REAL-TIME MONITORING OF CELL GROWTH RATE BY MEANS OF ELECTROCHEMICAL IMPEDANCE MEASUREMENT

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We investigated to clarify whether monitoring of cell growth rate by a real-time electrochemical impedance measurement on a cell chip was a useful tool for cytotoxicity assay. The cell chip consists of a four-well cell culture chamber incorporated with a three-electrode system on each well. The Indium Tin Oxide (ITO) electrode for impedance measurements is fabricated by sputtering on glass plate. Cells were grown onto the surfaces of ITO electrodes. Changes in cell status such as cell number, viability, morphology, and adherence were monitored and quantified by detecting sensor electrical impedance. For cell quantification and viability measurement, the data generated on the system correlated well with those from MTT assay. For cytotoxicity assessment, cells growing on ITO electrode were treated with toxicant, such as vincristine. The dynamic responses of the cells to the toxicants were continuously monitored by the system. In addition to cell viability, this assay provided dynamic information that can be used to identify maximum toxicity and reversibility of the toxic effects which are difficult to achieve by the endpoint assays and, therefore, the assay is more accurate for assessment of cytotoxicity. These results indicate that real-time monitoring of cell growth rate by electrochemical impedance measurement is a useful assay system for assessment of cytotoxic compounds such as anti-tumor drugs and toxins in the pharmacological and toxicological studies, and that this system have superior features such as labeling free, automatic detection and easy operation.

APPLICATION OF A SAMPLE POOLING METHOD FOR THE ACCELERATED ASSESSMENT OF THE RATE OF UPTAKE OF DRUGS BY THE BRAIN IN RATS

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The purpose of this study was to examine the feasibility of applying a sample pooling method to the accelerated estimation of the uptake clearance of drugs to the brain in rats. Brain uptake clearances (CLuptake) were estimated for five model compounds using the sample pooling method and an integration plot analysis. CLuptake was also evaluated for caffeine and theophylline by brain microdialysis. The parameters and throughput of the pooling method were compared with those of typically used standard methods. The correlation for CLuptake was statistically significant (p<0.005) between the integration plot and the current method; the throughput of evaluation was fifteen fold higher for the sample pooling method. A comparison of CLuptake values indicated that the three methods showed comparable results for caffeine while the CLuptake of theophylline using the proposed method was significantly different from those of the other methods. A kinetic analysis indicated that a compound with a slower CLuptake and longer half-life (e.g., theophylline) is more prone to error and that the lower limit of the CLuptake of 0.17 mL/min/g brain may be set so as to have an error less than 20 % of the estimation. These results suggest that the sample pooling method is applicable for use in the accelerated estimation of the uptake clearance of compounds in the brain for which the value is greater than 0.17 mL/min/g brain.