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Thallium(I) as a Potassium Probe in Biological Systems

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Summary Thallium(I) has been found to replace potassium in two enzymes, and thallium has been shown to have many possibilities as a potassium probe.

POTASSIUM ACTIVATION of enzymes is well known, but the effects of this element are extremely hard to define more closely as potassium is a poor probe. We have therefore set out to test the activity of thallium(I) which has several possible probe potentialities. Initially we examined two enzymes, pyruvate kinase and the vitamin B_{12}-dependent diol dehydratase. Table 1 shows that thallium(I) is ten times more effective in activating both enzymes due to a ten-fold increase in binding and not to a change in the maximum activity of the enzymes when the cation is at high concentration. This result has been observed in other biochemical systems[1,2] so that thallium(I) may be a general substitute for potassium. With this possibility in mind we have gone back to the study of thallium complexes with small ligands.

TABLE 1

The activation of enzymes by monovalent cations

	Diol-dehydrates		Pyruvate kinase	
	V_{max}	$\log_{10}K_M$	V_{max}	$\log_{10}K_M$
Lithium	inactive	small	inactive	small
Sodium	0·59	0·9		
Potassium ..	1·00	3·25	1·0	1·9
Ammonium ..	1·00	3·70		
Thallium	1·00	4·10	0·25	3·3
Rubidium ..	1·00	2·5		
Caesium	0·67	1·9	0·35	2·3

K_M is the binding constant of the metal to the enzyme and V_{max} the maximum velocity relative to potassium, and both are obtained from a study of the enzyme reaction kinetics.

Table 2 records some stability constants of thallium(I) complexes together with some data on potassium. Thallium binds several ligands at least ten times more strongly. Now several of these ligands have been chosen as they are the substrates of potassium-activated enzymes and we have gone on to consider the physical properties of the complexes. In addition to the possibility of using thallium-205 n.m.r.[2] we have examined the shifts in the u.v. absorption band of thallium(I) (Table 1), the quenching of fluorescence on complex formation, and the effect of thallium(I)

TABLE 2

The stability constants and absorption spectra of some thallium(I) *complexes at* 25° *and ionic strength* (μ) *of* 0·15M

Ligand	$\text{Log}_{10}K_{Tl}$ (±0·10)	λ_{max} (nm)	$\text{Log}_{10}K_K$ (medium)[a]
PO_4^{3-}	2·25	230	
HPO_4^{2-}	0·75	225	
$P_2O_7^{4-}$	3·05	227	2·3 (μ = 0)
$HP_2O_7^{3-}$	2·35	219	0·8 (μ = 1·0)
Ribose-5-phosphate^{2-}	0·90	219	
Adenosine-diphosphate^{3-}	1·20		
Adenosine-triphosphate^{4-}	2·00		1·15 (μ = 0·1)
Ethylenediaminetetra-acetate^{4-} ..	5·8[a]	246	1·00
Nitrilotriacetate^{3-}	4·4	243	

λ_{max} for the aquated Tl^I is at 213 nm.

[a] These constants are from "Stability Constants," *Chem. Soc. Special Publ. No.* 17, (eds. A. E. Martell and L.-G. Sillén), (1964).

on ligand nuclear resonances, *e.g.* of hydrogen and phosphorus. The magnitude of the shifts of the proton resonance of ethylenediaminetetra-acetate on complex formation are: $>CH_2$ of acetate $-0{\cdot}21$ p.p.m., ethylenic $>CH_2$ $-0{\cdot}17$ p.p.m. The shifts of the resonances of different phosphates are: pyrophosphate $-1{\cdot}4$; adenosine diphosphate α-P $-2{\cdot}0$, β-P $-1{\cdot}3$; adenosine triphosphate α-P $-0{\cdot}5$, β-P $-2{\cdot}2$, γ-P $-1{\cdot}0$ p.p.m. The complexes have been studied over the pH range 4·0—11·0. These shifts are as large as those found on complex formation with bivalent cations and should be easily followed in biological systems.

Apart from the use of thallium(I) in studying enzymes it should be useful in tackling the problem of potassium movement in membranes and its association with RNA. It is known that erythrocytes accumulate thallium in place of potassium.[3,4]

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