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Computer Simulation of Gd(III) Speciation in Human Interstitial Fluid

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Abstract: The speciation and distribution of Gd(III) in human interstitial fluid was studied by computer simulation. Meantime artificial neural network was applied to the estimation of log β values of complexes. The results show that the precipitate species, $GdPO_4$ and $Gd_2(CO_3)_3$, are the predominant species. Among soluble species, the free Gd(III), [Gd(HSA)] , [Gd(Ox)] and then the ternary complexes of Gd(III) with citrate are main species and $[Gd_3(OH)_4]$ becomes the predominant species at the Gd(III) total concentration of 2.2×10^{-2}mol/L.

Keywords: Computer simulation, gadolinium(III), speciation, human interstitial fluid.

The study on biological effects of rare earths is of great importance because more and more rare earths enter into the environment and human body *via* food chain *etc.*[1, 2] The research on rare earth speciation is a key to understand distribution, metabolism and biological effects of rare earths. As a continuation of our research on rare earth speciation in human body[3],soluble and insoluble speciations of Gd(III) in human interstitial fluid were studied in this work. Almost all the stability constants of the complexes of Gd(III), Ca(II) and Zn(II) with the low-molecular-weight biological ligands contained in this model were determined accurately under physiological conditions(T=37°C, I=0.15 mol/L)[3]. The binding constants of Gd(III) with inorganic ligands and proteins were mostly cited from references[2]. The binding constant of [Gd(HSA)] was estimated by artificial neural network.

Table 1 shows the distribution of Gd(III) species. At the background concentration of Gd(III) in human interstitial fluid (1.203×10^{-9} mol/L)[4], all the Gd(III) species are soluble and no precipitate appears. At the total concentration of $1.4x10^{-9}$ mol/L , $GdPO_4$ was firstly formed due to its high stability. When the total concentration of Gd(III) gets to 6.00×10^{-4} mol/L, another precipitate of $Gd_2(CO_3)_3$ begins to appear. From **Table 1**, it can be seen that when Gd(III) compounds enter into human body, $GdPO_4$ and $Gd_2(CO_3)_3$ are the main species. Since the precipitates are main species, most of Gd(III) are difficult to be transported and absorbed in human body. Distribution of soluble Gd(III) is shown in **Table 2**. When the total concentration of Gd(III) is below 5.988×10^{-4} mol/L, free Gd(III), [Gd(HSA)], [Gd(OX)] and Gd(III) ternary complexes with citrate are the main species. When the total concentration of Gd(III) reaches to 2.074×10^{-2} mol/L, $[Gd_3(OH)_4]$ begins to appear. With the increase of the total concentration of Gd(III) , $[Gd_3(OH)_4]$ gradually becomes the predominant species. At the same time, the percentages of the other soluble Gd(III) complexes

decrease obviously. It means Gd(III) entering into human interstitial fluid tends to form soluble hydroxyl compound under physiological conditions.

Table 1 Distribution of Gd(III) species(%) (37^oC, pH=7.4, I=0.15mol/L NaCl)

Species	Total concentration of Gd(III)(mol/L)				
	1.203×10^{-9}	1.4×10^{-9}	2.610×10^{-9}	6.00×10^{-4}	2.05×10^{-2}
$GdPO_4$	0.0	7.3	50.1	99	5.73
$Gd_2(CO_3)_3$	0.0	0.0	0.0	0.1	94.16
Soluble Gd(Ⅲ)	100.0	92.7	49.9	0.0	0.1
	(1.203×10^{-9})	(1.233×10^{-9})	(1.233×10^{-9})	(1.155×10^{-7})	(1.454×10^{-5})

*The values in parentheses are the concentrations of soluble Gd(Ⅲ) species

Table2 Distribution of the soluble Gd(III) species (%)(37^oC,pH=7.4,I=0.15mol/L NaCl)

Soluble Gd(Ⅲ)	Total concentration of Gd(III)(mol/L)					
	1.203×10^{-9}	1.000×10^{-7}	5.988×10^{-4}	2.074×10^{-2}	2.200×10^{-2}	2.30×10^{-2}
Free Gd(Ⅲ)	5.4	5.4	5.5	6.5	2.6	1.6
$[Gd_3(OH)_4]$	<1	<1	<1	1.0	78.9	88.3
$[Gd(Cit)(Gly)H_2]$	2.2	2.2	2.2	2.1	<1	<1
$[Gd(Cit)(Gln)H_2]$	3.1	3.1	3.1	3.0	<1	<1
[Gd(Cit)(Lac)]	10.0	10.0	9.9	9.5	1.7	<1
[Gd(Cit)(Leu)]	7.9	7.9	7.8	7.4	1.2	<1
[Gd(Cit)(Asp)]	7.7	7.7	7.6	5.3	<1	<1
[Gd(Ox)]	18.2	18.2	18.3	14.9	1.2	<1
[Gd(HSA)]	29.6	29.6	29.8	33.6	8.5	4.6
[Gd(IgG)]	3.1	3.1	3.1	3.5	1.1	<1
[Gd(OH)]	2.5	2.5	2.5	3.0	1.2	<1

*Cit=citrate,Gly=glycinate,Gln=glutaminate,Lac=lactate,Leu=leucinate,Asp=aspartate,Ox=oxalate HSA=Human Serum Albumin, IgG=immunoglobulin G

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