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## Electrochemotherapy Enhances the Curcumin Effect on TNBC Cells in a Dosage and Energy Dependent Manner

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Compared to other breast cancer phenotypes, triple negative breast cancer (TNBC) has a much lower five-year survival rate (30% compared to 66%) because it is refractive to standard chemotherapy since it lacks three main receptors. Thus, TNBC requires alternative treatment modalities. This motivates our study of treating TNB with electrochemotherapy (ECT) using curcumin, the yellow pigment of turmeric, which is loaded with anticancer phytochemicals with minimal side effects and lower expense than traditional chemotherapeutics.

We treat MDA-MB-231 cells, and aggressive, human TNBC cell line, with 10 $\mu$ M or 25 $\mu$ M curcumin exposed to four, ten or twenty 100  $\mu$ s electric pulses (EP) of 1200 V/cm to establish a correlation between the applied energy and cell death. The 24 h cell viability results show that combining EPs with curcumin effectively targets TNBCs in a curcumin dosage and EP energy density dependent manner. The viability for 10 $\mu$ M and 25 $\mu$ M curcumin alone samples did not differ significantly from control (100%). The viability was 32% and 43% for 20 and 10 EPs, respectively with no curcumin added; however, the viability was 17% and 85% for 10 and 4 pulses, respectively, with 25  $\mu$ M curcumin. The highest cell death (5% viability) was achieved for 20 pulses with 25  $\mu$ M curcumin. These results highlight the synergy of EP and curcumin against aggressive TNBC cells and the potential of using EP energy density to tune cellular responses. The low cost and natural herbal anticancer properties of curcumin could make this therapy an attractive alternative for TNBC treatment. Further potential tuning using a multi-electrode system was assessed using finite-element simulations. Such evaluations allow us to assess the field intensity and profile in the vicinity of a tumor target to help predict parameters for ultimate clinical applications. The implications of these results on guiding future in vivo work will be discussed.

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