Study on Speciation of Pr(III) in Human Blood Plasma by Computer Simulation

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Abstract: Speciation of Pr(III) in human blood plasma has been investigated by computer simulation. The speciation and distribution of Pr(III) has been obtained. It has been found that most of Pr(III) is bound to phosphate and to form precipitate. The results obtained are in accord with experimental observations.

Keywords: Speciation, praseodymium(III), computer simulation.

Biological effects of metal are controlled by its *in vivo* speciation [1,2]. It is not possible to determine *in vivo* speciation of metals with analytical methods so far. The low-molecular-weight complex distribution of biometal ions in blood plasma was studied by computer simulation[1]. Soluble species of rare earth were also reported [2,3]. However, insoluble species of rare earth in blood plasma have not been studied, it is the aim of this paper to study insoluble species by computer simulation.

We improved May's model, and constructed our computer model of Pr(III) speciation in human blood plasma[4,5]. To this model of Pr(III) speciation some proteins(transferrin, HSA and IgG) were added. Our studies show that ternary complexes of rare earths with biomolecules are important. For this reason, this model of Pr(III) speciation also included many important ternary complexes of Pr(III). The accurate determination of stability constants of complexes is very important to computer simulation of speciation. A lot of accurate stability constants of complexes of rare earths with biological ligands were determined under physiological conditions in our group, and were used in computer simulation by means of a computer program MINTEQA2.

The results from computer simulation are listed in **Table 1**. The concentration of Pr(III) used in the model of Pr(III) speciation is 3.55E-7 mol/L, and pH value is 7.0 4,5. It can be seen from **Table 1** that 99.4% of Pr(III) is bound to phosphate to form praseodymium phosphate. It is the most predominant species of all.

$Pr(OH)_3$ exists as an insoluble species in human blood plasma, though its content is exceedingly small. It can be expected that the content of $Pr(OH)_3$ increases at higher pH values. Soluble species consist of low-molecular-weight ligand complexes (amino-acid, carboxylate complexes *etc.*), protein complexes (transferrin, HSA and IgG complexes),

Table 1 The species and distribution of Pr(III)

Species	$PrPO_4$	$Pr(OH)_3$	$Pr(HPO_4)^+$	$Pr(HPO_4)_2^-$	Soluble species
Concentration (mol/L)	3.53E-7	8.03E-32	2.69E-31	1.33E-48	2.00E-9
Percentage distribution (%)	99.437	-	-	-	0.563

free Pr(III), and so on. Pr(III) forms precipitate of $PrPO_4$, as a result, it can make the absorption of Pr(III) in human body difficult. It has been found that rare earths administered to animals *via* oral can be excreted *via* urine or faeces, and accumulation in organs and tissues is quite low. It is obvious that the results obtained by computer simulation propose a convincing explanation for the pattern of excretion and accumulation reported *in vivo* biodistribution and metabolism studies.

Table 2 The species and distribution of phosphate

Species	$PrPO_4$	$Pr(HPO_4)^+$	$Pr(HPO_4)_2^-$	HPO_4^{2-}	$H_2PO_4^-$	H_3PO_4	PO_4^{3-}
Concentration (mol/L)	3.53 E-7	2.69 E-31	1.33 E-48	1.58 E-4	2.22 E-4	2.97 E-9	9.01 E-10
Percentage distribution (%)	0.094	Very small	Very small	41.539	58.366	Very small	Very small

The species and distribution of phosphate are presented in **Table 2**. The data in **Table 2** show that only 0.094% of phosphate is combined with Pr(III), and most of phosphate is available. For this reason rare earths are still bound to phosphate to form precipitate when their dose administered to animal increases. It will be seen from this that accumulation of rare earth in organs is still very low.

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