LIGHT-INDUCED TOXIC EFFECTS BY TAMOXIFEN: A CHEMOTHERAPEUTIC AND CHEMOPREVENTIVE AGENT

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Abstract: Tamoxifen is a powerful drug used to treat breast cancer patients, and more than 500,000 women in the U. S. are being treated with this drug. In our study, tamoxifen is found to be photomutagenic in Salmonella typhimurium TA102 at concentrations as low as 0.08 μM and reaches maximum photomutagenicity at 0.4 μM under a light dose equivalent to 20 min sunlight. These concentrations are comparable to the plasma tamoxifen concentration of 0.4 to 3 μM for patients undergoing tamoxifen therapy. The toxicity seems to be the result of DNA damage and/or lipid peroxidation caused by light irradiation of tamoxifen. The DNA damage caused by irradiation of ФХ174 DNA in the presence of tamoxifen appears to be formation of DNA-tamoxifen covalent adducts, not single strand/double strand cleavages, and there is no oxygen involvement. This is confirmed by EPR experiments that carbon-centered radicals are formed by light irradiation of tamoxifen and there is no singlet oxygen formation. Although superoxide radical is formed, it is not involved in DNA damage.

Keywords: Tamoxifen, phototoxicity, HaCaT keratinocytes, Salmonella TA102, DNA damage, Lipid peroxidation