158/1078-0432.ccr-04-0744.
31. Banaszak M, Górna I, Woźniak D, Przysławski J, Drzymała-Czyż S. The impact of curcumin, resveratrol, and cinnamon on modulating oxidative stress and antioxidant activity in type 2 diabetes: Moving beyond an anti-hyperglycaemic evaluation. Antioxidants. 2024;13(5):510. https://doi.org/10.3390/antiox13050510.
32. Shaw J, Raja SO, Dasgupta AK. Modulation of cytotoxic and genotoxic effects of nanoparticles in cancer cells by external magnetic field. Cancer Nanotechnol. 2014;5(1):2. https://doi.org/10.1186/s12645-014-0002-x.
33. Tomeh MA, Hadianamrei R, Zhao X. A review of curcumin and its derivatives as anticancer agents. Int J Mol Sci. 2019;20(5). https://doi.org/10.3390/ijms20051033.
34. Verma V. Relationship and interactions of curcumin with radiation therapy. World J Clin Oncol. 2016;7(3):275-83. https://doi.org/10.5306/wjco.v7.i3.275.
35. Marín-Palma D, Tabares-Guevara JH, Zapata-Cardona MI, Flórez-Álvarez L, Yepes LM, Rugeles MT, et al. Curcumin inhibits in vitro sars-cov-2 infection in vero e6 cells through multiple antiviral mechanisms. Molecules. 2021;26(22). https://doi.org/10.3390/molecules26226900.
36. Zhu Y, Bu S. Curcumin induces autophagy, apoptosis, and cell cycle arrest in human pancreatic cancer cells. Evid Based Complement Alternat Med. 2017;2017:5787218. https://doi.org/10.1155/2017/5787218.
37. Gurhan H, Barnes F. Impact of weak radiofrequency and static magnetic fields on key signaling molecules, intracellular ph, membrane potential, and cell growth in ht-1080 fibrosarcoma cells. Sci Rep. 2023;13(1):14223. https://doi.org/10.1038/s41598-023-41167-5.
38. Dini L, Abbro L. Bioeffects of moderate-intensity static magnetic fields on cell cultures. Micron. 2005;36(3):195-217. https://doi.org/10.1016/j.micron.2004.12.009.
39. Ji X, Zhang X. Impact of static magnetic fields on cells. InBiological effects of static magnetic fields. Singapore: Springer Nature Singapore; 2023. p. 133-85
40. Saletnik BA, Puchalska-Sarna A, Saletnik A, Lipa T, Dobrzanski B, Puchalski C. Static magnetic fields as a factor in modification of tissue and cell structure: A review. Int Agrophys. 2024;38(1). https://doi.org/10.31545/intagr/176998.
41. Fawzy RM, Abdel-Aziz AA, Bassiouny K, Fayed AM. Phytocompounds-based therapeutic approach: Investigating curcumin and green tea extracts on mcf-7 breast cancer cell line. J Genet Eng Biotechnol. 2024;22(1):100339. https://doi.org/10.1016/j.jgeb.2023.100339.
42. Woo J-H, Kim Y-H, Choi Y-J, Kim D-G, Lee K-S, Bae JH, et al. Molecular mechanisms of curcumin-induced cytotoxicity: Induction of apoptosis through generation of reactive oxygen species, down-regulation of bcl-x l and iap, the release of cytochrome c and inhibition of akt. Carcinogenesis. 2003;24(7):1199-208. https://doi.org/10.1093/carcin/bgg082.
43. Kocyigit A, Guler EM. Curcumin induce DNA damage and apoptosis through generation of reactive oxygen species and reducing mitochondrial membrane potential in melanoma cancer cells. Cell Mol Biol. 2017;63(11):97-105. https://doi.org/10.14715/cmb/2017.63.11.17.
44. Mortezaee K, Salehi E, Mirtavoos-mahyari H, Motevaseli E, Najafi M, Farhood B, et al. Mechanisms of apoptosis modulation by curcumin: Implications for cancer therapy. J cell physiol. 2019;234(8):12537-50. https://doi.org/10.1002/jcp.28122.
45. Wang H, Zhang X. Magnetic fields and reactive oxygen species. Int J Mol Sci. 2017;18(10):2175. https://doi.org/10.3390/ijms18102175.
46. Coballase-Urrutia E, Navarro L, Ortiz J, Verdugo-Díaz L, Gallardo J, Hernández ME, et al. Static magnetic fields modulate the response of different oxidative stress markers in a restraint stress model animal. BioMed research international. 2018;2018(1):3960408. https://doi.org/10.1155/2018/3960408.
47. Chota A, George BP, Abrahamse H. Interactions of multidomain pro-apoptotic and anti-apoptotic proteins in cancer cell death. Oncotarget. 2021;12(16):1615. https://doi.org/10.18632/oncotarget.28031.
48. Chimento A, D'Amico M, De Luca A, Conforti FL, Pezzi V, De Amicis F. Resveratrol, epigallocatechin gallate and curcumin for cancer therapy: Challenges from their pro-apoptotic properties. Life. 2023;13(2):261. https://doi.org/10.3390/life13020261.
49. Fatima F, Chourasiya NK, Mishra M, Kori S, Pathak S, Das R, et al. Curcumin and its derivatives targeting multiple signaling pathways to elicit anticancer activity: A comprehensive perspective. Curr Med Chem. 2024;31(24):3668-714. https://doi.org/10.2174/0929867330666230522144312.
50. Kim EC, Park J, Noh G, Park SJ, Noh K, Kwon IK, et al. Effects of moderate intensity static magnetic fields on osteoclastic differentiation in mouse bone marrow cells. Bioelectromagnetics. 2018;39(5):394-404. https://doi.org/10.1002/bem.22126.
51. Patel SS, Acharya A, Ray R, Agrawal R, Raghuwanshi R, Jain P. Cellular and molecular mechanisms of curcumin

in prevention and treatment of disease. Crit Rev Food Sci Nutr. 2020;60(6):887-939. https://doi.org/10.1080/10408398.2018.1552244.
52. Zablotskii V, Gorobets O, Gorobets S, Polyakova T. Effects of static and low-frequency magnetic fields on gene expression. J Magn Reson Imaging. 2025;62(2):317-34. https://doi.org/10.1002/jmri.29726.
53. Kalyanaraman B. Teaching the basics of cancer metabolism: Developing antitumor strategies by exploiting the differences between normal and cancer cell metabolism. Redox biol. 2017;12:833-42. https://doi.org/10.1016/j.redox.2017.04.018.
54. Shahbazi B, Najafabadi ZS, Goudarzi H, Sajadi M, Tahoori F, Bagheri M. Cytotoxic effects of pseudocerastes persicus venom and its hplc fractions on lung cancer cells. J Venom Anim Toxins Incl Trop Dis. 2019;25:e20190009. https://doi.org/10.1590/1678-9199-JVATITD-2019-0009.
55. Mansoury F, Babaei N, Abdi S, Entezari M, Doosti A. Changes in notch1 gene and its regulatory circrna, hsa_circ_0005986 expression pattern in human gastric adenocarcinoma and human normal fibroblast cell line following the exposure to extremely low frequency magnetic field. Electromagn Biol Med. 2021;40(3):375-83. https://doi.org/10.1080/15368378.2021.1891092.
56. Wang Z, Hao F, Ding C, Yang Z, Shang P. Effects of static magnetic field on cell biomechanical property and membrane ultrastructure. Bioelectromagnetics. 2014;35(4):251-61. https://doi.org/10.1002/bem.21847.
57. Kwon S, Yang W, Moon D, Kim KS. Comparison of cancer cell elasticity by cell type. J Cancer. 2020;11(18):5403-12. https://doi.org/10.7150/jca.45897.
58. Kim JM, Noh EM, Kwon KB, Kim JS, You YO, Hwang JK, et al. Curcumin suppresses the tpa-induced invasion through inhibition of pkcα-dependent mmp-expression in mcf-7 human breast cancer cells. Phytomedicine. 2012;19(12):1085-92. https://doi.org/10.1016/j.phymed.2012.07.002.