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Development of a novel integrated iontophoresis electrode consisting of metallic and drug-loaded layers[†]

T. Yoshioka*, N. Saito*, T. Ikoma*, N. Ohashi**, H. Haida***, S. Ando***, R. Wakita***,
H. Fukayama***, M. Umino****, and J. Tanaka*

KEY WORDS: (Metal) (Gel) (Integration) (Iontophoresis) (Local anesthesia)

1. Introduction

Iontophoresis is a drug delivery method that can be used to enhance the movement of ionic compounds or non-charged drug molecules by the application of external electric fields. Iontophoresis can transport ionic substance across skin or membranes into the body. Although iontophoresis needs a drug-loaded electrode, a metal electrode is unable to adsorb a large amount of drugs. Thus, the electrode that conjugates drug-absorbable gels is desired for sustainable administration. Alginic acid and chitosan have been widely studied as drug delivery carriers. Sodium alginate or chitosan form gels around electrodes by the pH change of the solution that was generated by electrolysis of water. In this study, we investigated the interface stability of the gels formed on a metal electrode by applying direct currents in the solutions in order to develop a novel iontophoresis electrode.

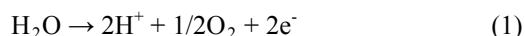
2. Materials and Methods

Al electrodes were cut into 2.5 x 1 x 0.01 cm pieces. The electrodes were ultrasonically washed three times with acetone for 10 min, and then dried under nitrogen gas flow. The cleaning procedure was completed by 10 min UV/ozone irradiation (ProCleaner 110, BioForce Nanosciences, Inc., USA). The electrochemical deposition cell was a two-electrode system, which consisted of a cylindrical polystyrene cell and metal electrodes. The deposition was obtained on Al electrodes that were set as anodes for alginic acid and as cathodes for chitosan. The Pt electrode was used as a counter electrode. The distance between two electrodes was 10 mm. Twenty mL of 0.5% sodium alginate aqueous solution or 0.2% chitosan solution was poured into the cylindrical polystyrene cell. The surface area of the electrodes exposed to the solution was adjusted to be 4 cm². The electrochemical deposition was conducted under application of a DC electric field with current densities of 1.0-5.0 mA/cm² for up to 3600 s at room temperature. The electrodes were dried at 37°C for 24 h. The surface of the electrodes was characterized by FT-IR. All measurements were performed using FT-IR spectrometer, model FT/IR-4100 (JASCO, Japan) equipped with PR-5101 system (JASCO, Japan). The incident angle

of the IR beam was set to be 60° from the surface normal.

3. Results and Discussion

Figure 1 shows the FT-IR spectra of the Al electrodes subjected to the electrochemical deposition process of alginic acid under the current density of 1 mA/cm² for 120 s, 300 s, and 600 s. The characteristic peaks at 1420 cm⁻¹ and 1600 cm⁻¹ were assigned to dissociated carboxyl groups (–COO⁻) of alginate, which corresponded to the symmetric and asymmetric C=O stretching vibration. The result indicated that the electrochemical process successfully deposited the alginate on the electrodes. The deposited mass on the electrodes was increased with an increase of the applied times. The band at 1740 cm⁻¹ was assigned to C=O stretching vibration of the undissociated carboxyl groups (–COOH). It was already described that alginic acid gels were formed around anode electrodes due to electrochemical decomposition of water [1]. According to the literature, the related reactions at the anode were expressed as follows;



Application of an electric field caused a pH decrease at the anode. In the aqueous solution, sodium alginate was dissociated to sodium ions and alginate molecules, and then the alginate molecules were protonated around the anode.



where the symbols Na-Alg and H-Alg denote sodium alginate and alginic acid, which are strong and weak electrolytes, respectively. The formed H-Alg turned to gels via hydrogen bonding between –COOH of H-Alg, which was confirmed in the FT-IR spectra shown in Fig. 1. Thus, the alginic acid layers were deposited through the proton-mediated gelation. The intensity of the peaks for –COOH at 1740 cm⁻¹ was increased with an increase of the applied times. This result indicated that the prolonged application leads to an increase of the hydrogen bonding in the layers in addition to an increase of the deposited amount.

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* Tokyo Institute of Technology, Tokyo, Japan

** National Institute for Materials Science, Tsukuba, Japan

*** Tokyo Medical and Dental University, Tokyo, Japan

**** TTI ellebeau, Inc., Tokyo, Japan

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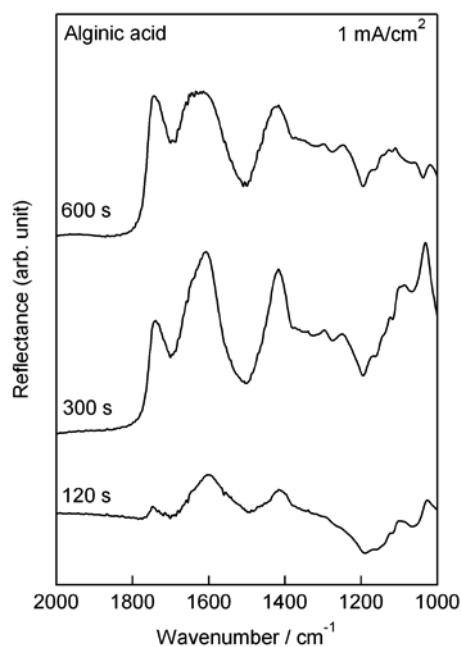


Fig. 1 FT-IR spectra of the Al electrodes subjected to the electrochemical deposition process of alginic acid.

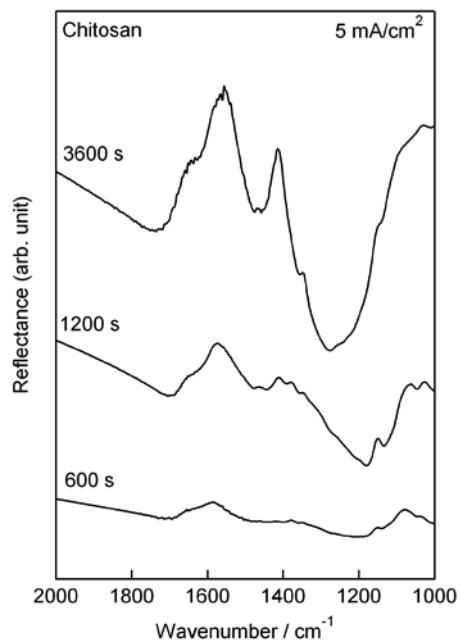
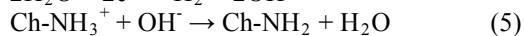


Fig. 2 FT-IR spectra of the Al electrodes subjected to the electrochemical deposition process of chitosan.

Figure 2 shows the FT-IR spectra of the Al electrodes subjected to the electrochemical deposition process of chitosan under the current density of 5 mA/cm² for 600 s, 1200 s, and 3600 s. The characteristic peaks at 1645 cm⁻¹ and 1570 cm⁻¹ were assigned to amide I and amide II of chitosan, respectively. Chitosan was also shown to deposit on the Al electrodes. The deposited mass of chitosan on Al was lower than that of alginic acid irrespective of longer applied time. It is suggested that the cathodic reactions were expressed as followed;



where the symbols Ch-NH_3^+ and Ch-NH_2 denote protonated and deprotonated chitosan, respectively. At the cathode, electrochemical decomposition of water resulted in an increase of pH as expressed in eq. (4). Then, the chitosan molecules lost their charge and formed insoluble deposits on the Al surface.

The results indicated that alginic acid and chitosan gels successfully deposited on the Al electrodes. However, their chemical stability was different. The alginic acid gels on Al did not exfoliate in ionic solution, while the chitosan gels easily exfoliated. It has been reported that there are a number of $-\text{OH}$ groups on the metal surface, and the groups existed mainly as $-\text{OH}_2^+$ at lower pH than an isoelectric point and as $-\text{O}^-$ at higher pH [2]. Since the electrochemical deposition of alginic acid occurred at acidic pH, the ionic interaction between $-\text{OH}_2^+$ on the surface and $-\text{COO}^-$ of the alginic acid could be exist. On the other hand, the chitosan gels deposited at a basic pH did not involve in ionic interaction between chitosan molecule and the Al surface.

4. Conclusion

Drug-absorbable gels of alginic acid or chitosan were successfully deposited on the Al electrodes.

References

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- [2] G. A. Parks: Chem. Rev., 65 (1965), pp. 177-198.