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Synergistic enhancement of antibiotic susceptibility of bacteria using nanosecond electric pulses

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Antibiotic resistance mechanisms render current antibiotics ineffective, necessitating higher concentrations of existing drugs, the development of new drugs, or the discovery of a method or mechanism to counter them [1]. Combining nanosecond electric pulses with tobramycin and rifampicin enhanced the cytotoxic effect for gram negative *Escherichia coli*, gram positive *Staphylococcus aureus*, and a Methicillin Resistant strain of *Staphylococcus aureus*. Specifically, we observed that individually applying 1000 pulses of 300 ns duration for a 20 kV/cm electric field or clinical doses between 2 and 20 ug/mL of tobramycin did not induce appreciable cell death; however, combining the pulse parameters and tobramycin resulted in more than a 3-log inactivation. Over a range of pulse and drug parameters, we observed a consistent 3-log synergy, which increased to 7-log reduction when combining tobramycin and rifampicin. This indicates the great advantage of combining electric pulses with a single drug, but indicates the dramatic improvement that can arise from combining multiple antibiotics [2] with electric pulses. This synergy arose on timescales of 15 minutes, compared to timescales of hours to days for antibiotics alone to achieve similar bacterial kill off.

[1] S. Reardon, "Antibiotic resistance sweeping developing world: bacteria are increasingly dodging extermination as drug availability outpaces regulation,"Nature, vol. 509, no. 7499, pp. 141–143, 2014.

[2] L. P. Kotra, J. Haddad, and S. Mobashery, "Aminoglycosides: perspectives on mechanisms of action and resistance and strategies to counter resistance,"Antimicrob. Agents Chemother., vol. 44, no. 12, pp. 3249–3256, 2000.

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