

THE PORE-STABILIZING EFFECT OF NISIN WITH NANOSECOND AND MICROSECOND PULSE BURSTS FOR ELECTROCHEMOTHERAPY

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Electrochemotherapy (ECT) is a technique that uses a pulsed electric field (PEF) to improve the transmembrane delivery of chemotherapeutic drugs. This process relies on creating hydrophilic pores in the cell membrane via electroporation. Consequently, managing the density, stability, and size of these pores is essential for ensuring effective drug administration. Nisin is a naturally occurring peptide known for its antibacterial properties, which can facilitate the aggregation of proteins at the edges of pores, possibly influencing pore resealing. Moreover, studies have demonstrated that nisin can boost the effectiveness of chemotherapy across a range of cancer cell lines, indicating it might offer synergistic anticancer benefits. The possibility of nisin enhancing drug delivery through changes in pore induction or resealing, along with its potential additional anticancer effects, raises optimism for its therapeutic use alongside ECT. However, the impact of nisin in the context of ECT has not yet been explored.

Consequently, the primary objective of this study is to collect experimental evidence that illustrates nisin's ability to influence pores created in the membranes of a cancer cells through electroporation. In this study, we combine electrochemotherapy using microsecond: 0.6–1.5 kV/cm × 100 μs × 8 (1 Hz) and nanosecond: 6 kV/cm × 300 ns × 100 (1, 10, 100 kHz and 1 MHz) electric field pulses. These electric field pulses were performed on a murine 4T1 cell line. Our findings indicate that nisin has a substantial impact on electroporation. The synergistic effects, which include enhanced permeabilization and molecular electrotransfer, become particularly profound with a higher pulse burst frequency. Furthermore, nisin lowers the permeabilization thresholds, influences the resealing of pores, and demonstrates anticancer effects comparable to those of traditional electrochemotherapy. Notably, nisin exerted no toxicity in breast cancer cells, which offers confidence in its potential use alongside electrochemotherapy.

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