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THRESHOLD INTENSITY OF 1.2 MHz CONTINUOUS ULTRASOUND IN DNA ALTERATION AND CELLULAR INACTIVATION

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Hokkaido University granted the degree of Doctor of Veterinary Medicine to the following three graduates of the Graduate School of Veterinary Medicine on 25 March, 1980.

The titles of their theses and other information are as follows:

**STUDY ON THE PURIFICATION, SUBCELLULAR LOCALIZATION, AND KINETIC MECHANISM OF PORCINE MITOCHONDRIAL ADENYLATE KINASE**

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**THRESHOLD INTENSITY OF 1.2 MHz CONTINUOUS ULTRASOUND IN DNA ALTERATION AND CELLULAR INACTIVATION**

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The present study was undertaken to elucidate the intensity effect of 1.2 MHz continuous ultrasound in DNA alteration and cellular inactivation.

To obtain biological data of the intensity effect, four criteria, viability, cell lysis, DNA synthesis, and DNA strand breaks, were applied to cultured mouse L cells. The cells in a log phase were harvested by trypsination. A sample placed in a polystyrene dish was held at a distance of 3 cm from a barium titanate transducer in water, and irradiated at various doses and intensities. The viability and cell lysis were assayed by their colony-forming ability and vital cell counting. DNA synthesis was estimated by incorporation of $^3$H-thymidine, and the number of DNA strand breaks was estimated by neutral sucrose gradient ultracentrifugation of $^3$H-thymidine labelled cells. Furthermore, the mechanical and chemical effects of ultrasound were investigated using the same irradiation apparatus. The experimental criterion by which cavitation was recognized here was the appearance of a chemical effect.
The apparent intensity effect and the intensity threshold were observed in mechanical, chemical and biological systems. The mechanical effect of ultrasound was observed at intensities over 0.3 W·cm⁻², and the chemical effect was clearly found at intensities over 1.3 W·cm⁻². The intensity thresholds of cell inactivation, viability, and cell lysis were close to those of the mechanical effect. The intensity threshold of the DNA strand breaks in the cells were equal to that of the cell inactivation. The perturbation of DNA synthesis was observed at intensities over 0.7 W·cm⁻², and this intensity threshold was close to the intensity region at which the difference between the colony-forming ability and cell lysis appeared.

Compared to the intensity threshold, it seemed probable that the initial cell inactivation of the ultrasound depended on the noncavitational mechanical shearing force. The alteration of DNA in the cells may be attributed to the DNA strand breaks rather than to DNA synthesis.

STUDIES ON THE ETIOLOGY OF SEPTICEMIC COLIBACILLOSIS IN NEONATAL PIGLET: THE RELATIONSHIP BETWEEN THE DISEASE AND INTESTINAL PERMEABILITY TO MACROMOLECULES

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