

The Potentiometric Performances of the Cation Selective Electrodes based on Tetracycline and Chemically Modified Tetracycline

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ABSTRACT:

Metal-binding antibiotics are very attractive choices as cation selective ionophores. The ability of tetracycline (TC) antibiotics to bind to metal ions has obtained much attention. TCs exhibit the potentiometric performance changes for various cations dependant on several experiment conditions. In this report, we investigated the potentiometric performance changes of TC as the modification of TC's possible metal binding site. We found that the selectivity alter with the blocking main binding site of ionophores for cations. And, additionally it is possible to control the selectivity of sensors with chemical modification of ionophores.

Keyword: Tetracycline, Ion selective electrode, Potentiometric performance, Modified tetracycline

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1. Introduction

The metal-binding antibiotics are very attractive choices as cation selective ionophores.¹⁻³⁾ The binding ability to metal ions of tetracycline (TC) antibiotics has obtained much attention because TCs have a very good affinity with divalent ions such as Mg(II) and Ca(II) ions.⁴⁻⁶⁾ Selectivity is obviously one of the most important characteristics of the sensors. In many cases, the ligand structure, cation size and complex formation or extractability are the major determining factors for selectivity. We also expect that the binding site modification of cation binding ionophores may cause a decisive effect on the selectivity toward certain cations by sensor based on those ionophores.

It has been reported that TC-based membrane electrodes showed different levels of selectivity toward both Ca(II) and Mg(II) based on membrane composition, especially on plasticizers.⁶⁻⁸⁾ In case of TC, the selectivity can vary with the plasticizers and additives employed.⁷⁾ In that report, we also pointed the possible binding site for

metal-TC complex through spectroscopic investigations. However, in a recent article, Rhee *et al.*⁸⁾ reported the binding site of Hg(II) ion with TC with calculation and NMR data. In their ¹HNMR results, they suggested that the binding model TC with Hg(II) ions in membrane is mainly a tricarbonylmethane functional group of ring A in TC (Fig. 1).

Here, modified TC (MTC) of blocking proposed binding sites was synthesized and the cation selective polymer membrane electrode was fabricated with. Then, the potentiometric performance of aforementioned electrode was

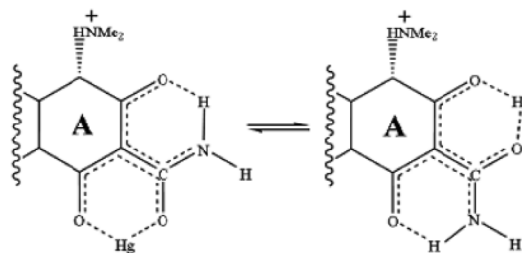


Fig. 1. A proposed binding structure of Hg(II) ion with tricarbonylmethane functional group of the ring A in TC.

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compared with that of TC-based membrane electrode. The potentiometric response - the slope towards several cations were influenced by MTC compared with TC. Thus, it is suggested that the results are due to the blocking of its binding site and are additionally possible to control the selectivity wanted with chemical modification of ionophores.

2. Experiments

2.1. Reagents and Apparatus

TC was purchased from Sigma (Saint Louis, MO, USA). Poly(vinyl chloride) (PVC), potassium tetrakis (4-chlorophenylborate) (KTpCIPB) and sebacate plasticizers (DOS) were supplied by Fluka (Ronkonkoma, NY, USA). Solvents and all other chemicals including nitrate salts of examined cations were analytical reagent grade. Solutions were prepared using deionized water. (Millipore, Billerica, MA, USA)

2.2. Preparation of modified tetracycline (MTC)

Modified TC was synthesized as follows : 0.5 mmol (0.1632 g) of K_2PdCl_4 was added to 5 ml of 0.5 mmol TC solution. After vigorous mixing for 3 hr, the solution was filtered with membrane filter and then dried under a vacuum. The final product was confirmed with NMR. The structure and NMR spectrum of modified TC is shown in Fig. 2.

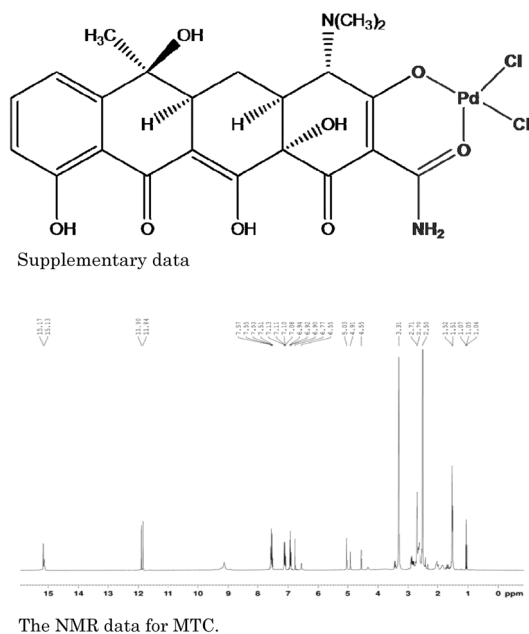


Fig. 2. The structure of Modified TC with palladium chloride.

2.3. Preparation and evaluation of polymer membranes and electrodes

PVC matrix membranes were prepared according to the method reported previously.³⁾ The ion selective electrode (ISE) membrane was prepared by mixing 1% TC, 33% PVC and 66% plasticizer (DOS) resulting in 200.0 mg, and 100 mol% of cation additive (KTpCIPB) were dissolved in 1 mL THF. The solution was cured to produce an elastic membrane. A small disk of 5.5 mm diameter was cut out from the PVC membrane and then mounted onto the end of electrode body (IS-561; Glasblaserei Möller, Zürich, Switzerland).

The potentiometric behavior of the membrane electrode was evaluated with the conventional ISE configuration. For all electrodes, a solution of 1×10^{-3} M $Hg(NO_3)_2$ was employed as the internal filling solution. The external reference electrode was an Orion sleeve-type double junction Ag/AgCl/KCl(saturated) electrode (Model 90-02).

3. Results and Discussion

Two of recent papers have reported the two different selectivity by ion selective membrane electrodes based on TC toward the cations.^{7,8)} The first of those papers,⁶⁾ by changing the plasticizer, sensors responded to the Ca and Mg ions with different selectivity. In that paper, authors suggested the binding site is keto-enolate site of TC. However, Rhee *et al.*⁸⁾ insisted that the binding site of Hg (II) ion with TC is mainly a tricarbonylmethane functional group of ring A in TC through NMR data and simulated calculation. These reports are ambiguous and in need of clarification.

Here, we expect that the binding site modification could alter the selectivity toward certain cations. Thus, in order to find the binding site of TC with cations in this membrane and investigate the selectivity changes with structure of ionophores, we chemically modified the TC as blocking tricarbonylmethane functional group of ring A on TC.

And the potentiometric performances of sensor based on MTC was compared with that of TC. The data is listed in Table 1. As shown in Table 1, the slope decreased significantly for the cations examined with sensor based on MTC. In the case of Hg(II) ion and Ca(II) ion, the slope decreased 52%, from 34.60 mV/dec to 16.66 mV/dec (with MTC), and 89%, from 27.8 mV/dec (with TC) to 3.20 mV/dec (with MTC), respectively. However, it exhibited relatively small decreases in cases of K^+ and NH_4^+ .

From those results, we could conclude that the main

Table 1. Potentiometric response properties (slope and detection limit) in sensor based on TC and modified TC.

	TC		MTC	
	Slope (mV/decade)	D.L. -log[M]	Slope (mV/decade)	D.L. -log[M]
Ca ²⁺	27.8 ^a	4.52	3.20	5.30
Na ⁺	9.03	4.85	4.64	4.65
Li ⁺	8.81	4.98	2.27	3.03
K ⁺	22.52	5.20	21.78	5.01
NH ₄ ⁺	21.99	5.20	18.46	4.90
Hg ²⁺	34.60 ^b	6.20	16.66	5.04

a : ref. 6 b; ref. 8

binding site of TC for divalent cations is tricarbonyl-methane functional group of ring A in TC, and monovalent ion such as K⁺ ion NH₄⁺ ion can coordinate to keto-enolate site of TC. The latter was supported by *in vivo* studies; K⁺ ion can coordinated to keto-enolate site of TC and histidine as octahedral structure.^{5,9)} Also NH₄⁺ ions shows similar response to K⁺ ions, it can be explained

by similar radii⁶⁾ on both ions, K⁺ ion and NH₄⁺ ion.

In summary, we found that the selectivity alter with the blocking main binding site of ionophores for cations. And, additionally it is possible to control the selectivity of sensors with chemical modification of ionophores.

References

1. W. E. Morf and W. Simon, *Helv. Chim. Acta*, **54**, 2683 (1971).
2. M. Schafer, G. M. Sheldrick, I. Bahner and H. Lackner, *Angew. Chem. Int.*, **37**, 2391 (1998).
3. I. R. Paeng, *Anal. Sci. Technol.*, **18**, 491 (2005).
4. J. M. Wessels, W. E. Ford, W. Szymczak and S. Schnider, *J. Phys. Chem. B*, **102**, 9323 (1998).
5. O. Scholz, P.; Schubert, M. Kintrop and W. Hillen, *Biochemistry*, **39**, 10914 (2000).
6. J. Baek, I. Rhee and K.-J. Paeng, *J. Kor. Electrochem. Soc.*, **9**, 132 (2006).
7. J. Baek, J.-S. Kim, I. Rhee and K.-J. Paeng, *Bull. Kor. Chem. Soc.*, **29**, 165 (2008).
8. J. Baek and I. Rhee, *J. Kor. Electrochem. Soc.*, **11**, 59 (2008)
9. O. J. Palm, D. Dalm, N. Mettew, J. Proft and W. Hindrichs, www.hasyllab.desy.de/science/annual_report/2005_report.