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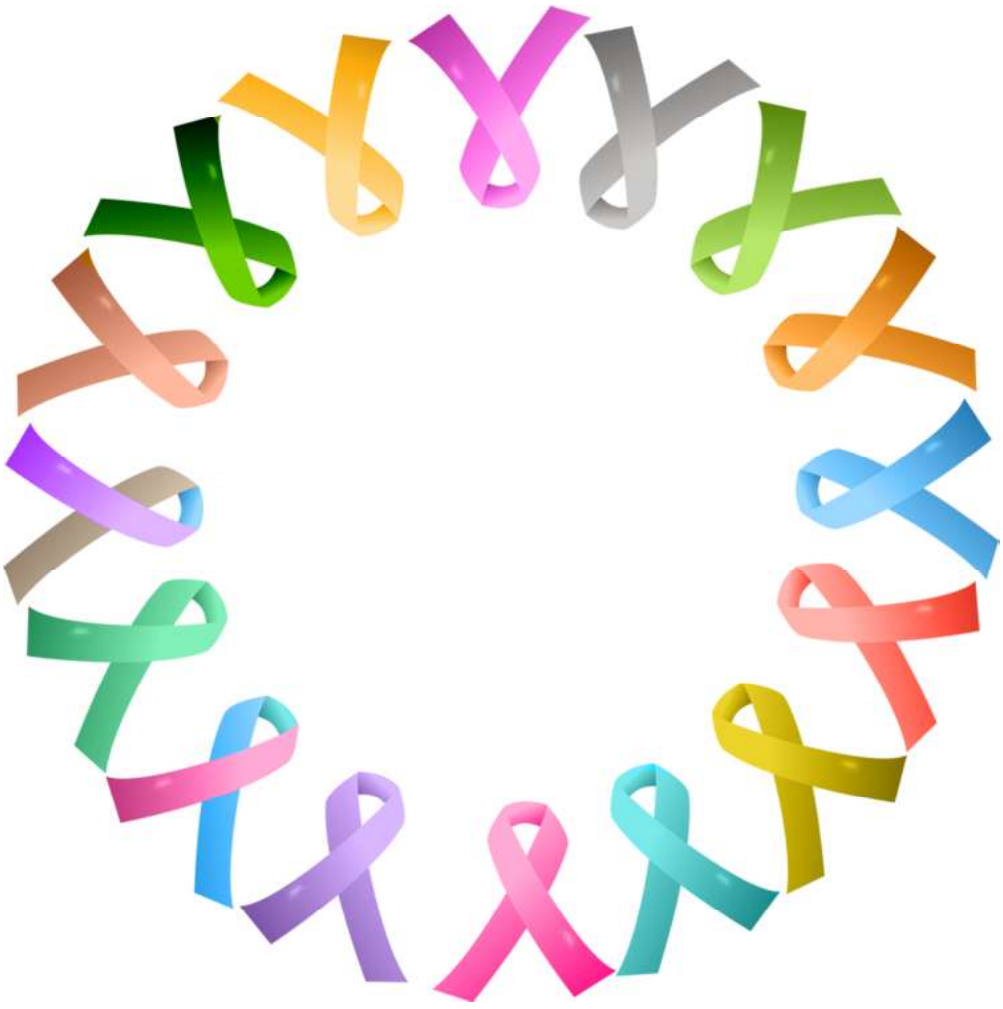

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2nd – 4th October 2023
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fibrosarcoma can be recommended for further clinical trials.
Keywords: BHK-21/C13, cell culture, drug effects, fibrosarcoma, hamsters, NF-kB
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Potential of Tamoxifen-based Copper(II) Dichloride in Breast Cancer Therapy

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Background: Estrogen receptor-positive (ER+) breast cancer accounts for approximately 70% of all cases and, concordantly, anti-estrogen therapies present a leading therapeutic choice. Interestingly, tamoxifen, which is the most commonly used drug, has also been proven effective in hormone-independent forms of breast cancer, suggesting the existence of intracellular off-targets. Frequent acquisition of therapy resistance presents a platform for the design of tamoxifen derivatives with a 2,2'-bipyridine unit enabling the coordination of transition metal moieties, such as copper(II) dichloride. Copper (Cu) is an essential element involved in the regulation of cellular growth and development. Disruption of its delicate homeostasis results in severe toxicity and hard medical conditions. Increased demand of cancer cells for this micronutrient makes it a valuable candidate for drug design in cancer treatment. The mechanism of action of Cu complexes is typically based on their ability to induce deadly oxidative stress. This study evaluated the efficacy of a copper–tamoxifen hybrid drug on a panel of breast cancer cell lines with varying receptor expression status. **Material and Methods:** The viability of breast adenocarcinoma cell lines MCF-7, MDA-MB-361, MDA-MB-231, 4T1 and glioma U251 was estimated by MTT and CV assays. Flow cytometric analysis of cells stained with annexin V-FITC/propidium iodide, ApoStat, acridine orange, dihydrorhodamine 123 (DHR), dihydroethidium (DHE) or 4-amino-5-methylamino-2',7'-difluorofluorescein diacetate (DAF) was used to evaluate cell death, caspase activity, autophagy, production of reactive oxygen and nitrogen species (ROS/RNS), respectively. **Results:** The Cu-tamoxifen hybrid drug displayed substantially higher hormone-receptor (HR) independent cytotoxic activity compared to previously reported metal complexes with a similar tamoxifen vector. Massive caspase-dependent apoptotic cell death is partially attenuated by an autophagic process that counteracts death signals. In contrast to the platinum analogue, the copper-based tamoxifen derivative reduces ROS/RNS that may be associated with the intracellular accumulation of the reduced form of CuI which is important for cuproptosis. **Conclusion:** This study demonstrates the potential of the copper–tamoxifen hybrid drug as an intriguing alternative to commonly used platinum complexes in treatment of cancer. Its safety and efficiency will be further estimated *in vivo*.
Keywords: Breast neoplasms, copper, tamoxifen, therapeutics

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The mechanism of action of ruthenium compounds on ovarian tumor cells OVCAR-3

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Abstract in extenso:
Background: From its discovery to the present day, cisplatin and structurally related platinum-based drugs represent an important class of compounds used in cancer therapy (1). The main problem in treatment and antitumor therapy is the occurrence of resistance to platinum-containing compounds and toxicity to healthy tissues. Researchers are for decades working on the development of new antitumor drugs that will successfully replace cisplatin and overcome