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NEW, NONCYCLIC IONOPHORES EXHIBITING SELECTIVE CATION TRANSPORT AGAINST THE CONCENTRATION GRADIENT

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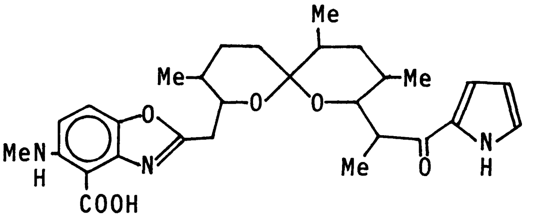
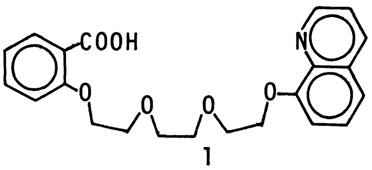
Some oligoethylene glycol derivatives containing both quinolyl and carboxyl terminal groups were prepared as synthetic ionophores. These polyethers can transport alkali ions selectively through liquid membrane against the concentration gradient. The rate of the active transport and the ion-selectivity with them change with changing the length of oxyethylene chain.

The phenomenon of ion transport across liquid membrane is receiving ever-increasing attention. A number of naturally occurring ionophores and synthetic ones as their model compounds are hitherto known which transport metal ions selectively and/or against the ion concentration gradient.1) As regard with synthetic noncyclic ionophores, although a number of their synthesis and selective complex formation with metal ions has been reported,2) only a few of ion transport with them has been known.3,4) These synthetic ionophores are substantially linear polyethers with hydroxy and carboxyl terminal groups like nigericin and monensin. A polyether antibiotic, A23187, is one of the best known Ca^{++} ionophores, which has pyrole and 8-carboxylbenzooxazole rings as terminal groups.5) However, there is no report about synthetic noncyclic ionophores containing both basic and acidic terminal groups like A23187. In this paper the author wishes to report the active ion transport with oligoethylene glycol derivatives containing basic and acidic ones.

The author et al. reported recently the preparation of triethylene glycol derivative containing ortho-carboxylphenyl and quinolyl terminal groups (1) and its complexation with alkali ions.6) Herein, some oligoethylene glycol derivatives with both carboxylphenyl or carboxylnaphtyl and quinolyl terminal groups as acidic and basic ones, respectively, are prepared.7) In order to modify the lipophilicity of the polyethers, naphtyl group was introduced in place of phenyl one, alternatively, ortho-phenylene group was introduced among oxyethylene chain (compounds 2a - 2c, and 3).



Acyclic Ionophore A23187



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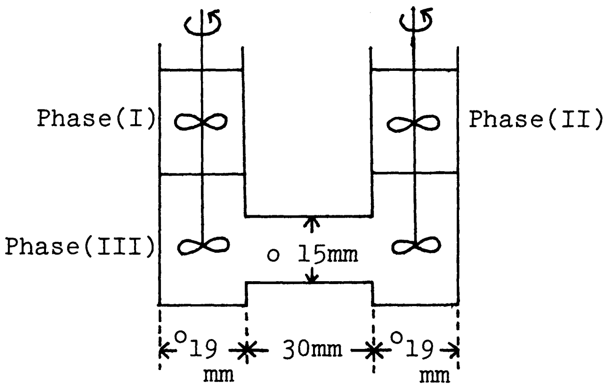
Transport of alkali ions across a chloroform liquid membrane with the synthetic polyethers prepared was examined within a U-type glass cell at 25 ± 0.2°C(Figure 1).

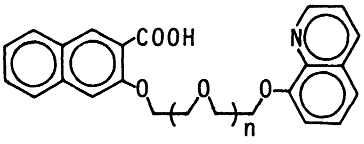
The amounts of the transported metal ion from Phase (I) to Phase (II) were determined by atomic absorption analysis. The experimental results are shown in Figures 2 - 4.

Fig. 1. U-type cell for ion transport



Phase(I): 15ml of 0.1N aqueous MOH solution;
Phase(II): 15ml of 0.1N MCl + 0.1N HCl soln.;
Phase(III): 30ml of $CHCl_3$ including 1.5×10^{-4} mole of synthetic polyether;
M : alkali metal (Li, Na, and K)

Synthetic Ionophores



2a (n = 1)
2b (n = 2)
2c (n = 3)

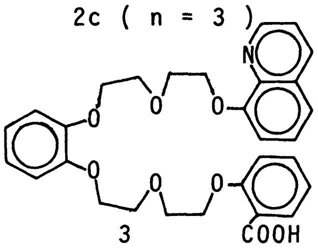


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Fig. 2. Active ion transport with (2a)

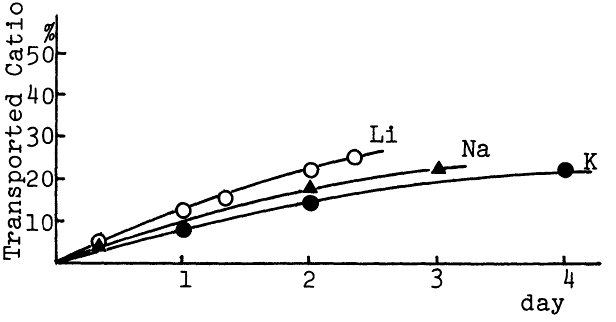


Fig. 3. Active ion transport with (2b)

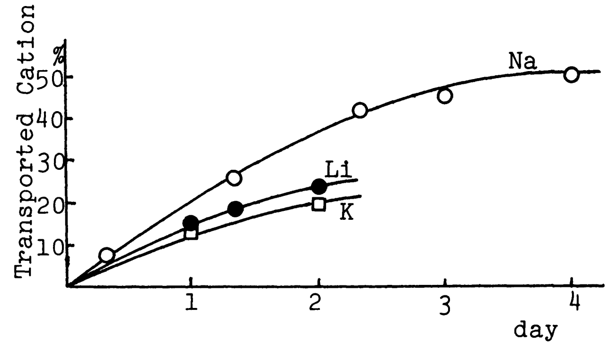
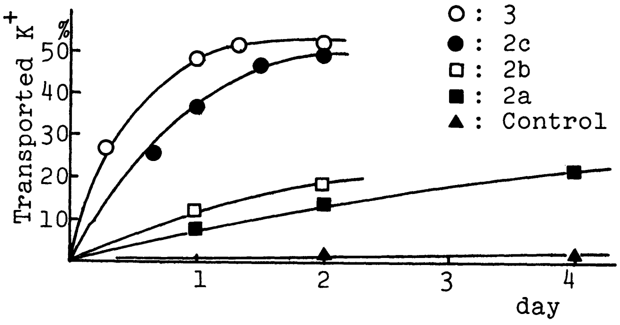


Fig. 4. Active ion transport of K^+ with synthetic ionophores



As indicated in Figures 2 - 4, the ion transport against the concentration gradient was observed with these synthetic ionophores in all cases. Additionally, the rate of ion transport depends upon the kind of ionophores, that is, the selectivity of ion transport was observed by the length of oxyethylene sequence of ionophores. Lithium ion was transported to some extent by these ionophores, independent of the length of oxyethylene chain as reported by Yamazaki et al.[3] It is difficult to explain the result only by the fitness of sizes between the cavity of pseudocyclic structure and lithium ion, although diethylene glycol derivative(2a) transports Li^+ a little more preferentially than Na^+ and K^+ (Figure 2). As seen in Figure 3, the largest rate of transport was observed in the case of Na^+. This result is consistent with the NMR spectroscopic behavior of (1) with alkali ions,6) in which it is suggested that sodium ion becomes very suitably incorporated into the cavity formed by the noncyclic polyether. Apparently, the fitness of sizes between metal ion and the inner cavity of ionophore, which forms pseudocyclic conformation, is important for uptake into Phase (III) from Phase (I) and transport to Phase (II). In Figure 4, the result of K$^+$ transport with four synthetic ionophores are shown. The rate of K$^+$ transport with them was decreased in the order as follows: (3) $>$ (2c) $>$ (2b) $>$ (2a) $\gg$ none. Thus, pentaethylene glycol derivative (3) transports most efficiently K$^+$ from Phase (I) to Phase (II) against the ion concentration gradient. Moreover, the transport of K$^+$ with (3) was also examined in the case that the potential difference between Phases (I) and (II) was clamped at 0 mV under the same conditions as described above. This made no difference to the above-observed result. This implies that the transport of alkali ion in this system is 'active'.8)

Next, the K$^+$ transport with (3) was attempted under the conditions that the initial ion concentration in Phase (II) was 2 to 5 times more than that in Phase (I) and other conditions were the same as described above. Surprisingly, 40 % to 50 % of initial amount of K$^+$ in Phase (I) transported to Phase (II) after 1 day in the presence of (3) in Phase (III) as seen in Figure 5. From Figures 4 and 5, the rate of K$^+$ transport is little affected by the increase of initial K$^+$ concentration in Phase (II) in the case (A). In the latter case (B), the final K$^+$ concentration in Phase (II) reaches almost ten times more than that in Phase (I).9)

Phase (I)	Phase (III)	Phase (II)
0.1N KOH 15 ml	(3): 1.5×10^{-4} mole $CHCl_3$ 30 ml	(A): 0.2N KCl + 0.1N HCl or (B): 0.5N KCl + 0.1N HCl 15 ml

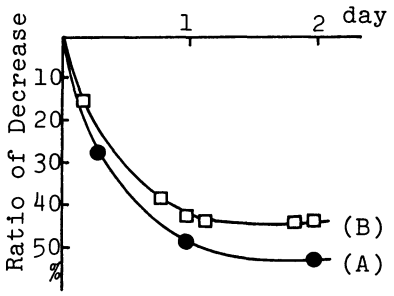
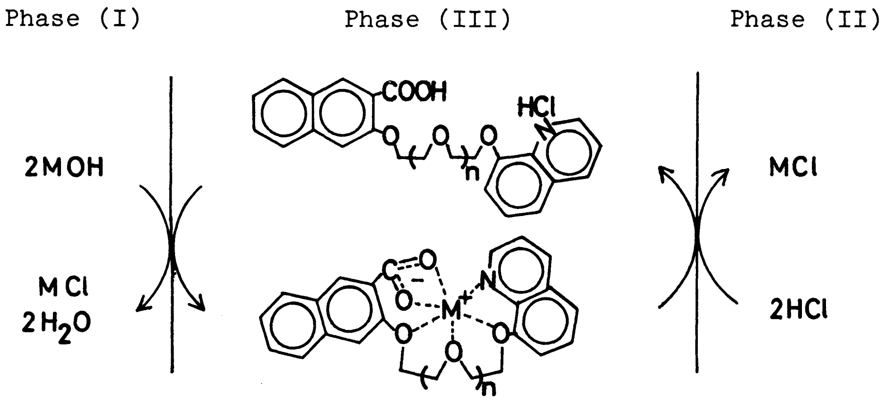


Fig.5. Decrease of K$^+$ amount in Phase (I)

Apparently, the ion transport seems to cease at the point where at most 50 % amount of ion in Phase (I) is carried to Phase (II) under these conditions.10) It is considered that HCl, which can be carried reversely from Phase (II) to Phase (I) as quinolynium salt because the ionophores contain basic quinolyl group, reacts with alkali hydroxide in Phase (I) to give alkali chloride.11) Therefore, the amount of ion transported from Phase (I) to Phase (II) is at maximum 50 % under these conditions as proposed sckeme in Figure 6. In this system, after metal ion is carried across Phase (III) to Phase (II), which is wrapped by pseudocyclic conformation of the polyether, the polyether becomes quinolynium salt at the boundary between Phase (II) and Phase (III) to be unable to form pseudocyclic conformation as indicated in Figure 6. Therefore, it is considered that the reverse ion transport from Phase (II) to Phase (I) can hardly occur and the ion transport from Phase (I) to Phase (II) can efficiently occur even under the condition that the initial ion concentration in Phase (II) is two to five times more than that in Phase (I).

Fig. 6. Ion transport scheme



Thus, these synthetic ionophores can clearly be endowed with ion-selectivity and enhance the active transport by designing of the molecules, that is, changing the length of oxyethylene chain, although amount of ion transported with them is at maximum 50 % of initial amount of ions in Phase (I).

The author and coworkers are continuing their investigation into synthetic ionophores and will report the transport phenomenon of other alkali ions, divalent metal ions and organic compounds, and the relation between structure of synthetic ionophores and their selectivity in due course.

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7) Synthesized according to Ref. 6). All new compounds reported gave satisfactory C, H, and N elementary analysis.
8) T. Shinbo, K. Kurihara, Y. Kobatake, and N. Kamo, Nature, 270, 277(1977).
9) The rate of transport and the final amount of ion transported are apparently affected by the large initial K$^+$ concentration in Phase (II). Under investigation concerning to the influence of ion concentration.
10) There is a possibility that the terminal amount of ion transported with them changes using buffered solution.
11) It was confirmed that chloride ion in Phase (I) increased with time.

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