magnetochemistry

MDPI

Review

Magnetic Fields as Biophysical Modulators of Anticancer Drug Action

Xin Yu [1,*] and Yue Lv [2]

[1] Department of Basic Medicine, Anhui Institute of Medicine, Hefei 230601, China
[2] Department of Radiation Oncology, The First Affiliated Hospital of Anhui Medical University, Hefei 230022, China; ayyfyly@163.com
* Correspondence: xinyu88@mail.ustc.edu.cn; Tel.: +86-19966131746

Abstract

Magnetic fields (MFs), including static (SMFs) and extremely low-frequency electromagnetic fields (ELF-EMFs), have recently emerged as potential modulators of anticancer drug responses. Evidence indicates that MFs can influence membrane transport, oxidative stress, DNA damage, apoptosis, and cell cycle regulation, thereby altering the efficacy of chemotherapeutics and targeted agents. These effects are strongly dependent on MFs' parameters and biological context, leading to synergistic, antagonistic and no-effect outcomes. However, inconsistent exposure protocols, limited reproducibility, and scarce clinical validation remain major obstacles. This review highlights current experimental findings, proposes mechanistic links between MFs and drug action, and outlines key challenges for advancing MF-based adjuvant strategies in oncology.

Keywords: magnetic field (MF); static magnetic field (SMF); extremely low frequency electromagnetic field (ELF-EMF); antitumor agents; cancer therapy

check for updates

Academic Editor: Carlos J. Gómez García

Received: 15 September 2025
Revised: 10 October 2025
Accepted: 10 October 2025
Published: 16 October 2025

Citation: Yu, X.; Lv, Y. Magnetic Fields as Biophysical Modulators of Anticancer Drug Action. *Magnetochemistry* **2025**, *11*, 89. https://doi.org/10.3390/magnetochemistry11100089

Copyright: © 2025 by the authors. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https://creativecommons.org/licenses/by/4.0/).

1. Introduction

Cancer is a multifactorial disease and remains the second leading cause of mortality worldwide, posing a profound global health and socioeconomic challenge [1]. Antitumor drugs—including conventional chemotherapeutic agents, targeted therapies, and other pharmacological interventions—play a central role in the treatment of malignant tumors, particularly in advanced or metastatic stages where surgical and radiotherapeutic options are limited. Yet, the long-term benefits of these therapies are often curtailed by drug resistance, tumor microenvironmental barriers, and dose-limiting toxicities [2–4]. A central challenge lies in selectively enhancing tumoricidal activity without exacerbating systemic burden.

In recent years, biophysical approaches have drawn increasing attention in oncology. Among them, magnetic fields (MFs) have emerged as a promising modality due to their non-invasive nature, tunability, and capacity to influence cellular and molecular processes [5]. The inhibitory effects of static magnetic fields (SMFs) and low-frequency electromagnetic fields (ELF-EMFs) have been studied against a wide variety of human cancer cell lines, such as fibrosarcoma [6], colon carcinoma [6–8], leukemia [9–11], breast cancer [12–14], lung cancer [15] and ascites carcinoma [16,17]. Clinical observations have further suggested that MFs may improve survival and alleviate symptoms in patients with advanced gastric cancer [18]. At the mechanistic level, MFs can modulate reactive oxygen species (ROS) generation [19], ion channel dynamics [20], apoptotic signaling [21], gene expression [22], and

drug transport [23], all of which are intimately related to tumor cell sensitivity to antitumor agents. These findings provide a rationale for combining MFs with pharmacological therapies to improve treatment outcomes. However, tumor treating fields (TTFs) have already demonstrated clinical success, particularly in glioblastoma, by applying low-intensity, intermediate-frequency alternating electric fields (~200 kHz) to disrupt mitotic spindle assembly and cytokinesis [24–26]. The approval of TTFs for clinical use underscores the therapeutic potential of non-invasive physical fields in cancer management, highlighting the feasibility of integrating physical biophysics with pharmacological interventions.

Given the "window effects" of MFs [27,28], variations in exposure parameters such as intensity, frequency, and duration can lead to diverse biological outcomes. In this review, we synthesize current evidence on MF–drug interactions, focusing on static and low-frequency fields. We categorize the synergistic effects of MFs and antitumor agents into four mechanistic domains: membrane transport, oxidative stress modulation, cell cycle regulation, and apoptosis induction. Through this framework, we aim to provide conceptual clarity and guide future studies toward clinical translation of MF-based adjuvant cancer therapies.

2. Methods

We systematically searched PubMed, Web of Science, and Scopus for studies published between 1996 and 2025 using the keywords "static magnetic field", "extremely low-frequency electromagnetic field", "anticancer drug", "chemotherapy", "targeted therapy", and "drug resistance". Inclusion criteria were: (1) original experimental studies (in vitro, in vivo) or clinical reports that investigated the biological effects of externally applied static or extremely low-frequency magnetic fields in combination with anticancer drugs; (2) clear description of MF exposure parameters (intensity, frequency, exposure duration) and drug treatment conditions; and (3) reported biological endpoints relevant to drug action (viability, apoptosis, ROS, drug uptake, tumor growth, survival). Exclusion criteria included purely theoretical papers without experimental data, studies lacking sufficient exposure or outcome details, and reports using high-frequency electromagnetic exposures outside the static/ELF range. Retrieved records were screened by title and abstract, followed by full-text assessment. Data were extracted into structured tables including experimental model, MF parameters, drug, endpoints, and principal outcomes. We apologize for any relevant studies not captured despite our efforts.

3. The Types of Magnetic Fields

Humans are exposed daily to artificial and naturally occurring MFs that originate from many different sources. For instance, there are MFs generated by permanent magnets and electromagnetic fields produced by electric currents. Based on whether the magnetic field strength and direction change over time, they can be categorized as static magnetic fields (SMFs) or dynamic/time-varying magnetic fields (TVMFs). Compared to TVMFs, SMFs exhibit certain advantages for investigating the mechanisms of magnetic field biological effects due to fewer variable parameters and the absence of thermal effects. Classification by magnetic field strength broadly includes weak magnetic fields (<1 mT), moderate magnetic fields (1 mT~1 T), strong magnetic fields (1 T~20 T), and ultra-strong magnetic fields ($\geq$20 T) [5]. While the variation rate of the intensity of the MF with spatial displacement is equal to zero, it is a uniform magnetic field; otherwise, it is a gradient magnetic field (GMF).

Time-varying magnetic fields, characterized by non-constant strength and direction, are often broadly divided based on frequency into extremely low-frequency electromagnetic fields (ELF-EMFs, <300 Hz), intermediate-frequency electromagnetic fields (IF-EMFs, 300 Hz~10 MHz), and radiofrequency electromagnetic fields (RF-EMFs,

10 MHz~300 GHz) [29]. For example, the power-frequency magnetic field generated by 50 Hz transmission lines belongs to ELF-EMFs, while the magnetic field produced by mobile phones falls under RF-EMFs. Furthermore, if the magnetic field distribution changes over time, TVMFs are subdivided into alternating magnetic fields (AMFs), pulsed magnetic fields (PMFs), and rotating magnetic fields (RMFs).

The biological effects of MFs are influenced by multiple parameters, including magnetic flux density (mT~T), frequency (Hz~MHz), exposure duration, and magnetic field type [30,31]. Different parameter combinations exert distinct influences on cellular behavior, potentially leading to inconsistent experimental outcomes. It is important to note that magnetic field-induced biological effects involve two fundamental molecular mechanisms: thermal effects and non-thermal effects. Based on the physical mechanisms, ELF-EMFs (<300 Hz) are regarded as non-thermal effects [32]. The non-thermal effect can be described as a direct interaction of MF with biological cells that is independent of any heating [33]. In the current review, we focus only on the biological effects of SMFs and ELF-EMFs in combination with chemotherapy, which have non-thermal effects.

4. SMF and Drugs

SMFs have emerged as a promising adjunct to enhance the efficacy of both conventional chemotherapeutics and targeted anticancer agents. They can modulate DNA damage, apoptosis, cell cycle progression, oxidative stress, and drug uptake, thereby potentiating the antitumor effects of drugs such as cisplatin, doxorubicin (DOX), 5-fluorouracil (5-FU), paclitaxel, and mTOR/EGFR inhibitors. The effects are highly dependent on drug type, molecular weight, cell line, SMF intensity, orientation, and exposure duration, with both synergistic and occasionally antagonistic outcomes reported. These findings underscore the potential of SMFs as a tailored adjuvant strategy in cancer therapy, warranting precise optimization of experimental parameters. The subsequent section will review the effects of SMF with different parameters on the efficacy of different types of chemotherapeutic drugs, as summarized in Table 1.

4.1. SMF and Cisplatin

Cisplatin, a broad-spectrum chemotherapeutic agent, exerts its antitumor effects through multiple cytotoxic mechanisms [34]. However, drug resistance and adverse side effects limit its therapeutic efficacy. Therefore, exploring the combined application of SMFs and cisplatin may provide new strategies to potentiate cisplatin therapy without compromising its antitumor activity.

Recent studies have reported synergistic effects of SMFs and cisplatin, although findings are not entirely consistent (Table 1). For example, exposure of human chronic myeloid leukemia K562 cells to an 8.8 mT SMF enhanced the cytotoxic effects of cisplatin, potentially by reducing P-glycoprotein (P-gp) expression or increasing DNA damage [10,35]. Similarly, research using K562 cells observed the appearance of differently shaped holes on the cell surface following combined treatment [36], suggesting that SMF application may alter membrane permeability and increase the influx of anticancer drugs. Indirect support for this hypothesis comes from another study demonstrating that exposure to 10, 15, and 25 mT SMFs promoted cisplatin uptake in human ovarian carcinoma A2780 cells [23]. This resulted in increased intracellular cisplatin accumulation and reduced cisplatin resistance in the cisplatin-resistant cell A2780-CP [23]. Further studies demonstrated that the combination of cisplatin and SMFs significantly enhanced the cytotoxic effect on both A2780 and A2780-CP by increasing DNA damage, upregulating the apoptosis genes P53/P21, and upregulating the drug uptake gene copper transporter 1 (CTR1) [37]. Xu et al. also found that SMF may be able to synergize with cisplatin to inhibit tumor cell growth by

inducing DNA damage, thereby activating cell cycle checkpoints, such as the arrested of G2/M phase cells [38]. Furthermore, the combination of a 10 mT SMF with cisplatin reduced cell viability and increased sensitivity to ROS in HeLa cells [39]. Consistent with these findings, our previous in vitro and in vivo studies also demonstrated that SMFs can enhance the anti-tumor efficacy of cisplatin and reduce its nephrotoxicity by modulating oxidative stress levels [40].

However, synergy is not universal. Continuous exposure to a 1 T SMF for 3 days failed to enhance cisplatin's cytotoxic effects against various cancer cells, including breast cancer and cervical cancer cell lines [41]. Treatment duration can also influence outcomes: in human neuroblastoma SH-SY5Y cells, a 2 h SMF-cisplatin combination decreased cell viability and mitochondrial mass while increasing apoptosis and ROS, whereas a 24 h treatment antagonized cisplatin toxicity [42]. Overall, these studies highlight that the combined effects of SMFs and cisplatin are strongly influenced by cell type, magnetic field strength, and exposure duration, emphasizing the need for systematic investigations to optimize treatment parameters for maximal therapeutic benefit.

4.2. SMF and DOX

The efficacy of DOX, another widely used chemotherapeutic agent, has also been shown to be enhanced by SMF with certain parameters exposure. Research by Hao et al. demonstrated that the combination of 8.8 mT SMF and DOX for 12 h significantly inhibited the metabolic activity of K562 cells, with notable alterations in cell structure and increased DNA damage observed [43]. This study indicated that SMF treatment led to a reduction in P-gp expression, which is crucial for mediating drug resistance, thereby enhancing the cytotoxic effects of DOX [43]. Continuous exposure to 8.8 mT SMF for 24 h also enhanced DOX-induced death in Hepa1-6 hepatocellular carcinoma cells, causing cell-cycle arrest at G1 and G2/M phases [38]. Similarly, combining 10 mT SMF with DOX reduced the effective dose required to kill MCF-7 cells, potentially minimizing side effects associated with high-dose DOX treatment [44]. Despite the high levels of glutathione (GSH) in cancer cells, the SMF was able to increase ROS production and lifespan at low doses of DOX treatment and overcome GSH-mediated drug resistance [44]. A recent study found that SMF enhances DOX-induced cytotoxicity in osteosarcoma cells by promoting ROS production, altering metal ion (iron and calcium) homeostasis, and increasing apoptosis [45]. In vivo, 8.8 mT SMF augmented the antitumor effects of DOX in mammary carcinoma–bearing mice, although the precise mechanisms were not fully explored [46]. Overall, these findings highlight the potential of integrating SMF with DOX to enhance therapeutic efficacy while potentially reducing drug-associated toxicity.

4.3. SMF and 5-FU/Paclitaxel/Topotecan

5-FU can exert its antitumor effect by interfering with DNA synthesis [47], and paclitaxel exerts its anticancer effect by stabilizing microtubule structure, arresting mitosis and inducing apoptosis [48]. Using four different human tumor cell lines (HeLa, HCT116, CNE-2Z, and MCF-7), Luo et al. demonstrated that a 1 T SMF enhanced the cytotoxicity of 5-FU and its combination with paclitaxel, and that the underlying mechanism may be related to the fact that 1 T SMFs can affect microtubules to disturb mitotic spindles and delay cells exit from mitosis [41]. Notably, under the same conditions, SMF did not enhance cisplatin activity, indicating a drug-specific effect [41]. In HL-60 leukemia cells, exposure to a 1 T SMF for 72 h led to suppressed metabolic activity, both alone and in combination with multiple chemotherapeutic agents including 5-FU, cisplatin, doxorubicin, and vincristine [49]. Further, SMF synergized with paclitaxel in K562 cells by increasing DNA damage and cell membrane permeability, thereby reducing the effective starting

concentration of paclitaxel [50]. Consistently, Gellrich et al. reported that SMF enhanced the antitumor activity of paclitaxel by increasing tumor microvessel permeability [9]. Together, these findings suggest that SMF can augment the effects of 5-FU and paclitaxel, primarily through modulation of microtubule dynamics and tumor microenvironment properties.

Topotecan, a topoisomerase I inhibitor derived from plant alkaloids, also displayed enhanced tumor-suppressing activity when combined with a 1 T SMF. Interestingly, this effect was orientation-dependent: an upward-directed SMF increased topotecan efficacy, whereas a downward-directed SMF did not produce synergy [51]. This finding highlights the importance of SMF orientation as a critical experimental parameter.

Table 1. Summary of the effect of SMF on the antitumor activity of drugs.

Cell Lines/Animal	Agent Co-Used	SMF Intensity	Exposure Time	Critical Endpoint	Interaction	Refs
K562	Cisplatin	8.8 mT	8 h	Enhanced the killing potency; inhibited metabolic activity, increased cisplatin uptake, and decreased P-gp expression	Potentiation	[35]
K562		8.8 mT	12 h	Enhanced the anticancer effect, reducing the efficient killing concentration; increased DNA damage	Potentiation	[10]
Heap1-6		8.8 mT	24 h	Promoted the killing of tumor cells; increased the ratio of cells arrested in G2/M phase, enhanced DNA damage and caused larger holes in the cell membrane	Potentiation	[38]
K562		9 mT	12 h	Altered membrane permeability; holes appear on the cell surface	Potentiation	[36]
A2780 and A2780-CP cell lines		10, 15 and 25 mT	24/48/96 h	Increased the effect of cisplatin on cell viability percent and decreased the resistance of A2780-CP cells; produced large, verruca shaped structures at the surface of the cell membrane, increased drug uptake	Potentiation	[23]
A2780 and A2780-CP cell lines		15 mT	24/48/96 h	Increased DNA damage and cell death; elevated expression levels of p53, p21, and CTR1, with no significant effect on Bcl2 expression levels	Potentiation	[37]
Hela		10 mT	48 h	Decreased cell viability; increased ROS levels	Potentiation	[39]

Table 1. *Cont.*

Cell Lines/Animal	Agent Co-Used	SMF Intensity	Exposure Time	Critical Endpoint	Interaction	Refs
SH-SY5Y	Cisplatin	31.7–232.0 mT	2 h	Decreased cell viability; overexpression of the apoptosis-related cleaved caspase-3 protein, increase in ROS production and reduction in the number of mitochondria	Potentiation	[42]
			24 h	Antagonizing cisplatin toxicity; decreased levels of cleaved caspase-3 and ROS production	Antagonism	
MDA-MB231 cell/mice		0.2–0.4 T	24 h/24 d	Increased anti-tumor effects and reduced side effects; altered levels of oxidative stress	Potentiation	[40]
HeLa, HCT116, CNE-2Z and MCF7		1 T	3 d	No effect on the antitumor effect of cisplatin	No effect	[41]
K562	DOX	8.8 mT	12 h	Enhanced the cytotoxicity; altered cellular ultrastructure, cell cycle arrest in G2/M phase, increased DNA damage, decreased P-gp expression	Potentiation	[43]
Heap1-6		8.8 mT	24 h	Promote the killing of tumor cells; cells were almost arrested in G1 and G2/M phase, enhanced DNA damage and caused larger holes in the cell membrane	Potentiation	[38]
MCF-7		10 mT	24/48 h	Decreased required dose of chemotherapy drugs; boosted the generation and lifetime of ROS	Potentiation	[44]
G292		3, 6, 12, 24 mT	24 h	Enhanced cytotoxicity; promoted ROS production, altering iron and calcium homeostasis, and increased apoptosis	Potentiation	[45]
Breast cancer transplant mice		110 mT	4 × 4 h	Promoted tumor regression	Potentiation	[46]

Table 1. *Cont.*

Cell Lines/Animal	Agent Co-Used	SMF Intensity	Exposure Time	Critical Endpoint	Interaction	Refs
HeLa, HCT116, CNE-2Z and MCF7	5-FU/5-FU+ Paclitaxel	1 T	3 d	Increased anti-tumor effects; caused abnormal mitotic spindles	Potentiation	[41]
K562	Paclitaxel	8.8 mT	24 h	Reduced effective concentration; increased DNA damage, alteration of cell membrane permeability	Potentiation	[50]
A-Mel-3-tumor-bearing hamsters	Paclitaxel	587 mT	2 h	Improved antitumoral efficacy; inhibited tumor angiogenesis and increased tumor microvessel permeability	Potentiation	[9]
A172	TMZ	0.5 mT		Reduced cell viability more effectively	Potentiation	[52]
HepG2	Capsaicin	0.5 mT	72 h	Enhance the anti-cancer effect; increased the binding efficiency of capsaicin for the TRPV1 channel	Potentiation	[53]
Primary cultures and cell lines	Different apoptosis inducing agents	6 mT	24/48 h	Promotion/inhibition of apoptosis; interfered with apoptosis in a cell type- and exposure time-dependent manner	Potentiation/Antagonism	[54]
MDA-MB-468/T47D	TRAIL	3 mT	24 h	Induced apoptosis; cell cycle arrest at the G2/M phase, decreased survivin protein, and downregulated Cdc2 expression.	Potentiation	[55]
MCF-7	Vitamin D	0.2 T	3 h	Inhibition of cell proliferation	Potentiation	[56]
LLC-1 tumor-bearing mice	EGFR inhibitor cetuximab	587 mT	2 h/d, 13 d	Interfered with the effects of cetuximab; Interference of SMF and EGFR signaling	Antagonism	[57]
CNE-2Z, HCT116 c	EGFR inhibitor afatinib	1 T	3 d	Increased the antitumor efficacy; Inhibition of the EGFR pathway	Potentiation	[58]
CNE-2Z	mTOR inhibitor Torin 2	1 T	3 d	Increased the antitumor efficacy; Inhibition of the mTOR pathway	Potentiation	[59]

Table 1. *Cont.*

Cell Lines/Animal	Agent Co-Used	SMF Intensity	Exposure Time	Critical Endpoint	Interaction	Refs
HCT116, LoVo	Topotecan	Upward 1 T	2 d	Inhibition of cell proliferation; DNA synthesis	Potentiation	[51]
		Downward 1 T		Does not affect cellular proliferation	No effect	
Mice bearing GIST-T1	Imatinib mesylate	9.4 T	200 h	Improved the anti-tumor effect, reduced its toxicity and improved the mice mental health	Potentiation	[60]
Patients with advanced malignancy	Standard multi-agent chemotherapy regimens	3–28 mT	15 min	No differences in the white blood cell count and the platelet count in control and treated groups	No effect	[61]
Advanced lung cancer patients receiving chemotherapy	/	0.4 T, rotating frequency of 7.5 Hz	2 h/d, 21 d	Improved life quality and modulated blood cytokine concentration in advanced lung cancer patients	Potentiation	[62]
HL-60	Mixture of antineoplastic drugs 5-FU, cisplatin, doxorubicin and vincristine	1 T	72 h	Metabolic activity retardation	Potentiation	[49]

4.4. SMF and Molecularly Targeted Drugs

SMFs interact with molecularly targeted therapies, such as mTOR and EGFR inhibitors, in a drug-dependent manner, showing either synergistic or antagonistic effects that appear to be influenced by drug size, mechanism of action, and magnetic field strength. mTOR (mammalian target protein of rapamycin) inhibitors and EGFR (epidermal growth factor receptor) inhibitors are two important classes of targeted antitumor drugs that exert anticancer effects by interfering with the signaling pathways of tumor cells [63]. 1 T SMF enhances the antitumor efficacy of mTOR inhibitors on CNE2Z cells [59] and EGFR inhibitors on CNE2Z and HCT116 cells [58]. Interestingly, however, the combination of SMF with cetuximab—a monoclonal antibody targeting EGFR—produced antagonistic effects in Lewis lung carcinoma (LLC-1) mouse models: while either SMF or cetuximab alone significantly inhibited tumor growth, their combination failed to yield additional benefit [57]. Considering the SMF alone can inhibit EGFR activation and increase the efficacy of small-molecule EGFR inhibitors [58], whereas in combination with the SMF it antagonizes the efficacy of large-molecule EGFR-targeting antibodies [57], these findings suggest that drug molecular weight and binding modality may critically influence SMF–drug interactions, alongside other determinants such as field parameters, drug class, and tumor type.

Beyond moderate-intensity SMFs, strong SMFs have also been explored. A study employing a 9.4 T SMF demonstrated both intrinsic antitumor activity and synergistic effects with imatinib mesylate [60]. Prolonged SMF exposure (200 h) alone inhibited tumor growth by 62.88%, while its combination with 20 mg/kg imatinib achieved a tumor inhibition rate of 92.75%, comparable to the efficacy of high-dose imatinib (80 mg/kg). Notably, the high-dose regimen induced severe adverse effects, including reduced body weight gain, liver dysfunction, and depressive-like behavior, whereas the SMF-combined low-dose regimen substantially mitigated these toxicities, particularly behavioral abnormalities. These findings underscore the dual advantage of strong SMFs in enhancing efficacy and alleviating drug-associated side effects, pointing toward their translational potential in targeted therapy.

4.5. SMF and Other Drugs

Beyond classical agents such as cisplatin, DOX, and 5-FU, SMFs have also been investigated in combination with a variety of other drugs. For instance, co-treatment with apoptosis-inducing agents under a 6 mT SMF produced divergent results: while apoptosis was inhibited in several primary and tumor cell types, apoptosis was paradoxically enhanced in T-cell lymphoma 3DO cells [54]. This observation highlights the strong influence of cellular context on SMF–drug interactions. A more targeted example involves tumor necrosis factor-related apoptosis-inducing ligand (TRAIL), which exerts potent antitumor activity through selective engagement of death receptors on cancer cells, sparing normal tissues. Exposure to a 3 mT SMF significantly promoted TRAIL-induced apoptosis in resistant breast cancer cells by downregulating Cdc2 and subsequently survivin [55]. Importantly, SMF did not sensitize untransformed human mammary epithelial cells to TRAIL-mediated apoptosis, suggesting that this combination may offer a selective and safe strategy for overcoming TRAIL resistance in breast cancer [55].

SMFs have also been shown to modulate the effects of other bioactive agents. Pacini et al. reported that SMF abrogated the proliferative action of low-dose vitamin D on MCF-7 breast cancer cells while enhancing the anti-proliferative activity of high-dose vitamin D [56]. Similarly, a 2018 study demonstrated that SMF exposure potentiated the anticancer effect of the natural compound capsaicin in HepG2 hepatocellular carcinoma cells through a mitochondria-dependent apoptotic pathway. This synergism was proposed to arise from

an SMF-facilitated increase in capsaicin binding efficiency to its receptor channels on the cell surface [53].

4.6. Clinical Research

Compared with extensive cell and animal studies, clinical investigations on the effects of MFs in cancer therapy remain limited. In 2003, Joseph et al. conducted a Phase I trial to evaluate whether SMFs could alter chemotherapy metabolism and toxicity in patients with advanced cancer [61]. No significant increase in chemotherapy-related toxicity, assessed by white blood cell and platelet counts, was observed compared with historical controls [61]. While this study demonstrated the safety of combining SMF with chemotherapy, it did not provide evidence regarding its impact on antitumor efficacy. More recently, Zhu et al. performed a randomized, double-blind, controlled trial to assess 0.4 T rotating SMF therapy in lung cancer patients [62]. The results showed no significant reduction in tumor burden or prolongation of progression-free survival, suggesting that MF alone has minimal direct antitumor effects and does not enhance the efficacy of chemotherapy in this setting [62]. Factors such as short treatment duration, low MF intensity, and advanced disease stage may have contributed to these outcomes. Notably, MF exposure was associated with improved quality of life in patients receiving chemotherapy, indicating potential utility as a supportive adjuvant therapy [62]. Overall, these findings underscore that clinical application of SMFs in oncology requires rigorous safety evaluation, careful optimization of treatment parameters, and long-term studies to fully assess risks and potential benefits.

5. ELF-EMF and Drugs

Accumulating evidence indicates that ELF-EMFs can modulate the activity of chemotherapeutic drugs. In vitro and animal studies show that ELF-EMFs may enhance apoptosis, oxidative stress, and differentiation, thereby improving the efficacy of agents such as temozolomide, methotrexate, 5-FU, doxorubicin, and cisplatin. They may also help overcome drug resistance and allow for dose reduction. However, the outcomes vary considerably with cancer type, EMF parameters, and drug specificity. Clinical data remain limited, with small pilot studies suggesting benefits in reducing toxicity and improving tolerance but lacking survival evidence. Overall, ELF-EMFs hold promise as adjuvants in chemotherapy, yet their application requires standardized protocols and rigorous clinical validation. The following section will present a compendium of the effects that differing parameters of ELF-EMF have on the anti-cancer effects of a variety of chemotherapeutic agents, as summarized in Table 2.

5.1. ELF-EMF and Cisplatin/Carboplatin

Platinum-based chemotherapeutics, such as cisplatin and carboplatin, are widely used in cancer treatment, and accumulating evidence indicates that their efficacy can be either enhanced or attenuated by ELF-EMF exposure, depending on cellular and experimental contexts. Most studies suggest that ELF-EMFs can enhance the efficacy of platinum-based chemotherapeutic agents by modulating cellular processes. For example, the combination of ELF-EMF with cisplatin significantly increased the sensitivity of cisplatin-resistant ovarian cancer cells to the drug, achieving this effect by inducing apoptosis and modulating the expression of key genes, such as P53 and MMP-2 [64]. Similarly, in MCF-7 and SH-SY5Y cells, cisplatin + ELF-EMF co-treatment enhanced the downregulation of non-homologous end-joining pathway-related genes compared with cisplatin alone, suggesting that ELF-EMF may potentiate cisplatin cytotoxicity by sensitizing cells to DNA double-strand breaks [65]. Consistent with this, exposure to 50 Hz ELF-EMF in combination with cisplatin and bleomycin increased drug sensitivity in MCF-7 cells, but not in SH-SY5Y

cells, an effect linked to cell-type-specific differences in DNA repair gene expression (e.g., GADD45A, XRCC1, Ku70, Ku80) [66]. These findings indicate that ELF-EMF may enhance cisplatin efficacy by modulating DNA repair pathways, thereby improving tumor selectivity while sparing neuronal cells.

In vivo evidence further supports these observations. Yuan et al. reported that combined exposure to cisplatin and a superimposed MF (SMF + 50 Hz ELF-EMF) significantly enhanced antitumor effects in both nephroblastoma and neuroblastoma cell lines, as well as in G401 nephroblastoma xenografts in nude mice [67]. The combined treatment not only reduced tumor mass but also caused only mild liver injury, while MF exposure alone did not impair liver or kidney function [67]. Similarly, in Ehrlich carcinoma models, ELF-EMF + cisplatin co-treatment significantly increased DNA damage and inhibited tumor growth [68]. Together, these studies reinforce the potential of ELF-EMF as a promising adjuvant to platinum-based chemotherapy.

However, not all findings are consistent. In the AT478 carcinoma cells, exposure to 50 Hz, 1 mT ELF-EMF for a period of 16 min resulted in a reduction in the effects of cisplatin-induced oxidative stress and DNA damage, as well as a further decrease in MDA levels, suggesting an antagonistic effect [69]. In contrast, ELF-EMF alone increased oxidative stress, raising the possibility that EMF effects are highly context-dependent [69]. Likewise, in human glioblastoma cells, carboplatin cytotoxicity was attenuated when combined with 50 Hz, 70 G ELF-EMF for 24 h, though the underlying mechanisms remain unclear [70]. Taken together, these studies highlight that while ELF-EMF can enhance the anticancer activity of cisplatin by promoting DNA damage and apoptosis, conflicting reports underscore that the outcomes are strongly dependent on cell type, field strength, and exposure duration. Future work should systematically evaluate different MF parameters across multiple tumor models to establish reproducible therapeutic benefits.

5.2. ELF-EMF and Temozolomide

Temozolomide (TMZ) is the standard first-line chemotherapeutic agent for glioblastoma multiforme, yet resistance limits its efficacy in 60–75% of patients [71,72]. Recent studies indicate that ELF-EMF exposure can potentiate the cytotoxic effects of TMZ, providing a promising approach to overcome drug resistance in GBM. For instance, Zeinab et al. demonstrated that the combination of TMZ with a 100 Hz, 100 G ELF-EMF markedly enhanced apoptosis in U87 and T98G glioblastoma cells [73]. This was associated with upregulation of P53, Bax, and Caspase-3, alongside downregulation of Bcl-2 and Cyclin-D1. ROS production and expression of the redox-sensitive gene HO-1 were also elevated, suggesting that ELF-EMF may strengthen TMZ's pro-apoptotic activity through oxidative stress and redox-regulatory mechanisms. In addition, combined treatment was shown to decrease stem cell marker expression and promote differentiation of glioblastoma cells, offering a potential strategy to overcome TMZ resistance [74]. Consistent with these findings, studies in glioblastoma A172 cells reported that SMFs (50 G) or ELF-EMFs (10 Hz, 50 G) combined with TMZ reduced cell viability more effectively than TMZ alone [52]. This effect was accompanied by increased free radical generation and enhanced p53 gene and protein expression, supporting a role for MF–mediated oxidative stress and p53 pathway activation in sensitizing cells to TMZ. Similarly, in T98 and A172 glioblastoma cells, exposure to 50 Hz, 70 G EMF synergized with TMZ to inhibit cell proliferation and migration while partially reversing TMZ resistance [75]. Mechanistically, these effects were linked to p53 upregulation, Cyclin-D1 suppression, and modulation of MGMT (O6-methylguanine DNA methyltransferase) expression.

In summary, TMZ not only exerts antitumor effects through apoptosis but also induces differentiation in glioblastoma cells. Importantly, ELF-EMF can amplify these effects,

enabling the possibility of achieving comparable therapeutic efficacy with lower TMZ doses, thereby reducing treatment-associated toxicity.

5.3. ELF-EMF and Antimetabolites (MTX/5-FU)

Current evidence indicates that ELF-EMF can modulate the cytotoxicity of antimetabolite drugs, but the direction and magnitude of this effect depend strongly on the drug type, cancer cell line, and field parameters. Stratton et al. reported that ELF-EMFs enhanced methotrexate cytotoxicity by inducing transient membrane damage, thereby facilitating increased drug uptake in cancer cells [76]. This so-called "dose-loading" effect enabled effective treatment at much lower drug concentrations. However, another study showed that 25 Hz pulsed EMF exposure (1.5 mT, 2 h/day for 3 days) did not alter methotrexate cytotoxicity in MCF-7 breast cancer cells, suggesting that EMF modulation of chemotherapy is not universal and may be highly condition-specific [77].

In the case of 5-FU, Han et al. demonstrated that pre-exposure of MCF-7 cells to 50 Hz, 1 mT EMF for 12 h enhanced the antiproliferative effects of 5-FU, whereas no such effect occurred in normal MCF10A breast epithelial cells [78]. This selective sensitization of tumor cells may result from intrinsic cellular differences or culture conditions. Importantly, this raises the possibility that ELF-EMF could be used to synchronize tumor cells into specific cell-cycle phases, thereby improving the efficacy of cycle-specific chemotherapeutic agents. Conversely, other studies reported opposing results. For example, exposure of Caco-2 colon cancer cells to 4 mT ELF-EMF for 10 min significantly reduced the therapeutic efficacy of 5-FU [79]. These conflicting findings underscore that the outcome of ELF-EMF–drug combinations is highly context-dependent and can vary between synergistic and antagonistic interactions.

5.4. ELF-EMF and Anthracyclines/Other Drugs

The interaction between ELF-EMF and anthracyclines or multidrug-resistant cancers is complex, showing both synergistic and antagonistic effects that are dependent on the tumor model and treatment sequence. In MCF-7 breast cancer cells, 50 Hz, 20 mT ELF-EMF enhanced DOX-induced ROS generation, apoptosis, and cell-cycle arrest, thereby potentiating its antiproliferative activity [80]. In contrast, in SH-SY5Y neuroblastoma cells, exposure to 50 Hz, 1 mT ELF-EMF increased resistance to doxorubicin, reducing its cytotoxicity in a persistent, low-intensity–sensitive manner [81]. In uterine sarcoma MES-SA cells, ELF-EMF markedly enhanced the cytotoxicity of cisplatin, doxorubicin, and daunorubicin, with cisplatin + EMF reducing cell viability by approximately 60% [82]. In the drug-resistant MES-SA/Dx5 variant overexpressing MDR1, EMF also potentiated cisplatin activity, though its effects on doxorubicin and daunorubicin were considerably weaker [82]. Interestingly, etoposide, despite being an MDR1 substrate, was unaffected by EMF exposure [82]. These findings suggest that EMF does not directly modulate MDR1 activity but may enhance drug uptake through alternative influx pathways, thereby partially overcoming drug resistance. Similar observations were reported in HepG2 cells, where EMF potentiated cisplatin, mitomycin C, and doxorubicin activity, but not etoposide [83].

The sequence of EMF exposure relative to chemotherapy is also a critical determinant. BEMER (a low-frequency pulsed EMF device) pretreatment for 8 min failed to enhance sensitivity to cisplatin, gemcitabine, or cetuximab [84]. By contrast, simultaneous BEMER therapy combined with HPMA copolymer-based DOX yielded a synergistic antitumor effect [85]. Similarly, exposing multidrug-resistant colon cancer cells simultaneously to PEMFs (1.5 mT, 1–25 Hz) and chemotherapy agents (vincristine, mitomycin C, or cisplatin) significantly increased cytotoxicity in a frequency- and drug-specific manner, whereas post-treatment EMF exposure produced minimal or no benefit [86].

Table 2. Summary of the effect of EMF on the antitumor activity of drugs.

Cell Lines/Animal	Agent Co-Used	EMF		Exposure Time	Critical Endpoint	Interaction	Refs
		Frequency	Intensity				
PC12, THP-1 and HeLa	Methotrexate	10 Hz	0.3 mT	30 min	Enhanced cellular uptake of methotrexate; induced transient plasma membrane pores/damage	Potentiation	[76]
MCF-7		25 Hz	1.5 mT	2 h/d, 3 d	Not alter cytotoxicity	No effect	[77]
MCF-7, SH-SY5Y	Cisplatin	50 Hz	0.50 mT	30 min (15 min field-on/15 min field-of)	Down-regulation of the genes involved in non-homologous end-joining pathway GADD45A mRNA levels were increased, mRNA levels of XRCC4, Ku80, Ku70 and DNA-PKcs were down-regulated.	Potentiation	[65]
G401, CHLA255, N2a cells		50 Hz	5.1 mT (Superimposed SMF)	2 h/d, 3 d	Decreased cell proliferation and induced cell apoptosis	Potentiation	[67]
G401 Tumor Model in Nude Mice				80 min/d, 15 d	Decreased of tumor mass		
i.p. injection of Ehrlich ascites cells		50 Hz	10 mT	1 h/d, 2 weeks	Tumor growth inhibition; increased DNA damage	Potentiation	[68]
A2780		50 Hz	20 mT	2 h	Potentiated cisplatin-induced apoptosis. increased P53 gene expression and decreased MMP-2 expression	Potentiation	[64]
MES-SA and MES-SA/Dx5		50 Hz	50 mT	−4 h	Enhanced the cytotoxicity	Potentiation	[82]
HepG2		50 Hz	50 mT	−4 h	Enhanced the cytotoxicity	Potentiation	[83]
AT478		50 Hz	1 mT	16 min	Reduced ROS and antioxidant enzyme activity (SOD, GSH-Px); reduced DNA damage; significantly reduced MDA levels.	Antagonism	[69]

Table 2. *Cont.*

Cell Lines/Animal	Agent Co-Used	EMF		Exposure Time	Critical Endpoint	Interaction	Refs
		Frequency	Intensity				
MCF-7	Cisplatin + Bleomycin	50 Hz	0.50 mT	30 min (15 min field-on/15 min field-of)	Increased drug sensitivity	Potentiation	[66]
SH-SY5Y	Cisplatin + Bleomycin	50 Hz	0.50 mT	30 min (15 min field-on/15 min field-of)	Drug sensitivity has not changed	No effect	[66]
U-87	Carboplatin	50 Hz	7 mT	24 h	Increased cell viability; reduced carboplatin-induced caspase-3 protein expression	Antagonism	[70]
A172	TMZ	10 Hz	5 mT	96 h	Inhibited cell viability, increased free radical production, and upregulating p53 gene and protein expression	Potentiation	[52]
T98, A172		50 Hz	7mT	6 h/d, multiple days	Enhanced the cytotoxicity of TMZ, inhibited cell migration; upregulating p53 expression, downregulating cyclin-D1, and partially affecting MGMT expression	Potentiation	[75]
U87, T98		100 Hz	10 mT	144 h	Increased cell apoptosis; increased expression of P53, Bax, and Caspase-3, decreased expression of Bcl-2 and Cyclin-D1, increased generation of ROS, and up-regulated expression of the HO-1 gene.	Potentiation	[73]
U87		100 Hz	10 mT	122 h,144 h	Enhanced the effects of TMZ; decreased expression of tumor stem cell markers (CD133, Nestin, and Notch4), increased expression of the differentiation marker GFAP, increased intracellular calcium concentration, SOD activity, and MDA levels	Potentiation	[74]

Table 2. *Cont.*

Cell Lines/Animal	Agent Co-Used	EMF		Exposure Time	Critical Endpoint	Interaction	Refs
		Frequency	Intensity				
SH-SY5Y	DOX	50 Hz	1 mT/100 μT	5 d/10 d	Reduced cytotoxicity; improvements in the activity of the major antioxidant and detoxification defensive systems, as well as by the activation of crucial regulators of the cellular redox environment.	Antagonism	[81]
MCF-7		50 Hz	20 mT	24 h	Inhibition of cell growth and proliferation; increased ROS production and promotion of apoptosis and enhanced arrest of MCF-7 cells in the G0-G1 phase	Potentiation	[80]
MES-SA and MES-SA/Dx5		50 Hz	50 mT	−4 h	MF does not directly modulate MDR1 activity but may instead facilitate anticancer drug uptake by influencing influx pathways	Potentiation	[82]
HepG2		50 Hz	50 mT	−4 h	Enhanced the cytotoxicity	Potentiation	[83]
MES-SA and MES-SA/Dx5	Daunorubicin	50 Hz	50 mT	−4 h	MF does not directly modulate MDR1 activity but may instead facilitate anticancer drug uptake by influencing influx pathways	Potentiation	[82]
HepG2	Mitomycin C	50 Hz	50 mT	−4 h	Enhanced the cytotoxicity	Potentiation	[83]
MES-SA and MES-SA/Dx5	Etoposide	50 Hz	50 mT	−4 h	Not alter cytotoxicity	No effect	[82]
HepG2		50 Hz	50 mT	−4 h	Not alter cytotoxicity	No effect	[83]
MCF-7	5-Fu	50 Hz	1 mT	Pre-exposure for 12 h	Enhanced antiproliferative effect; promoted DNA synthesis, induced entry into the S phase, and upregulated the expression levels of cell cycle-related proteins Cyclin D1 and Cyclin E (no effect on apoptosis and P53 expression)	Potentiation	[78]
Caco-2		50 Hz	4 mT	10 min	Reduced CT and ECT treatment efficacy	Antagonism	[79]

Table 2. *Cont.*

Cell Lines/Animal	Agent Co-Used	EMF		Exposure Time	Critical Endpoint	Interaction	Refs
		Frequency	Intensity				
UTSCC1, A549, MiaPaCa, DLD1	Cetuximab	30 Hz (BEMER therapy)	~13 μT	8 min	Not enhance the sensitivity of cancer cells	No effect	[84]
EL4 tumor-bearing mice	HPMA-bound doxorubicin	BEMER therapy	3.5–35 μT	30 min/4 h or continuous exposure, multiple days	Synergistic antitumor effect	Potentiation	[85]
HCA-2/1cch	Vincristine	1 Hz	1.5 mT	synchronous exposure for 1 h/after drug treatment, EMF treatment: 2 h/d, 2d	When EMF was applied simultaneously with drugs, a significant synergistic enhancement effect was observed; when EMF was applied after drug treatment, only a very weak or no synergistic effect was observed.	Potentiation/No effect	[86]
	Mitomycin C	25 Hz					
	Cisplatin	25 Hz					
Hodgkin's lymphoma patients	ABVD (Adriamycin, Bleomycin, Vinblastine and Dacarbazine)	1 to 100 Hz	1 to 100 μT	/	Reduced the side effects of chemotherapy, specifically Myelotoxicity, reduced the oxidative stress	Potentiation	[87]

5.5. Clinical Research

Platinum Clinical investigations combining ELF-EMF with chemotherapy remain limited, often constrained by small sample sizes and short follow-up periods. One notable device, SEQEX, can generate 30 different electromagnetic waveforms with intensities ranging from 1 to 100 μT and frequencies between 1 and 100 Hz. Rossi et al. conducted a pilot study in 18 patients with Hodgkin's lymphoma undergoing chemotherapy, in which nine patients received adjunctive ELF-EMF treatment while nine served as controls. The results showed that ELF-EMF exposure reduced oxidative stress and chemotherapy-induced bone marrow toxicity, thereby potentially improving patients' quality of life [87]. While these findings are encouraging, the long-term safety and therapeutic relevance of ELF-EMF remain uncertain. Larger, randomized, multicenter trials are needed to validate these preliminary observations and to determine their applicability across diverse cancer types.

6. Mechanistic Insights: How MFs Modulate Drug Response

SMFs and ELF-EMFs have been shown to enhance the efficacy of chemotherapeutic agents through multifaceted interactions at the cellular and molecular levels. These interactions can be broadly classified into four core biological processes: membrane transport, cell cycle regulation, oxidative stress modulation, and apoptosis induction (Figure 1). While each mechanism has been independently reported, it is important to note that these processes are not isolated but interconnected, and their interplay is highly context-dependent, varying with magnetic field parameters, drug type, and cellular phenotype.

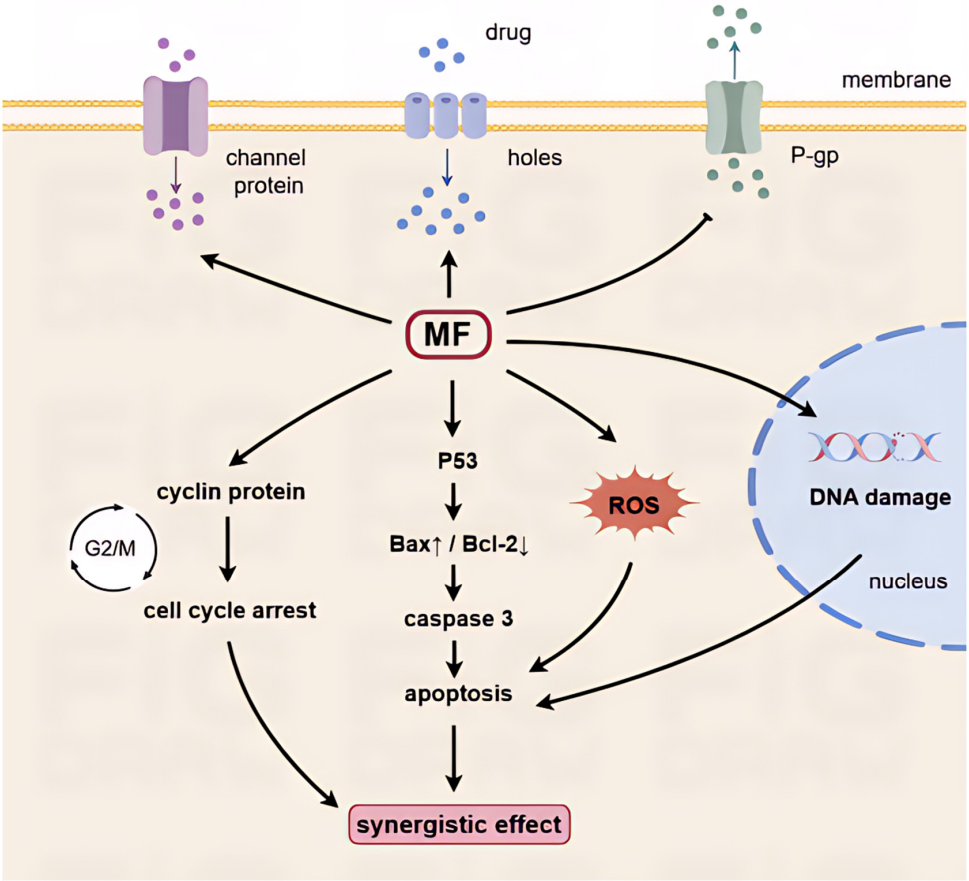

Figure 1. Mechanistic model of magnetic field-assisted antitumor drugs. Magnetic fields modulate multiple cellular processes to enhance chemotherapeutic efficacy. They remodel membrane structure and drug transporter expression to increase intracellular drug accumulation; perturb cell cycle checkpoints

to sensitize tumor cells to phase-specific cytotoxicity; elevate ROS levels and disrupt redox homeostasis, overcoming antioxidant-mediated drug resistance; and amplify apoptosis via DNA damage and pro-apoptotic signaling. These pathways are interconnected, with ROS, DNA damage, and altered membrane dynamics creating feedback loops that collectively enhance drug response. Directionality, intensity, and duration of MF exposure critically influence these outcomes.

6.1. Membrane Permeability and Drug Transport

The plasma membrane serves as the primary interface between MFs and cells, and its biophysical properties can be modulated by MF exposure, thereby influencing drug influx and efflux. Experimental evidence suggests that MFs can reorganize phospholipid bilayers due to diamagnetic anisotropy, reducing acyl chain flexibility and increasing membrane rigidity [88,89]. This restructuring alters lipid raft dynamics, potentially modifying the function of membrane-embedded proteins such as transporters and ion channels [90,91]. Several investigations have demonstrated that exposure to SMFs or ELF-EMFs in combination with chemotherapeutic agents such as cisplatin, paclitaxel, and methotrexate induces morphological changes in the cell membrane [23,36,38,50,76]. These alterations include the formation of holes or protrusions on the cell membrane surface, which have the potential to enhance the absorption of the drug by tumor cells [23,76].

P-gp, a transmembrane glycoprotein, functions as an ATP-dependent efflux pump that actively transports intracellular drugs out of cells, contributing to multidrug resistance [92,93]. In K562 cells, exposure to SMFs reduced P-gp expression, resulting in increased retention of cisplatin and Adriamycin [35,43]. This suggests that MFs can partially overcome drug resistance by modulating transporter activity. Conversely, MFs may also enhance drug influx. Higher expression levels of CTR1 are positively correlated with intracellular accumulation of platinum-based agents such as cisplatin, leading to improved therapeutic outcomes [94,95]. When cisplatin was combined with SMF, not only were the cytotoxic effects enhanced in both sensitive and resistant ovarian cancer cells, but CTR1 expression was also significantly upregulated, thereby facilitating drug entry [37].

In addition to regulating transporter activity, MFs may influence drug transport through calcium signaling. Co-treatment with ELF-EMFs and temozolomide (TMZ) in U87 cells elevated intracellular Ca^{2+} levels [74]. Since calcium signaling controls key cellular processes, including apoptosis, gene expression, and drug uptake, MF-induced modulation of calcium homeostasis represents another mechanism by which MFs can enhance chemotherapeutic efficacy [96].

Collectively, these findings indicate that MFs can modulate membrane structure and function, regulate both efflux and influx transporters, and influence intracellular signaling pathways, all of which contribute to altered drug permeability and retention in tumor cells. These changes at the membrane level can also influence downstream processes such as calcium signaling, oxidative stress, and apoptosis, thereby linking membrane effects to broader cellular responses.

6.2. Cell Cycle Perturbation and Mitotic Arrest

The cell cycle consists of G1, S, G2 and M phases, which are closely related to cell differentiation, growth and death [97]. MFs can potentiate the efficacy of chemotherapeutic agents by disrupting cell cycle progression, modulating checkpoint regulators, and inducing phase-specific arrest. For instance, SMFs enhanced G2/M arrest in K562 and Hepa1-6 cells exposed to cisplatin or Adriamycin, accompanied by elevated DNA damage and cell ultrastructure alteration [38,43].

The cell cycle is tightly regulated by a series of cyclins and cyclin-dependent kinase (CDKs), which are the checkpoints for cell cycle progression at each stage [98]. Exposure to ELF-EMFs promoted more MCF-7 cells to enter the S phase of cell cycle by upregulating

Cyclin E and Cyclin D1, and because cells in S phase are more sensitive to 5-FU, this leads to an increase in the cytotoxic effect of 5-FU on the cancer cells [78]. However, under these conditions, ELF-EMFs did not affect apoptosis or p53 expression, indicating that their chemo-sensitizing effect in this context is likely mediated by cell cycle redistribution rather than apoptotic signaling [78].

In the case of Adriamycin, ELF-EMF co-treatment induced G0/G1 arrest and DNA degradation in MCF-7 cells, supporting its role in augmenting cell cycle blockade [80]. Moreover, 1 T SMFs disrupted mitotic spindle formation and delayed mitotic exit in multiple tumor cell lines (e.g., HCT116, MCF-7), synergizing with 5-FU and paclitaxel to suppress proliferation [41].

Taken together, these findings suggest that MFs can modulate cell cycle kinetics in a phase- and drug-dependent manner. By forcing tumor cells into phases of heightened drug susceptibility or disrupting mitotic processes, MFs increase the vulnerability of cancer cells to chemotherapeutic agents, thereby offering a potential strategy to enhance treatment efficacy.

6.3. Oxidative Stress and Redox Modulation

ROS are both effectors and regulators of chemotherapy-induced cytotoxicity [99]. MFs can modulate this redox balance, often shifting it toward a pro-oxidant state when combined with chemotherapeutic agents. The free radical recombination hypothesis suggests that the MF can influence the level of free radicals by regulating the singlet and triplet states of unpaired electrons [100,101]. Through this mechanism, MFs can enhance the oxidative stress induced by anticancer drugs. Experimental studies provide compelling evidence for this synergy. MF exposure increases ROS production in tumor cells, thereby amplifying the cytotoxicity of agents such as DOX, TMZ, and cisplatin [39,73,80]. In spite of high a GSH (a key antioxidant) level in cancer cell, SMF boosts the generation and lifetime of ROS at low dose of DOX and overcame to GSH mediated drug resistance [44]. This suggests that MFs may help circumvent redox buffering mechanisms employed by cancer cells for drug evasion.

Malondialdehyde (MDA) is a marker of oxidative stress and is produced during the attack of free radicals to membrane lipoproteins [102]. Superoxide dismutase (SOD) plays an important role to protect the cell against formation of oxygen free radicals [103]. In U87 glioblastoma cells, combined exposure to ELF-EMFs and TMZ elevated both MDA levels and SOD activity, underscoring the dual modulation of oxidative damage and antioxidant response [74]. Clinically, Rossi et al. demonstrated that ELF-EMF treatment reduced chemotherapy-induced oxidative stress and bone marrow toxicity in Hodgkin's lymphoma patients, highlighting its potential translational relevance [87].

Together, these findings suggest that MFs act as redox modulators that intensify ROS-driven cytotoxicity, disrupt antioxidant defenses, and potentially alleviate chemotherapy resistance.

6.4. Apoptosis Induction and DNA Damage Enhancement

Apoptosis is a form of programmed cell death and a target for anti-tumor therapy, which plays an important role in cancer treatment [104]. MFs have been shown to potentiate pro-apoptotic signaling and exacerbate DNA damage, thereby amplifying tumor cell death. For example, 0.5 mT SMFs enhanced the anticancer activity of the natural compound capsaicin in HepG2 cells via the mitochondrial-dependent apoptotic pathway [53]. Similarly, in vitro studies demonstrated that ELF-EMF inhibited proliferation, induced apoptosis in nephroblastoma and neuroblastoma cells, and improved the efficacy of cisplatin [67]. In glioblastoma U87 cells, ELF-EMF combined with TMZ triggered apoptosis through

upregulation of Bax, Caspase-3, and P53, alongside downregulation of Bcl-2 [73]. This synergistic effect is also supported by the findings that exposure to MF leads to an increase in the production of ROS [39,73,80], a key regulator of apoptosis [105].

In general, the process of apoptosis that is induced by genotoxins is primarily attributable to DNA damage [106], with DNA double-strand breaks (DSBs) being considered among the most severe forms of DNA lesions [107]. Repetitive exposure to ELF-EMF has been demonstrated to induce DNA damage and the accumulation of DSBs, thereby triggering apoptosis in Hela and MCF7 cell lines [12,108]. Importantly, co-treatment with EMFs and cisplatin further suppressed the expression of non-homologous end-joining repair genes, suggesting that MFs may sensitize tumor cells to DNA damage by impairing repair capacity and thus enhance the efficacy of DNA-targeting chemotherapies [65]. In some cases, upward-directed 1 T SMF enhanced the effect of topotecan, a DNA synthesis inhibitor, whereas a downward-directed field did not [51]. Mechanistically, upward SMFs appear to synergize with topotecan by exacerbating the formation of positive DNA supercoiling and inhibiting its relaxation, thereby strongly suppressing cancer cell proliferation, while downward SMFs lack this cooperative effect.

6.5. Integration and Crosstalk

Collectively, the effects of MFs on cancer cells cannot be fully explained by any single mechanism. Instead, these pathways operate in concert: membrane alterations regulate calcium signaling and drug uptake, oxidative stress amplifies DNA damage and apoptotic cascades, and cell cycle arrest is often triggered in parallel with genotoxic stress. Apoptosis thus emerges as a downstream integration point of these events. Recognizing this mechanistic crosstalk is critical for understanding why MF–drug interactions produce diverse experimental outcomes and may help identify parameter "windows" that consistently favor therapeutic synergy.

7. Key Challenges and Scientific Controversies

Despite encouraging preclinical evidence, the integration of MFs into cancer chemotherapy remains hindered by a number of critical scientific and translational challenges. These barriers span from experimental inconsistencies to unresolved mechanistic ambiguities and technological constraints.

7.1. Lack of Parameter Standardization

A major limitation in current research is the heterogeneity of MF exposure protocols. Across published studies, field strength varies from micro-tesla to several tesla, frequencies span from static to 100 hertz, and exposure durations range from minutes to days (As shown in Tables 1 and 2). Moreover, studies rarely justify the selected parameters or explore dose–response relationships systematically. This variability makes it difficult to compare findings, establish reproducibility, or develop consensus guidelines for therapeutic use. It should be noted that the biological effects of magnetic fields appear to occur within specific intensity- and frequency-dependent "windows," yet these ranges remain difficult to generalize due to variations in experimental models, field parameters, and drug types. Future research should adopt standardized reporting frameworks (e.g., MF exposure logs), explore threshold/plateau effects, and define reproducible "therapeutic windows" for MF parameters.

7.2. Mechanistic Ambiguity and Biological Complexity

Although various mechanisms have been proposed—membrane modulation, ROS generation, DNA damage, and cell cycle arrest—none have been fully validated in vivo, and most are context-dependent, varying with cell type, genetic background, and microen-

vironmental conditions. For example, the same MF exposure may enhance 5-FU effect in one cell line, but this effect was not observed in another [78]. Using the same experimental parameters, MF enhanced the antitumor effects of 5-FU and its combination with paclitaxel, but not with cisplatin [41]. It is currently unclear what causes these results. We recommend that employ multi-omics profiling (transcriptomics, metabolomics, phosphorproteomics) under MF exposure to identify conserved molecular signatures and regulatory nodes.

7.3. Limited In Vivo and Clinical Translation

While numerous in vitro studies show synergistic effects, in vivo validation is sparse, and human clinical trials are virtually nonexistent or inconclusive. Only a handful of clinical studies have evaluated MF-assisted chemotherapy, with generally neutral or quality-of-life–oriented outcomes [62]. Furthermore, lack of scalable, precise, and safe MF-generating devices for human treatment limits real-world feasibility. In future, researchers should design animal studies with clinically relevant tumor models and develop wearable or targeted MF delivery systems that enable spatial control and integration with standard therapy. Next, initiate early-phase safety-focused trials to evaluate tolerability and pharmacodynamic effects of MF exposure in humans.

7.4. Interdisciplinary Gaps and Engineering Challenges

Progress in MF–chemo synergy is inherently multidisciplinary, requiring coordination between physics, bioengineering, oncology, and pharmacology. However, most studies are conducted in disciplinary silos, resulting in oversimplified biological models or suboptimal MF systems. We propose to foster collaboration between materials scientists, magnetic engineers and oncologists. At the same time, develop open-source MF exposure platforms and modeling tools for experimental standardization.

7.5. Need for Predictive and Personalized Approaches

Current research assumes that MF effects are broadly applicable across cell types and drug classes. However, preliminary evidence suggests that MF–drug synergy is highly specific, depending on cell type (e.g., epithelial vs. hematopoietic), drug class (e.g., alkylating agents vs. topoisomerase inhibitors), patient redox status or genetic background. Thus, machine learning or systems pharmacology can be used to predict MF-drug synergism based on cellular or patient characteristics and to identify biomarkers of MF responsiveness to guide clinical applications.

8. Conclusions and Future Perspective

Over the past two decades, growing evidence has shown that magnetic fields—particularly SMFs and ELF-EMFs—can modulate biological pathways that critically influence the efficacy of antitumor agents. By altering membrane permeability, redox balance, cell cycle progression, and apoptotic signaling, MFs have emerged as promising biophysical adjuvants in cancer therapy.

Despite these advances, current research remains fragmented and predominantly preclinical. Most findings rely on in vitro models with limited translational relevance, and while the mechanistic insights are biologically plausible, they require further validation in more complex systems. Variability in MF parameters, tumor types, and drug-specific responses underscores the need for standardized protocols and a system-level investigative framework.

Looking ahead, progress will depend on several strategic directions. Mechanistic precision can be achieved through multi-omics approaches and real-time imaging to unravel the molecular dynamics of MF–drug interactions. Technological innovation is required to develop spatially controllable, cost-effective, and clinically compatible MF delivery systems.

Greater preclinical rigor, including the use of patient-derived xenografts and organoid models, will provide more predictive insights than traditional cell lines. Equally important is clinical exploration, with carefully designed early-phase trials focusing on safety, pharmacodynamics, and biomarker identification. Finally, considering the heterogeneity of MF responses, the integration of predictive modeling and MF-sensitivity biomarkers may enable the development of personalized therapeutic strategies.

In summary, MF-based modulation of antitumor agents represents a novel, non-invasive, and potentially transformative approach to enhance drug efficacy while mitigating systemic toxicity. Although significant challenges remain, the convergence of biophysics, oncology, and system pharmacology offers fertile ground for innovation. With interdisciplinary collaboration and methodological rigor, MF-assisted therapies may evolve into a valuable component of future precision oncology.

Author Contributions: Conceptualization, X.Y. and Y.L.; investigation, X.Y. and Y.L.; validation, X.Y. and Y.L.; resources, X.Y.; writing—original draft preparation, X.Y.; writing—review and editing, X.Y. and Y.L.; visualization, X.Y.; supervision, X.Y.; project administration, X.Y. All authors have read and agreed to the published version of the manuscript.

Funding: This work was supported by the Natural Science Research Project of Anhui Educational Committee (2024AH050860) and High-Level Talents Research Startup Fund Project of Anhui Institute of Medicine (2024RC007).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflicts of interest.

Abbreviations

The following abbreviations are used in this manuscript:

MF	Magnetic Field
SMF	Static Magnetic Field
ELF-EMF	Extremely Low-Frequency Electromagnetic Field
RF-EMF	Radiofrequency Electromagnetic Field
TVMF	Time-Varying Magnetic Field
GMF	Gradient Magnetic Field
ROS	Reactive Oxygen Species
P-gp	P-glycoprotein
GSH	Glutathione
MDA	Malondialdehyde
SOD	Superoxide Dismutase
TMZ	Temozolomide
DOX	Doxorubicin
5-FU	5-Fluorouracil
EGFR	Epidermal Growth Factor Receptor
mTOR	Mammalian Target of Rapamycin
CDK	Cyclin-Dependent Kinase
CDC2	Cell Division Cycle 2
MDR1	Multidrug Resistance Protein 1
CTR1	Copper Transporter 1
GFAP	Glial Fibrillary Acidic Protein
DSB	Double-Strand Break
TRAIL	Tumor Necrosis Factor-Related Apoptosis-Inducing Ligand

IC50	Half Maximal Inhibitory Concentration
CD133, Nestin, Notch4	Cancer Stem Cell Markers
TRPV1	Transient Receptor Potential Vanilloid 1
HO-1	Heme Oxygenase-1
DNA-PKcs	DNA-dependent Protein Kinase Catalytic Subunit
Ku70/Ku80/XRCC4	DNA Repair Proteins
GADD45A	Growth Arrest and DNA Damage-inducible 45 Alpha

References

1. Sung, H.; Ferlay, J.; Siegel, R.L.; Laversanne, M.; Soerjomataram, I.; Jemal, A.; Bray, F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA Cancer J. Clin.* **2021**, *71*, 209–249. [CrossRef] [PubMed]
2. Kuderer, N.M.; Desai, A.; Lustberg, M.B.; Lyman, G.H. Mitigating acute chemotherapy-associated adverse events in patients with cancer. *Nat. Rev. Clin. Oncol.* **2022**, *19*, 681–697. [CrossRef] [PubMed]
3. Nussinov, R.; Tsai, C.-J.; Jang, H. Anticancer drug resistance: An update and perspective. *Drug Resist. Updates* **2021**, *59*, 100796. [CrossRef]
4. Behranvand, N.; Nasri, F.; Emameh, R.Z.; Khani, P.; Hosseini, A.; Garssen, J.; Falak, R. Chemotherapy: A double-edged sword in cancer treatment. *Cancer Immunol. Immunother.* **2021**, *71*, 507–526. [CrossRef]
5. Zhang, X.; Yarema, K.; Xu, A. *Biological Effects of Static Magnetic Fields*; Springer: Singapore, 2017.
6. Martino, C.F.; Portelli, L.; McCabe, K.; Hernandez, M.; Barnes, F. Reduction of the earth's magnetic field inhibits growth rates of model cancer cell lines. *Bioelectromagnetics* **2010**, *31*, 649–655. [CrossRef]
7. Destefanis, M.; Viano, M.; Leo, C.; Gervino, G.; Ponzetto, A.; Silvagno, F. Extremely low frequency electromagnetic fields affect proliferation and mitochondrial activity of human cancer cell lines. *Int. J. Radiat. Biol.* **2015**, *91*, 964–972. [CrossRef]
8. Wang, T.; Nie, Y.; Zhao, S.; Han, Y.; Du, Y.; Hou, Y. Involvement of midkine expression in the inhibitory effects of low-frequency magnetic fields on cancer cells. *Bioelectromagnetics* **2011**, *32*, 443–452. [CrossRef]
9. Gellrich, D.; Becker, S.; Strieth, S. Static magnetic fields increase tumor microvessel leakiness and improve antitumoral efficacy in combination with paclitaxel. *Cancer Lett.* **2014**, *343*, 107–114. [CrossRef] [PubMed]
10. Chen, W.-F.; Qi, H.; Sun, R.-G.; Liu, Y.; Zhang, K.; Liu, J.-Q. Static Magnetic Fields Enhanced the Potency of Cisplatin on K562 Cells. *Cancer Biother. Radiopharm.* **2010**, *25*, 401–408. [CrossRef]
11. Provenzano, A.E.; Amatori, S.; Nasoni, M.G.; Persico, G.; Russo, S.; Mastrogiacomo, A.R.; Gambarara, A.; Fanelli, M. Effects of Fifty-Hertz Electromagnetic Fields on Granulocytic Differentiation of ATRA-Treated Acute Promyelocytic Leukemia NB4 Cells. *Cell. Physiol. Biochem.* **2018**, *46*, 389–400. [CrossRef]
12. Crocetti, S.; Beyer, C.; Schade, G.; Egli, M.; Fröhlich, J.; Franco-Obregón, A. Low Intensity and Frequency Pulsed Electromagnetic Fields Selectively Impair Breast Cancer Cell Viability. *PLoS ONE* **2013**, *8*, e72944. [CrossRef]
13. Mousavi, M.; Baharara, J.; Shahrokhabadi, K. The Synergic Effects of *Crocus sativus* L. and Low Frequency Electromagnetic Field on VEGFR2 Gene Expression in Human Breast Cancer Cells. *Avicenna J. Med. Biotechnol.* **2014**, *6*, 123–127.
14. Buckner, C.A.; Buckner, A.L.; Koren, S.A.; Persinger, M.A.; Lafrenie, R.M. Exposure to a specific time-varying electromagnetic field inhibits cell proliferation via cAMP and ERK signaling in cancer cells. *Bioelectromagnetics* **2018**, *39*, 217–230. [CrossRef] [PubMed]
15. Ren, J.; Ding, L.; Xu, Q.; Shi, G.; Li, X.; Li, X.; Ji, J.; Zhang, D.; Wang, Y.; Wang, T.; et al. LF-MF inhibits iron metabolism and suppresses lung cancer through activation of P53-miR-34a-E2F1/E2F3 pathway. *Sci. Rep.* **2017**, *7*, 749. [CrossRef]
16. Novikov, V.V.; Novikov, G.V.; Fesenko, E.E. Effect of weak combined static and extremely low-frequency alternating magnetic fields on tumor growth in mice inoculated with the Ehrlich ascites carcinoma. *Bioelectromagnetics* **2009**, *30*, 343–351. [CrossRef]
17. Ali, F.M.; El-Gebaly, R.H.; Hamad, A.M. Combination of bacteriolytic therapy with magnetic field for Ehrlich tumour treatment. *Gen. Physiol. Biophys.* **2017**, *36*, 259–271. [CrossRef]
18. Chen, Z.; Liu, H.; Wang, H.; Wu, C.; Feng, H.; Han, J. Effect of low-frequency rotary magnetic fields on advanced gastric cancer: Survival and palliation of general symptoms. *J. Cancer Res. Ther.* **2018**, *14*, 815–819. [CrossRef]
19. Poniedziałek, B.; Rzymski, P.; Karczewski, J.; Jaroszyk, F.; Wiktorowicz, K. Reactive oxygen species (ROS) production in human peripheral blood neutrophils exposed in vitro to static magnetic field. *Electromagn. Biol. Med.* **2013**, *32*, 560–568. [CrossRef] [PubMed]
20. Jimenez, H.; Wang, M.; Zimmerman, J.W.; Pennison, M.J.; Sharma, S.; Surratt, T.; Xu, Z.-X.; Brezovich, I.; Absher, D.; Myers, R.M.; et al. Tumour-specific amplitude-modulated radiofrequency electromagnetic fields induce differentiation of hepatocellular carcinoma via targeting $Ca_V3.2$ T-type voltage-gated calcium channels and Ca^{2+} influx. *EBioMedicine* **2019**, *44*, 209–224. [CrossRef] [PubMed]

21. Lei, H.; Xu, Y.; Guan, R.; Li, M.; Hui, Y.; Gao, Z.; Yang, B.; Xin, Z. Effect of gyromagnetic fields on human prostatic adenocarcinoma cells. *OncoTargets Ther.* **2015**, *8*, 3489–3497. [CrossRef]
22. Fang, F.; Liu, C.; Huang, Q.; Dong, C.; Zhang, G.; Jiang, J.; Lu, S. Effect of static magnetic field on gene expression of human umbilical cord mesenchymal stem cells by transcriptome analysis. *Adv. Med. Sci.* **2024**, *69*, 281–288. [CrossRef]
23. Jalali, A.; Zafari, J.; Jouni, F.J.; Abdolmaleki, P.; Shirazi, F.H.; Khodayar, M.J. Combination of static magnetic field and cisplatin in order to reduce drug resistance in cancer cell lines. *Int. J. Radiat. Biol.* **2019**, *95*, 1194–1201. [CrossRef] [PubMed]
24. Ballo, M.T.; Conlon, P.; Lavy-Shahaf, G.; Kinzel, A.; Vymazal, J.; Rulseh, A.M. Association of Tumor Treating Fields (TTFields) therapy with survival in newly diagnosed glioblastoma: A systematic review and meta-analysis. *J. Neuro-Oncol.* **2023**, *164*, 1–9. [CrossRef]
25. Moser, J.C.; Salvador, E.; Deniz, K.; Swanson, K.; Tuszynski, J.; Carlson, K.W.; Karanam, N.K.; Patel, C.B.; Story, M.; Lou, E.; et al. The Mechanisms of Action of Tumor Treating Fields. *Cancer Res.* **2022**, *82*, 3650–3658. [CrossRef] [PubMed]
26. Fisher, J.P.; Adamson, D.C. Current FDA-Approved Therapies for High-Grade Malignant Gliomas. *Biomedicines* **2021**, *9*, 324. [CrossRef] [PubMed]
27. Markov, M.S. Angiogenesis, magnetic fields and 'window effects'. *Cardiology* **2010**, *117*, 54–56. [CrossRef]
28. Zhu, Y.-M.; Xu, D.; Ren, H.; Geng, J.; Xu, K. Metagenomic insights into the "window" effect of static magnetic field on nitrous oxide emission from biological nitrogen removal process at low temperature. *J. Environ. Manag.* **2021**, *298*, 113377. [CrossRef]
29. Repacholi, M.H. An overview of WHO's EMF project and the health effects of EMF exposure. In Proceedings of the International Conference on Non-Ionizing Radiation at UNITEN (ICNIR 2003) Electromagnetic Fields and Our Health, Kuala Lumpur, Malaysia, 20–22 October 2003.
30. Wang, H.; Zhang, X. Magnetic Fields and Reactive Oxygen Species. *Int. J. Mol. Sci.* **2017**, *18*, 2175. [CrossRef]
31. Yu, X.; Li, J.; Yang, X.; Fang, Z.; Zhang, X. Biological effects of magnetic field combined with irradiation. *Chem. Life* **2019**, *39*, 849–858. [CrossRef]
32. Engstrom, S. Physical mechanisms of non-thermal extremely-low-frequency magnetic-field effects. *Ursi Radio Sci. Bull.* **2004**, *77*, 95–106.
33. Israel, M.; Zaryabova, V.; Ivanova, M. Electromagnetic field occupational exposure: Non-thermal vs. thermal effects. *Electromagn. Biol. Med.* **2013**, *32*, 145–154. [CrossRef]
34. Rottenberg, S.; Disler, C.; Perego, P. The rediscovery of platinum-based cancer therapy. *Nat. Rev. Cancer* **2021**, *21*, 37–50. [CrossRef]
35. Zhang, K.; Chen, W.; Bu, T.; Qi, H.; Sun, R.; He, X. Decreased P-glycoprotein is associated with the inhibitory effects of static magnetic fields and cisplatin on K562 cells. *Bioelectromagnetics* **2014**, *35*, 437–443. [CrossRef]
36. Liu, Y.; Qi, H.; Sun, R.G.; Chen, W.F. An investigation into the combined effect of static magnetic fields and different anticancer drugs on K562 cell membranes. *Tumori* **2011**, *97*, 386–392. [CrossRef]
37. Zafari, J.; Rastegar-Pouyani, N.; Jouni, F.J.; Najjar, N.; Azarshin, S.Z.; Jafarzadeh, E.; Abdolmaleki, P.; Shirazi, F.H. Static magnetic field reduces cisplatin resistance via increasing apoptosis pathways and genotoxicity in cancer cell lines. *Sci. Rep.* **2024**, *14*, 5792. [CrossRef]
38. Xu, L.; Guo, W.; Liu, Y.; Zhang, X.; Yu, J.; Wu, W.; Zhao, T. Synergistic inhibitory effect of static magnetic field and antitumor drugs on Hepa1-6 cells. *Chin. J. Biotechnol.* **2015**, *31*, 1363–1374.
39. Kamalipooya, S.; Abdolmaleki, P.; Salemi, Z.; Jouni, F.J.; Zafari, J.; Soleimani, H. Simultaneous application of cisplatin and static magnetic field enhances oxidative stress in HeLa cell line. *Vitr. Cell. Dev. Biol.-Anim.* **2017**, *53*, 783–790. [CrossRef]
40. Yu, X.; Ji, X.; Fan, Y.; Yu, B.; Wang, X.; Feng, C.; Zhang, L.; Song, C.; Zhang, X. Static Magnetic Fields Protect against Cisplatin-Induced Kidney Toxicity. *Antioxidants* **2022**, *12*, 73. [CrossRef]
41. Luo, Y.; Ji, X.; Liu, J.; Li, Z.; Wang, W.; Chen, W.; Wang, J.; Liu, Q.; Zhang, X. Moderate intensity static magnetic fields affect mitotic spindles and increase the antitumor efficacy of 5-FU and Taxol. *Bioelectrochemistry* **2016**, *109*, 31–40. [CrossRef] [PubMed]
42. Vergallo, C.; Ahmadi, M.; Mobasheri, H.; Dini, L. Impact of Inhomogeneous Static Magnetic Field (31.7–232.0 mT) Exposure on Human Neuroblastoma SH-SY5Y Cells during Cisplatin Administration. *PLoS ONE* **2014**, *9*, e113530. [CrossRef]
43. Hao, Q.; Wenfang, C.; Xia, A.; Qiang, W.; Ying, L.; Kun, Z.; Runguang, S. Effects of a moderate-intensity static magnetic field and adriamycin on K562 cells. *Bioelectromagnetics* **2011**, *32*, 191–199. [CrossRef]
44. Verdom, B.H.; Abdolmaleki, P.; Behmanesh, M. The Static Magnetic Field Remotely Boosts the Efficiency of Doxorubicin through Modulating ROS Behaviors. *Sci. Rep.* **2018**, *8*, 990. [CrossRef]
45. Rajabi, F.; Hajipour-Verdom, B.; Abdolmaleki, P. Static magnetic field promotes the doxorubicin toxicity effects on osteosarcoma cells. *Sci. Rep.* **2025**, *15*, 11902. [CrossRef]
46. Gray, J.R.; Frith, C.H.; Parker, J.D. In vivo enhancement of chemotherapy with static electric or magnetic fields. *Bioelectromagnetics* **2000**, *21*, 575–583. [CrossRef]
47. Azwar, S.; Seow, H.F.; Abdullah, M.; Jabar, M.F.; Mohtarrudin, N. Recent Updates on Mechanisms of Resistance to 5-Fluorouracil and Reversal Strategies in Colon Cancer Treatment. *Biology* **2021**, *10*, 854. [CrossRef]
48. Zhu, L.; Chen, L. Progress in research on paclitaxel and tumor immunotherapy. *Cell. Mol. Biol. Lett.* **2019**, *24*, 40. [CrossRef]

49. Sabo, J.; Mirossay, L.; Horovcak, L.; Sarissky, M.; Mirossay, A.; Mojzis, J. Effects of static magnetic field on human leukemic cell line HL-60. *Bioelectrochemistry* **2002**, *56*, 227–231. [CrossRef]
50. Sun, R.-G.; Chen, W.-F.; Qi, H.; Zhang, K.; Bu, T.; Liu, Y.; Wang, S.-R. Biologic effects of SMF and paclitaxel on K562 human leukemia cells. *Gen. Physiol. Biophys.* **2012**, *31*, 1–10. [CrossRef]
51. Yang, X.; Li, Z.; Polyakova, T.; Dejneka, A.; Zablotskii, V.; Zhang, X. Effect of static magnetic field on DNA synthesis: The interplay between DNA chirality and magnetic field left-right asymmetry. *FASEB BioAdvances* **2020**, *2*, 254–263. [CrossRef]
52. Ashta, A.; Motalleb, G.; Ahmadi-Zeidabadi, M. Evaluation of frequency magnetic field, static field, and Temozolomide on viability, free radical production and gene expression (p53) in the human glioblastoma cell line (A172). *Electromagn. Biol. Med.* **2020**, *39*, 298–309. [CrossRef]
53. Chen, W.-T.; Lin, G.-B.; Lin, S.-H.; Lu, C.-H.; Hsieh, C.-H.; Ma, B.-L.; Chao, C.-Y. Static magnetic field enhances the anticancer efficacy of capsaicin on HepG2 cells via capsaicin receptor TRPV1. *PLoS ONE* **2018**, *13*, e0191078. [CrossRef]
54. Tenuzzo, B.; Chionna, A.; Panzarini, E.; Lanubile, R.; Tarantino, P.; Di Jeso, B.; Dwikat, M.; Dini, L. Biological effects of 6 mT static magnetic fields: A comparative study in different cell types. *Bioelectromagnetics* **2006**, *27*, 560–577. [CrossRef]
55. Lin, T.; Wan, L.; Qi, X.; Shi, W.; Lin, J. A moderate static magnetic field enhances TRAIL-induced apoptosis by the inhibition of Cdc2 and subsequent downregulation of survivin in human breast carcinoma cells. *Bioelectromagnetics* **2014**, *35*, 337–346. [CrossRef]
56. Pacini, S.; Aterini, S.; Pacini, P.; Ruggiero, C.; Gulisano, M.; Ruggiero, M. Influence of static magnetic field on the antiproliferative effects of vitamin D on human breast cancer cells. *Oncol. Res.* **1999**, *11*, 265–271.
57. Gellrich, D.; Schmidtmayer, U.; Eckrich, J.; Hagemann, J.; Becker, S.; Strieth, S. Modulation of Exposure to Static Magnetic Field Affects Targeted Therapy of Solid Tumors In Vivo. *Anticancer Res.* **2018**, *38*, 4549–4555. [CrossRef]
58. Zhang, L.; Wang, J.; Wang, H.; Wang, W.; Li, Z.; Liu, J.; Yang, X.; Ji, X.; Luo, Y.; Hu, C.; et al. Moderate and strong static magnetic fields directly affect EGFR kinase domain orientation to inhibit cancer cell proliferation. *Oncotarget* **2016**, *7*, 41527–41539. [CrossRef]
59. Zhang, L.; Yang, X.; Liu, J.; Luo, Y.; Li, Z.; Ji, X.; Wang, W.; Zhang, X. 1 T moderate intensity static magnetic field affects Akt/mTOR pathway and increases the antitumor efficacy of mTOR inhibitors in CNE-2Z cells. *Sci. Bull.* **2015**, *60*, 2120–2128. [CrossRef]
60. Tian, X.; Wang, C.; Yu, B.; Fan, Y.; Zhang, L.; Zhang, X. 9.4 T static magnetic field ameliorates imatinib mesylate-induced toxicity and depression in mice. *Eur. J. Nucl. Med. Mol. Imaging* **2023**, *50*, 314–327. [CrossRef]
61. Salvatore, J.R.; Harrington, J.; Kummet, T. Phase I clinical study of a static magnetic field combined with anti-neoplastic chemotherapy in the treatment of human malignancy: Initial safety and toxicity data. *Bioelectromagnetics* **2003**, *24*, 524–527. [CrossRef]
62. Zhu, M.; Yang, Z.; Yu, H.; Zhu, Q.; Xu, Y.; Li, Y.; Li, C.; Zhao, W.; Liang, Z.; Chen, L. The efficacy and safety of low-frequency rotating static magnetic field therapy combined with chemotherapy on advanced lung cancer patients: A randomized, double-blinded, controlled clinical trial. *Int. J. Radiat. Biol.* **2020**, *96*, 943–950. [CrossRef]
63. Bozec, A.; Ebran, N.; Radosevic-Robin, N.; Sudaka, A.; Monteverde, M.; Toussan, N.; Etienne-Grimaldi, M.; Nigro, C.L.; Merlano, M.; Penault-Llorca, F.; et al. Combination of mTOR and EGFR targeting in an orthotopic xenograft model of head and neck cancer. *Laryngoscope* **2016**, *126*, E156–E163. [CrossRef]
64. Baharara, J.; Hosseini, N.; Farzin, T.R. Extremely low frequency electromagnetic field sensitizes cisplatin-resistant human ovarian adenocarcinoma cells via P53 activation. *Cytotechnology* **2016**, *68*, 1403–1413. [CrossRef]
65. Sanie-Jahromi, F.; Saadat, I.; Saadat, M. Effects of extremely low frequency electromagnetic field and cisplatin on mRNA levels of some DNA repair genes. *Life Sci.* **2016**, *166*, 41–45. [CrossRef]
66. Sanie-Jahromi, F.; Saadat, M. Different profiles of the mRNA levels of DNA repair genes in MCF-7 and SH-SY5Y cells after treatment with combination of cisplatin, 50-Hz electromagnetic field and bleomycin. *Biomed. Pharmacother.* **2017**, *94*, 564–568. [CrossRef]
67. Yuan, L.; Wang, C.; Zhu, K.; Li, H.; Gu, W.; Zhou, D.; Lai, J.; Zhou, D.; Lv, Y.; Tofani, S.; et al. The antitumor effect of static and extremely low frequency magnetic fields against nephroblastoma and neuroblastoma. *Bioelectromagnetics* **2018**, *39*, 375–385. [CrossRef]
68. El-Bialy, N.S.; Rageh, M.M. Extremely Low-Frequency Magnetic Field Enhances the Therapeutic Efficacy of Low-Dose Cisplatin in the Treatment of Ehrlich Carcinoma. *BioMed Res. Int.* **2013**, *2013*, 189352. [CrossRef]
69. Bułdak, R.J.; Polaniak, R.; Bułdak, Ł.; Żwirska-Korczala, K.; Skonieczna, M.; Monsiol, A.; Kukla, M.; Duława-Bułdak, A.; Birkner, E. Short-term exposure to 50 Hz ELF-EMF alters the cisplatin-induced oxidative response in AT478 murine squamous cell carcinoma cells. *Bioelectromagnetics* **2012**, *33*, 641–651. [CrossRef]
70. Amiri, M.; Basiri, M.; Eskandary, H.; Akbarnejad, Z.; Esmaeeli, M.; Masoumi-Ardakani, Y.; Ahmadi-Zeidabadi, M. Cytotoxicity of carboplatin on human glioblastoma cells is reduced by the concomitant exposure to an extremely low-frequency electromagnetic field (50 Hz, 70 G). *Electromagn. Biol. Med.* **2018**, *37*, 138–145. [CrossRef]

71. Wijaya, J.H.; Hulou, S.; Lucke-Wold, B.; V, W.B.G.; Lamprecht, C.B.; Ruchika, F.; Schneider, B.; Foster, D.; Abolfazli, P.; Quintero-Consuegra, M.D.; et al. Socioeconomic status as a determinant of survival in glioblastoma: A systematic review and meta-analysis. *Neurosurg. Rev.* **2025**, *48*, 500. [CrossRef]
72. Chamberlain, M.C. Temozolomide: Therapeutic limitations in the treatment of adult high-grade gliomas. *Expert Rev. Neurother.* **2010**, *10*, 1537–1544. [CrossRef]
73. Akbarnejad, Z.; Eskandary, H.; Dini, L.; Vergallo, C.; Nematollahi-Mahani, S.N.; Farsinejad, A.; Abadi, M.F.S.; Ahmadi, M. Cytotoxicity of temozolomide on human glioblastoma cells is enhanced by the concomitant exposure to an extremely low-frequency electromagnetic field (100 Hz, 100 G). *Biomed. Pharmacother.* **2017**, *92*, 254–264. [CrossRef]
74. Ahmadi-Zeidabadi, M.; Akbarnejad, Z.; Esmaeeli, M.; Masoumi-Ardakani, Y.; Mohammadipoor-Ghasemabad, L.; Eskandary, H. Impact of extremely low-frequency electromagnetic field (100 Hz, 100 G) exposure on human glioblastoma U87 cells during Temozolomide administration. *Electromagn. Biol. Med.* **2019**, *38*, 198–209. [CrossRef] [PubMed]
75. Dehghani-Soltani, S.; Eftekhar-Vaghefi, S.H.; Babaee, A.; Basiri, M.; Mohammadipoor-Ghasemabad, L.; Vosough, P.; Ahmadi-Zeidabadi, M. Pulsed and Discontinuous Electromagnetic Field Exposure Decreases Temozolomide Resistance in Glioblastoma by Modulating the Expression of O^6-Methylguanine-DNA Methyltransferase, Cyclin-D1, and p53. *Cancer Biother. Radiopharm.* **2021**, *36*, 579–587. [CrossRef]
76. Stratton, D.; Malibha-Pinchbeck, M.; Inal, J. Extremely low-frequency magnetic fields significantly enhance the cytotoxicity of methotrexate and can reduce migration of cancer cell lines via transiently induced plasma membrane damage. *Biochem. Biophys. Res. Commun.* **2022**, *626*, 192–199. [CrossRef] [PubMed]
77. Laqué-Rupérez, E.; Ruiz-Gómez, M.; de la Peña, L.; Gil, L.; Martínez-Morillo, M. Methotrexate cytotoxicity on MCF-7 breast cancer cells is not altered by exposure to 25 Hz, 1.5 mT magnetic field and iron (III) chloride hexahydrate. *Bioelectrochemistry* **2003**, *60*, 81–86. [CrossRef]
78. Han, Q.; Chen, R.; Wang, F.; Chen, S.; Sun, X.; Guan, X.; Yang, Y.; Peng, B.; Pan, X.; Li, J.; et al. Pre-exposure to 50 Hz-electromagnetic fields enhanced the antiproliferative efficacy of 5-fluorouracil in breast cancer MCF-7 cells. *PLoS ONE* **2018**, *13*, e0192888. [CrossRef]
79. Alkis, M.E.; Akdag, M.Z.; Kandemir, S.I. Influence of extremely low-frequency magnetic field on chemotherapy and electrochemotherapy efficacy in human Caco-2 colon cancer cells. *Electromagn. Biol. Med.* **2022**, *41*, 177–183. [CrossRef] [PubMed]
80. 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*, 884. [CrossRef]
81. Falone, S.; Santini, S.; Cordone, V.; Cesare, P.; Bonfigli, A.; Grannonico, M.; Di Emidio, G.; Tatone, C.; Cacchio, M.; Amicarelli, F. Power frequency magnetic field promotes a more malignant phenotype in neuroblastoma cells via redox-related mechanisms. *Sci. Rep.* **2017**, *7*, 11470. [CrossRef]
82. Shibaki, R.; Kakikawa, M. Different effects of magnetic field on drug activity in human uterine sarcoma cell lines MES-SA and MES-SA/Dx5. *Electromagn. Biol. Med.* **2022**, *41*, 343–351. [CrossRef]
83. Kakikawa, M.; Maeda, T.; Yamada, S. Combined Effect of 60 Hz Magnetic Fields and Anticancer Drugs on Human Hepatoma HepG2 Cells. *IEEE J. Electromagn. RF Microwaves Med. Biol.* **2019**, *3*, 56–60. [CrossRef]
84. Storch, K.; Dickreuter, E.; Artati, A.; Adamski, J.; Cordes, N. BEMER Electromagnetic Field Therapy Reduces Cancer Cell Radioresistance by Enhanced ROS Formation and Induced DNA Damage. *PLoS ONE* **2016**, *11*, e0167931. [CrossRef] [PubMed]
85. Říhová, B.; Etrych, T.; Šírová, M.; Tomala, J.; Ulbrich, K.; Kovář, M. Synergistic effect of EMF–BEMER-type pulsed weak electromagnetic field and HPMA-bound doxorubicin on mouse EL4 T-cell lymphoma. *J. Drug Target.* **2011**, *19*, 890–899. [CrossRef] [PubMed]
86. Ruiz-Gómez, M.; de la Peña, L.; Prieto-Barcia, M.; Pastor, J.; Gil, L.; Martínez-Morillo, M. Influence of 1 and 25 Hz, 1.5 mT magnetic fields on antitumor drug potency in a human adenocarcinoma cell line. *Bioelectromagnetics* **2002**, *23*, 578–585. [CrossRef]
87. Rossi, E.; Corsetti, M.T.; Sukkar, S.; Poggi, C. Extremely Low Frequency Electromagnetic Fields Prevent Chemotherapy Induced Myelotoxicity. *Electromagn. Biol. Med.* **2007**, *26*, 277–281. [CrossRef]
88. Braganza, L.F.; Blott, B.H.; Coe, T.J.; Melville, D. The superdiamagnetic effect of magnetic fields on one and two component multilamellar liposomes. *Biochim. Biophys. Acta* **1984**, *801*, 66–75. [CrossRef]
89. Petrov, E.; Martinac, B. Modulation of channel activity and gadolinium block of MscL by static magnetic fields. *Eur. Biophys. J.* **2007**, *36*, 95–105. [CrossRef]
90. Triantafilou, M.; Morath, S.; Mackie, A.; Hartung, T.; Triantafilou, K. Lateral diffusion of Toll-like receptors reveals that they are transiently confined within lipid rafts on the plasma membrane. *J. Cell Sci.* **2004**, *117*, 4007–4014. [CrossRef]
91. Zhang, X.; Min, X.; Yang, F. Conformational basis of the phospholipid requirement for the activity of SR Ca^{2+}-ATPase. *Chem. Phys. Lipids* **1998**, *97*, 55–64. [CrossRef]
92. Germann, U. P-glycoprotein—A mediator of multidrug resistance in tumour cells. *Eur. J. Cancer* **1996**, *32*, 927–944. [CrossRef]
93. Silva, R.; Vilas-Boas, V.; Carmo, H.; Dinis-Oliveira, R.J.; Carvalho, F.; Bastos, M.d.L.; Remião, F. Modulation of P-glycoprotein efflux pump: Induction and activation as a therapeutic strategy. *Pharmacol. Ther.* **2015**, *149*, 1–123. [CrossRef]

94. Kilari, D.; Guancial, E.; Kim, E.S. Role of copper transporters in platinum resistance. *World J. Clin. Oncol.* **2016**, *7*, 106–113. [CrossRef]
95. Spreckelmeyer, S.; Orvig, C.; Casini, A. Cellular Transport Mechanisms of Cytotoxic Metallodrugs: An Overview beyond Cisplatin. *Molecules* **2014**, *19*, 15584–15610. [CrossRef]
96. Monteith, G.R.; Davis, F.M.; Roberts-Thomson, S.J. Calcium Channels and Pumps in Cancer: Changes and Consequences. *J. Biol. Chem.* **2012**, *287*, 31666–31673. [CrossRef]
97. Otto, T.; Sicinski, P. Cell cycle proteins as promising targets in cancer therapy. *Nat. Rev. Cancer* **2017**, *17*, 93–115. [CrossRef]
98. Moreno-Layseca, P.; Streuli, C.H. Signalling pathways linking integrins with cell cycle progression. *Matrix Biol.* **2014**, *34*, 144–153. [CrossRef] [PubMed]
99. Gorrini, C.; Harris, I.S.; Mak, T.W. Modulation of oxidative stress as an anticancer strategy. *Nat. Rev. Drug Discov.* **2013**, *12*, 931–947. [CrossRef] [PubMed]
100. Van Huizen, A.V.; Morton, M.; Kinsey, K.; Von Kannon, V.K.; Saad; Birkholz, B.; Czajka, C.; Cyrus, C.; Barnes, B.; Beane, B. Weak magnetic fields alter stem cell-mediated growth. *Sci. Adv.* **2019**, *5*, eaau7201. [CrossRef]
101. Barnes, F.; Greenebaum, B. Role of radical pairs and feedback in weak radio frequency field effects on biological systems. *Environ. Res.* **2018**, *163*, 165–170. [CrossRef] [PubMed]
102. Cui, X.; Gong, J.; Han, H.; He, L.; Teng, Y.; Tetley, T.; Sinharay, R.; Chung, K.F.; Islam, T.; Gilliland, F.; et al. Relationship between free and total malondialdehyde, a well-established marker of oxidative stress, in various types of human biospecimens. *J. Thorac. Dis.* **2018**, *10*, 3088–3197. [CrossRef]
103. Obrenovich, M.E.; Li, Y.; Parvathaneni, K.; Yendluri, B.B.; Palacios, H.H.; Leszek, J.; Aliev, G. Antioxidants in Health, Disease and Aging. *CNS Neurol. Disord. Drug Targets* **2011**, *10*, 192–207. [CrossRef]
104. Mohammad, R.M.; Muqbil, I.; Lowe, L.; Yedjou, C.; Hsu, H.-Y.; Lin, L.-T.; Siegelin, M.D.; Fimognari, C.; Kumar, N.B.; Dou, Q.P.; et al. Broad targeting of resistance to apoptosis in cancer. *Semin. Cancer Biol.* **2015**, *35*, S78–S103. [CrossRef] [PubMed]
105. Simon, H.-U.; Haj-Yehia, A.; Levi-Schaffer, F. Role of reactive oxygen species (ROS) in apoptosis induction. *Apoptosis* **2000**, *5*, 415–418. [CrossRef] [PubMed]
106. Roos, W.P.; Kaina, B. DNA damage-induced cell death by apoptosis. *Trends Mol. Med.* **2006**, *12*, 440–450. [CrossRef] [PubMed]
107. Citterio, E. Fine-tuning the ubiquitin code at DNA double-strand breaks: Deubiquitinating enzymes at work. *Front. Genet.* **2015**, *6*, 282. [CrossRef]
108. Kim, J.; Ha, C.S.; Lee, H.J.; Song, K. Repetitive exposure to a 60-Hz time-varying magnetic field induces DNA double-strand breaks and apoptosis in human cells. *Biochem. Biophys. Res. Commun.* **2010**, *400*, 739–744. [CrossRef]

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.