

# Spectroelectrochemical Studies of Molecular Association with Polyamidoamine Dendrimers at Liquid | Liquid Interfaces

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# Spectroelectrochemical Studies of Molecular Association with Polyamidoamine Dendrimers at Liquid|Liquid Interfaces

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Molecular association behavior and interfacial mechanism of polyamidoamine dendrimers for anionic porphyrins and bioactive species at the polarized water|1,2-dichloroethane (DCE) interface as a model of biomembrane were studied through potential modulated fluorescence (PMF) spectroscopy. In aqueous solutions, zinc(II) porphyrin associated with the dendrimers was stabilized without protolytic demetalation in a wide range of pH. On the other hand, the free base porphyrin was readily protonated following the formation of the J-aggregates of diprotonated species. PMF measurement at the interface revealed that the dendrimers incorporating porphyrin molecules were transferred across the positively polarized interface accompanied by the adsorption process, whereas the porphyrins released from the dendrimers were transferred at the negatively polarized interface. In addition, the ion association stability between the dendrimer and the porphyrin was quantitatively estimated from the negative shift of the transfer potential of the porphyrins. Although ionizable drugs were not effectively associated with the dendrimers in the aqueous solutions, PMF results of the fluorescent dipyridamole (DIP) indicated that the interfacial mechanisms of DIP species were significantly modified by the dendrimers, depending on the pH conditions. Flavin derivatives were effectively associated with the dendrimer in the aqueous solution. The interfacial adsorption of the anionic flavin derivatives was inhibited by forming associates with the dendrimer, while the associates were transferred across the interface in the positive potential region.

## ABSTRACT

Dendrimers are non-traditional polymers which have a well-defined molecular structure and have attracted much attention as molecular capsule for drug delivery systems (DDS) and separation sciences. It is worth investigating molecular encapsulation behavior and charge transfer reaction of dendrimers at an interface between two immiscible electrolyte solutions (ITIES) where metal ions and organic molecules are transferred. In order to evaluate the potential ability of dendrimers as molecular capsule, molecular encapsulation behavior of amino and carboxylate-terminated polyamidoamine (PAMAM) dendrimers and the interfacial behavior at the polarized water|1,2-dichloroethane (DCE) interface were investigated through potential modulated fluorescence (PMF) spectroscopy. The association between the dendrimers and the porphyrins or bioactive species was significantly dependent on the pH condition and the generation of dendrimers. In aqueous solutions, the spectroscopic results indicated that zinc(II) 5,10,15,20-tetrakis(4-sulfonatophenyl)porphyrin ( $\text{ZnTPPS}^{4-}$ ) associated with the positively charged fourth generation (G4) PAMAM dendrimer was highly stabilized without protolytic demetalation in a wide range of pH. On the other hand, the free base porphyrin ( $\text{H}_2\text{TPPS}^{4-}$ ) was readily protonated under acidic conditions even in the presence of the dendrimers accompanied by forming the J-aggregates of diprotonated species, ( $\text{H}_4\text{TPPS}^{2-}$ )<sub>n</sub>. PMF measurement at the water|DCE interface revealed that the dendrimers incorporating porphyrin molecules were transferred across the positively polarized interface accompanied by the adsorption process, whereas the porphyrins released from the dendrimers were transferred at the negatively polarized interface. The ion association stability between the dendrimer and the porphyrin estimated from the negative shift of the transfer potential of the porphyrins exhibited relatively strong interaction between  $\text{ZnTPPS}^{4-}$  and the higher generation dendrimer. In the bioactive species systems, ionizable drugs, i.e. dipyridamole (DIP), propranolol (PRO) and warfarin (WAR), were

not effectively associated with the dendrimers in the aqueous solutions. PMF results of the fluorescent DIP indicated that the monoprotonated form,  $\text{HDIP}^+$ , was transferred across the water|DCE interface accompanied by the adsorption process and the interfacial mechanisms of the DIP species were significantly modified by the dendrimers, depending on the pH conditions. Flavin derivatives, especially riboflavin (RF) and lumichrome (LC), were effectively associated with the dendrimer in the aqueous solution. The interfacial adsorption of the anionic flavin derivatives was inhibited by forming associates with the dendrimer, while the associates were transferred across the interface in the positive potential region. Present results demonstrated that the potential ability of the dendrimers as molecular capsule and drug transporter.

## 学位論文審査報告書（甲）

1. 学位論文題目（外国語の場合は和訳を付けること。）

Spectroelectrochemical Studies of Molecular Association with Polyamidoamine Dendrimers at Liquid|Liquid Interfaces（液液界面におけるポリアミドアミンデンドリマーによる分子会合反応の分光電気化学的研究）

2. 論文提出者（1）所 属 物質科学 専攻

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3. 審査結果の要旨（600～650字）

提出学位論文について、各審査委員による予備審査を実施した後、平成28年1月28日に口頭発表会および論文審査委員会を開催し、以下のように判定した。

混ざり合わない水相と有機相の液液界面は、物質の液液分配を利用した分離化学や不均一反応において重要な二次元特異反応場であり、生体膜のモデル反応場としても利用されている。本論文では、規則的な三次元階層構造を有する多分岐高分子であるポリアミドアミンデンドリマーと様々な分子の会合挙動を分光電気化学的に研究し、液液界面における反応機構を解明した。デンドリマーは分析試薬や色素増感剤として重要な水溶性ポルフィリン化合物と静電相互作用による会合体を形成し、水溶液中ではポルフィリン化合物のプロトン付加や金属解離反応の抑制、液液界面では会合状態と相間移動反応の電気化学的制御が可能であることを示した。さらに、液液界面で隔てられたポルフィリン化合物とフェロセン誘導体の間で生じる不均一光誘起電子移動反応では、デンドリマーとの会合体形成によって反応効率が向上することを明らかにした。また、様々なイオン性薬剤分子やフラビン化合物との会合反応を詳細に解析し、静電的あるいは疎水性相互作用による会合体形成と界面吸着反応への影響を明らかにした。本論文の成果は、デンドリマーを新規な分離検出反応や薬物動態制御などに応用する上で重要な指針を与えるものであり、博士（理学）の学位に値すると判断した。

4. 審査結果（1）判定（いずれかに○印） ☒ 合格 ・ ☐ 不合格

（2）授与学位 博士（理学）