Electrochemical Measurement of Antiglaucoma Drug Brimonidine Using Boron-Doped Diamond Microelectrodes

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Glaucoma is the leading cause of blindness in Japan [1]. The standard treatment for glaucoma is to lower intraocular pressure with eye drops, but there are still many unknowns regarding intraocular pharmacokinetics. Here, we proposed an electrochemical method using boron-doped diamond (BDD) electrodes to observe changes in intraocular drug concentrations over time. BDD shows excellent electrochemical properties and biocompatibility [2], allowing it to be applied as a sensor for measuring drugs *in vivo*. In this study, we performed the electrochemical measurements of the popular antiglaucoma drug brimonidine tartrate (BRM). Firstly, the electrochemical properties of BRM were evaluated by cyclic voltammetry (CV) measurements using a three-electrode configuration: a BDD plate electrode as the working electrode (WE) and the counter electrode (CE), and an Ag/AgCl (sat. KCl) electrode as the reference electrode (RE). In CV measurement, a reduction signal of BRM was observed at -0.4 V and below. Subsequently, we performed continuous measurements using a BDD microelectrode as WE. Chronoamperometry (CA) measurements applying -0.5 V showed highly linear concentration dependence in phosphate buffer but not in aqueous humor (Fig. 1 (a)). The adsorption of biological materials to the surface of the electrode was thought to be the primary cause of this degradation in the sensor's sensitivity. To address this, a potential-step method (consisting of -0.2 V applied for 29.5 s and -1.5 V for 0.5 s) was established. This method includes a phase where a particular potential (-0.2 V) is applied, which induces no electrochemical reaction on the electrode surface, thereby preventing adsorption. By using this method, a reduction signal of BRM in aqueous humor was observed (Fig.1 (b)). The optimized potential-step method was applied to *in vivo* measurements with anesthetized mice. The BDD microelectrode was inserted into the right cornea. CE and RE were placed on the surface of the left eye. 5 μL of 6 mM BRM was administered to the right eye. The reduction signal of BRM started to increase ~2 min after the administration (Fig. 2). The signal returned to the original level 17 minutes after administration (Fig. 2). This result indicates the possibility of *in vivo* monitoring of drug concentration changes in the eye.

References

[1] The Japan Glaucoma Society, J. Jpn. Ophthalmol. Soc., 126(2022) 85-177.
[2] Y. Einaga, J. Appl.Electrochem., 40(2010) 1807 – 1816.

Figures

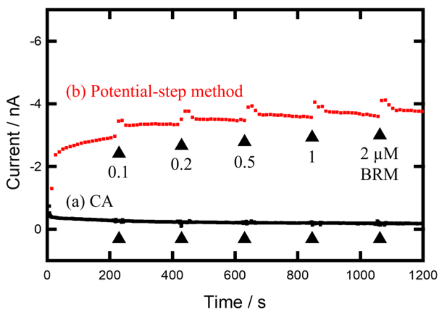

Figure 1: Continuous measurements in aqueous humor, (a) CA (b) potential-step method.

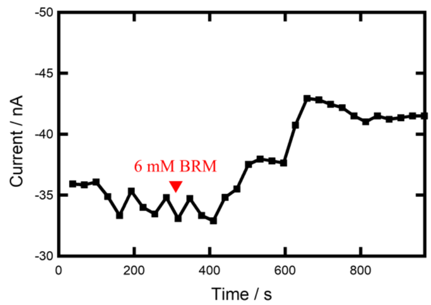

Figure 2: *In vivo* measurements with mice (moving average of 2 intervals).