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In vitro studies on the use of Extremely Low Frequency (ELF) Electromagnetic Fields as a means of increasing the effectiveness of anticancer drugs

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INTRODUCTION & AIM

Extremely low frequency (ELF) electromagnetic field (EF) is an innovative way of treating cancer. It affects various biological processes in cells, such as proliferation, metabolism and cell cycle, which play a key role in the development of cancer cells. Intercellular interactions based on the electromagnetic field regulate cell migration and morphogenesis. These processes are closely related to the function of the centrosome and intercellular communication. EF induces apoptosis and increases the sensitivity of drug-resistant tumor cells to cytostatics. The mechanisms important in EF effects on cancer cells are impact on the cell cycle, apoptosis, proliferation and angiogenesis [1,2]. This processes that play an important role in cancer development. EF appears to be a promising direktion in cancer therapy [3]. Particularly important is the sensitization of cancer cells through the use of PE to cytostatics. In order to be able to appropriately select PE parameters that appear to be specific for a given cancer type and the effect on appropriate cytostatics, especially in drug-resistant cancers, these studies should be conducted on cell cultures.

The aim of the study was to design and construct a device enabling the assessment of the effect of electromagnetic fields on cell cultures of various cancer cell lines (including those collected from patients) and various PE conditions.

A laboratory research station was designed, which allows for testing the effect of a specific value of the magnetic induction of an electromagnetic field in the ELF frequency band and determining the optimal time of exposure to the field. The device also allows for culturing selected cell lines and using anticancer drugs in the appropriate concentration. The central element of the station is a solenoid, in the workspace of which cell culture plates can be placed. The parameters of the electromagnetic field are in the low frequency range, up to 300 Hz, and the maximum set magnetic induction of 2.5 mT.

METHOD

DESIGN OF APPARATUS FOR EXPOSURE TO AN ALTERNATING MAGNETIC FIELD

For the purpose of conducting research on cancer cells, a research apparatus has been constructed that allows exposure to an alternating electromagnetic field in the extremely low frequency range. The main component of the system is a solenoid fed from a signal generator via a power amplifier. Using a graduated voltmeter of the output signal from the power amplifier, it is possible to set a specific value of magnetic induction and control its value. In order to simplify the measurement system, the ammeter was dispensed with by scaling the voltmeter by setting a scaling constant B[mT] / U[V]. The block diagram of the test bench is shown in Figure 1.

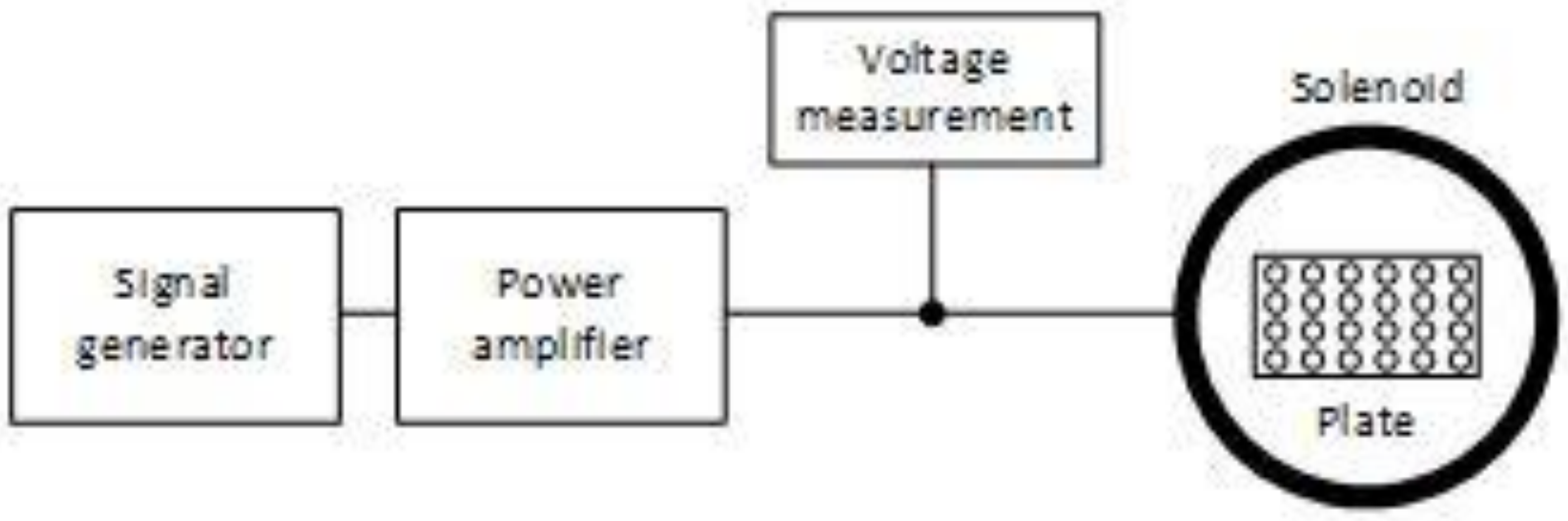

Fig.1. Block diagram of the test stand for exposure to an alternating inductive field

RESEARCH EXPERIMENT ON CULTURES OF CANCER CELL LINES

Research experiments on the effect of magnetic fields on the growth of human cancer cells LoVo (colon cancer), MC7 (breast cancer) and A431 (epidermoid cancer) were carried out on a designed laboratory bench. 96-well test plates with the cells was placed in the center of a solenoid. It was investigated, that the center of the plate and maximum 5cm away characterized constant exposure to the magnetic field. In experiment 20 to 400 μM concentrations o cisplatin were tested. The control cultures of cells were treated with cisplatin alone, without magnetic field exposure. Cell lines were cultured in an incubator at 5% CO_2, 37°C and 95% humidity (Fig.2).

Fig.2. View of the designed solenoid (a) and the inside of the incubator with cultures of control cell lines and cells exposed to magnetic induction in the solenoid (b)

RESULTS & DISCUSSION

TESTING THE UNIFORMITY OF MAGNETIC INDUCTION EXPOSURE IN THE SOLENOID

In order to confirm the obtained values of the electromagnetic field in the designed device, tests were carried out to determine the value of magnetic induction and its distribution in the space of the exposure system. A test plate with 24, 48 or 96 cells was placed in the central point of the test space.The normalized distribution of magnetic induction B/Bcenter at a frequency of 60 Hz in the working space is shown in the graph in Fig. 3, where Bcenter is the value of induction at the central point of the electromagnet. The graph shows the distribution of induction inside the electromagnet in the horizontal x-axis and the vertical y-axis (subsequent planes) relative to the geometric center of the coil.

Laboratory measurements of magnetic induction carried out when forcing a current flow in the solenoid of 2.5 A, confirm the calculated maximum value of magnetic induction at the geometric center of the coil of 2.5 mT

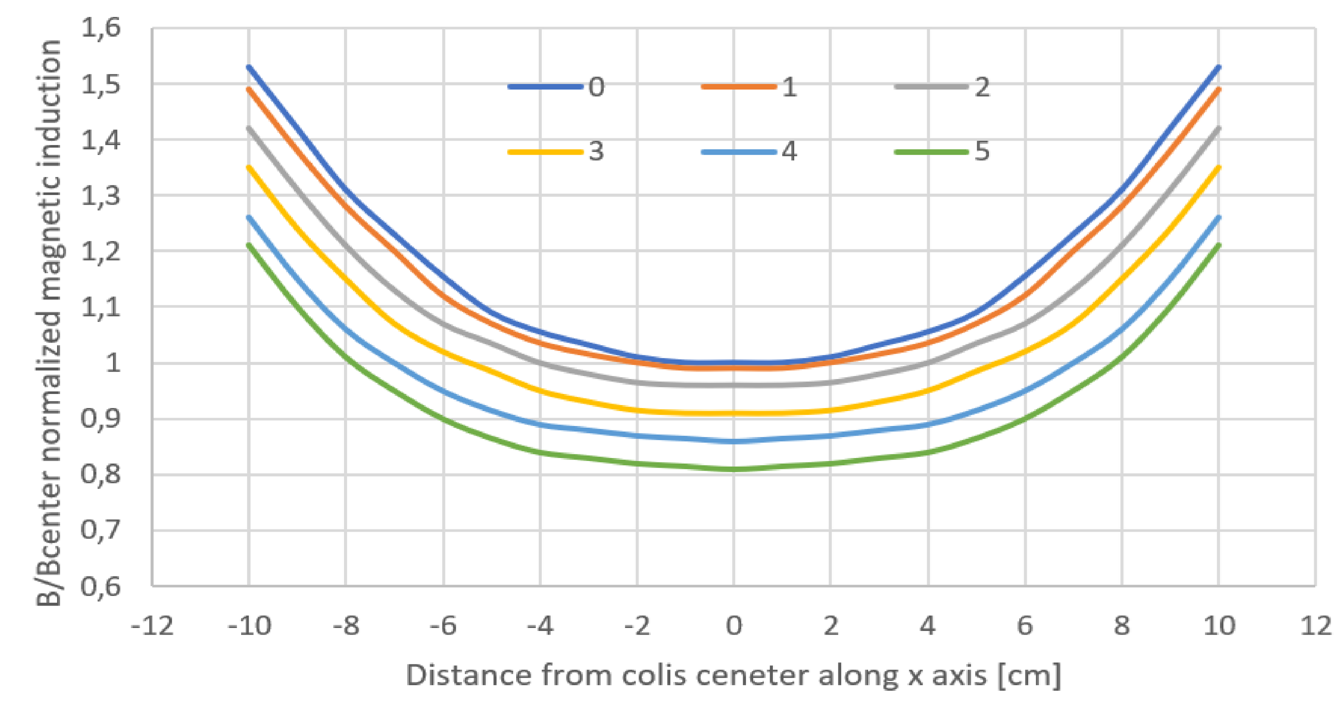

Fig.3 Relative distribution of normalized magnetic induction B/Bcenter in the exposure coil along the horizontal x-axis and vertical y-axis (0,1,2,3,4,5 - y-axis distance from the center point of the coil [cm])

EXPERIMENTAL RESULTS

In the experiment carried out, the effect of magnetic induction with a frequency of 60 Hz and values of 1.25mT and 2.5mT on cisplatin-treated cancer cell cultures was evaluated. To assess cytotoxicity and cell viability MTT assay was performed. Laboratory tests were performed on tumor cells exposed to magnetic fields in a cycle of daily 30min exposure conducted for 5 consecutive days.

The pro-proliferative effect was observed at higher cisplatin concentrations exposed to PE 1.5 mT.

The magnetic induction value was increased to 2.5 mT and the increased exposure value led to a significant modification of the response of tumor cells to cisplatin treatment.

A significant reduction in LoVo tumor cell viability was observed and the cytotoxic effect of cisplatin was significantly enhanced by the altered magnetic field parameters (Fig.4).

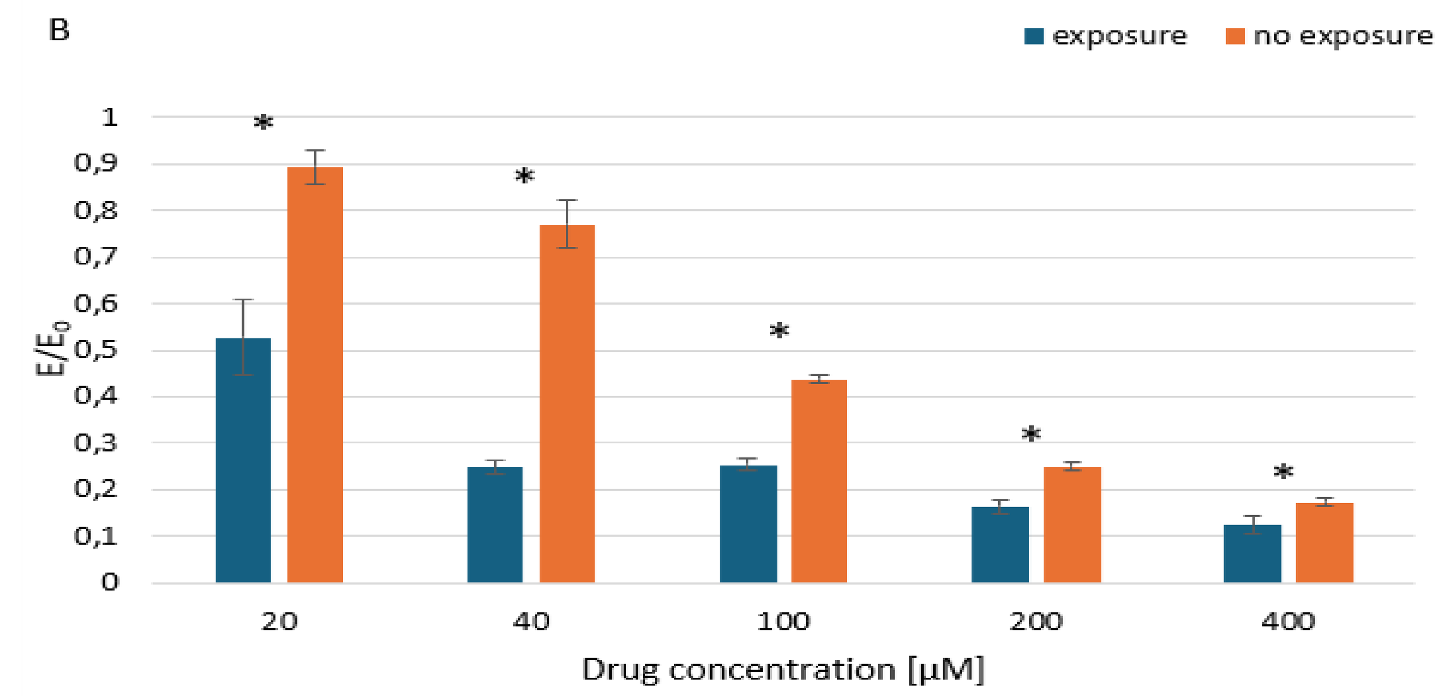

Fig.4 Evaluation of the viability of LoVo cells exposed to 60 Hz and 2,5 mT magnetic fields in cycles of 30 minutes of daily exposure conducted for 5 consecutive days; *p<0.05 statistically significant differences were observed between the groups treated with both the magnetic field and cisplatin, compared to those treated with cisplatin alone.

CONCLUSION

The described method allows for an effective and fast way to check the influence of EF on the pharmacological effect of the drug for a given type of cancer and select the appropriate EF parameters, allowing for a reduction in the cytostatic dose while maintaining the effectiveness of the therapy. The conducted studies demonstrate that a magnetic field with specific parameters can significantly influence the response of cancer cells to cisplatin treatment. The application of a magnetic field may either promote cell proliferation at higher cytostatic concentrations or, with appropriately adjusted parameters, lead to enhanced cytotoxicity.

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