Computer modelling of the chemical speciation of Americium (III) in human body fluids

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Abstract. A muti-phase equilibrium model consisted of muti-metal ion and low molecular mass ligands in human body fluid has been constructed to discuss the speciation of Am^{3+} in gastric juice, sweat, interstitial fluid, intracellular fluid and urine of human body, respectively. Computer simulations indicated that the major Am(III) species were Am^{3+}, $[AmCl]^{2+}$ and $[AmH_2PO_4]^{2+}$ at pH <2.9 and the solid phase $AmPO_4$ became dominant with higher pH value when [Am] = 1×10^{-7} mol/L in gastric juice model and percentage of $AmPO_4$ increased with [Am]. in sweat system, Am(III) existed with soluble species at pH4.2~pH7.5 when [Am] = 1×10^{-7} mol/L and Am(III) existed with Am^{3+} and $[AmOH]^{2+}$ at pH6.5 when [Am] < 3×10^{-10} mol/L or [Am] > 5×10^{-8} mol/L . With addition of EDTA, the Am(III) existed with soluble $[AmEDTA]^-$ whereas the Am(III) existed with insoluble $AmPO_4$ when [Am] > 1×10^{-12} mol/L at interstitial fluid. The major Am(III) species was $AmPO_4$ at pH7.0 and [Am]=4×10^{-12} mol/L in intracellular fluid, which implied Am(III) represented strong cell toxicity. The percentage of Am(III) soluble species increased at lower pH hinted that the Am(III), in the form of aerosol, ingested by macrophage, could released into interstitial fluid and bring strong toxicity to skeleton system. The soluble Am(III) species was dominant when pH<4.5 despite the major Am(III) species was solid $AmPO_4$ when pH>4.5 when [Am] = 1×10^{-10} mol/L in human urine, so it was favorable to excrete Am(III) from kidney by taking acid materials.

KEYWORDS: body fluid; thermodynamic equilibrium; speciation; Am3+; toxicity

1. Introduction

Americium, a synthetic element with most hazardous isotopes ^{241}Am(α emitter, $T_{1/2}$=432.2 a, E=5.485 MeV(85.1%), E=5.442 MeV(13.3%)) and ^{243}Am (α emitter, $T_{1/2}$=7370 a, E=5.275 MeV (87.4%), E=5.233 MeV (11.0%)) has been widely produced and used in nuclear industry, and become a environmental unfriend contamination. Based on the long toxicity to human[1]， a lot of investigations had been focused on the determination[2] and venture evaluation[3] of Americium. Americium in waste water and polluted soil could come into human body by ingesting food, inhalating aerosol or skin penetration. Same to the other metal ion, the speciation of Americium dominate its distribution, metabolization and excretion in human body[4]. In despite of the exact species could hardly been mensurated in experiment, the computer modelling with thermodynamic equilibrium methodology could play important role in prediction speciation of trace element in environment[5-8]. Investigation of the speciation of Be^{2+} and UO_2^{2+} in the human body fluids imlpied [7,8] thermodynamic equilibrium methodology was valueable in exploring nuclides toxicity. This paper present the speciation of Am^{3+} in human body fluids by computer modeling mothed.

2. Models and motheds

The Composition and pH value of human body fluid had been reviewed by Guyton [9] and Iyengar[10], the metal ion and low weigh molecule ligand and their concentration in human body fluids involving in this thermodynamic equilibrium were listed in table 1 and table 2. The Elements of the two table have included the major matel ions and organic ligands of body fluids and could describe effectively the reality. The formation constants of Am^{3+}complexes were listed in table 3 and the other formation

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constants of other metal ions or/and ligands were provided by SC-Databases[11]. All calculations were carried out using the Hyperquad 2000 program[12]. Before calculations, the formation constants were adjusted to certain values on considering the exact tempture of 37℃ and the ionic strength of equilibrium systems were adjusted to certain values according to different body fluid. Adsorption and unequilibrium have been ignored in all calculations.

Table 1 Composition and pH value of human body fluid

Element	Intracellular fluid/μmol·L^{-1}	Interstitial fluid /μmol·L^{-1}	Sweat /μmol·L^{-1}	Gastric juice /μmol·L^{-1}
K^+	140000.00	4000.00	6.74	10524.00
Na^+	14000.00	139000.00	105.76	54543.00
Ca^{2+}	0.00	1200.00	4.77	
Mg^{2+}	20000.00	700.00	0.05	
PO_4^{3-}	11000.00	2000.00	0.02	1419.00
CO_3^{2-}	10000.00	28300.00		
SO_4^{2-}	1000.00	500.00		
Cl^-	4000.00	108000.00	43.59	84000.00
F^-			0.06	29.00
Cu^{2+}				4.00
(pH)	6.0~7.4	7.4	4.2～7.5	1.0～3.5

Table 2 Composition and pH value of human urine

Element	Concentration/μmol·L^{-1}	Element	Concentration/μmol·L^{-1}	Element	Concentration/μmol·L^{-1}
Al^{3+}	27.33	F^-	84.21	PO_4^{3-}	18820.02
AsO_4^{3-}	1.72	F^{e2+}	5.67	Pb^{2+}	0.23
$B(OH)_4^-$	79.44	Ga^{3+}	0.60	Rb^+	26.57
Ba^{2+}	0.52	Ge^{2+}	19.28	SO_4^{2-}	33125.00
Be^{2+}	14.44	I^-	2.02	Sn^{2+}	0.22
Br^-	49.11	K^+	64850.81	Sr^{2+}	2.56
Ca^{2+}	5285.46	Li^+	102.73	TeO_4^{2-}	4.15
Ce^{3+}	0.23	Mg^{2+}	4681.11	Ti^{3+}	8.66
Cl^-	146666.67	Mn^{2+}	10.99	V^{2+}	0.44
Co^{2+}	0.38	MoO_4^{2-}	0.66	WO_4^{2-}	0.16
Cr^{3+}	0.50	Na^+	174075.16	Zn^{2+}	6.91
Cs^+	0.12	NbO_3^-	3.88	pH	4.2～8.0
Cu^{2+}	0.77	Ni^{2+}	1.85		

Table 3 Formation constants of Am3+complexes

Species	logβ or logKsp	Ref.
$[AmOH]^{2+}$	7.6	1
$[Am(OH)_2]^+$	13.9	1
$Am(OH)_3(aq)$	16.3	1
$[AmCl]^{2+}$	1.05	1
$[AmSO_4]^+$	3.85	1
$[Am(SO_4)_2]^-$	5.40	1
$[AmH_2PO_4]^{2+}$	21.22	1
$[AmCO_3]^+$	7.80	1
$[Am(CO_3)_2]^-$	12.30	1

$[Am(CO_3)_3]^{3-}$	15.20	1
$[Am(CO_3)_5]^{6-}$	-4.90	1
$Am(OH)_3$ (am)	-25.00	1
$Am(OH)_3$ (cr)	-26.8	1
$AmPO_4$ (am)	-24.79	1
$Am_2(CO_3)_3$ (cr)	-33.40	1
$Am(OH)(CO_3)$ (cr)	-21.2	1

3. Results and discussion

3.1 Speciation of Am^{3+} in gastric juice

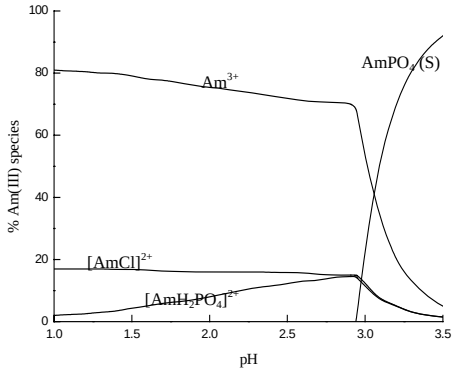

Fig. 1 Relationship of speciation of Am(III) and pH in gastric juice

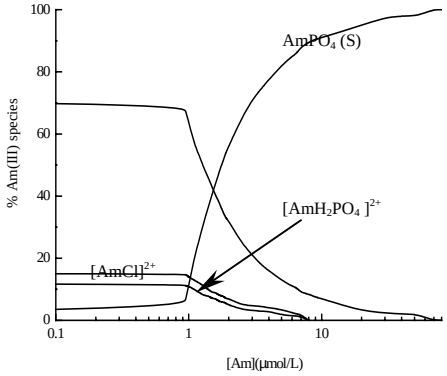

Fig. 2 Relationship of speciation of Am(III) and [Am] in gastric juice

Stomach is the organ for human to digest food, because of strong acidity of gastric juice and its normal pH value is 1.0~3.5[11]. The soluble Am(III) species in stomach, digested by gastric juice after taking up from food or water, may came into interstitial fluid, otherwise, the insoluble species would egest in the form of dejecta. The Am(III) present stronger toxicity when came into blood plasma than egested by dejecta. Fig.1 showed the speciation of Am(III) in gastric juice when the concentration of Am(III) was 0.1μmol/L. Fig.1 told us Am(III) existed with soluble species such as Am^{3+}, $[AmCl]^{2+}$ and $[AmH_2PO_4]^{2+}$ when the pH value of gastric juice was as lower as 2.9. and solid $AmPO_4$ came forth when pH value was only higher than 2.9.So, high percentage of Am(III) may invade to blood system. Fig.2 also told us the percentage of solid $AmPO_4$ increased with pH when pH more than 2.9, which implied it was favorble to prevent absorption from Am(III) by improving the pH value of gastric juice, for example, takeing alkaline material such as $NaHCO_3$. Fig.2 showed the relationship between speciation and the concentration of Am(III) when pH was 2.5, which told us the soluble species dominated when Am(III) was lower than 1μmol/L. Fig.2 suggested that Am(III) may invade

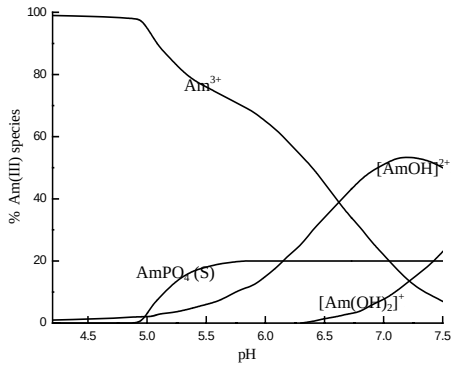

Fig. 3 Relationship of speciation of Am(III) and pH in sweat

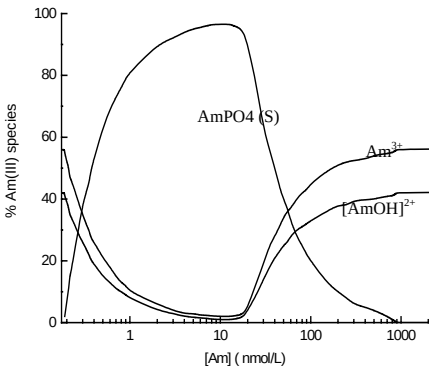

Fig. 4 Relationship of speciation of Am(III) and [Am] in sweat

to blood system again.

3.2 Speciation of Am^{3+} in sweat

It is well know that skin penetration is one of the major route of radionuclides uptake. Am(III) species dissolved in sweat may penetrate skin into interstitial fluid and behaved higher toxicity, whereas the solid Am(III) species in sweat behaved lower toxicity that was similar as Am(III) in gastric juice. Fig.3 showed the Am(III) speciation in sweat when Am(III) was 0.1μmol/L. From Fig.3, we knowed Am(III) existed mainly in soluble species at pH range from4.2 to7.5, the nomal sweat pH range[10]. Am^{3+}, the smallest molecule of Am(III) species, was the dominant when pH value was lower than 5.0. So, Am(III) adsorbed on human skin may enter interstitial fluid get across the route of sweat. Fig.4 showed the speciation of Am(III) in sweat at pH 6.5. Fig.4 told us high proportion of Am^{3+} and $[Am(OH)_2]^+$ species appeared when the concentration of Am(III) was lower than 0.3nmol/L or more than 50nmol/L. Skin of workers and researchers who operate Am may be contaminated by the Am aerosol or Am dust etc. Results of Fig.3 and Fig.4 indicated it was important to emphasize the prevention aimed at skin.

3.3 Speciation of Am^{3+} in interstitial fluid

Am^{3+} could arrive at every organ of human by the transportation of interstitial fluid. the speciation of Am(III) play important role in its toxicity. Fig.5 showed the speciation of Am^{3+} in interstitial fluid. From Fig.5 one could see that the major Am(III) species was solid $AmPO_4$ when Am(III) was more than 0.001nmol/L and the percentage of $AmPO_4$ increased with the concentration，which implied Am(III)could not be easily evacuated from blood plasma. The solid $AmPO_4$ may precipitate on the surface of hyroxyapatite, the inorganic phase of skeleton, when $AmPO_4$ pass by bone in blood. And then, Am(III) may come into the inner during bone rebuilding to behave toxicity lifelong. Chelation therapy is one of the best treatment for heavy metal ion toxicosis in which poisonous metal ion combine ligand to form charged complexes which could evacuate in urine. Fig.6 showed the influence of addition of 0.001 mol/L of EDTA on the speciation of Am(III) in interstitial fluid. In Fig.6, all of Am(III) existed in the form of $[AmEDTA]^-$ when Am(III) was lower than 70nmol/L. If EDTA was 10mmol/L，the concentration of Am(III), which made all of Am(III) existed in the form of $[AmEDTA]^-$ increased to 10μmol/L. So，EDTA was effective in cleaning up Am(III) in interstitial fluid.

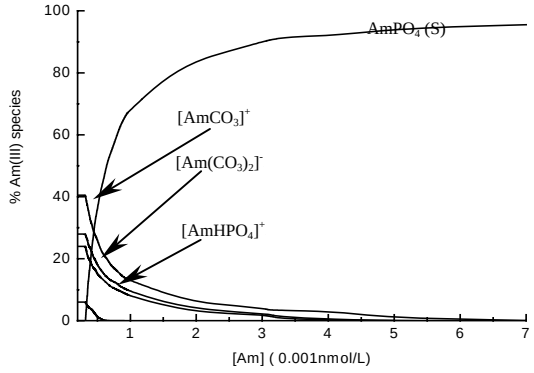

Fig.5 Influence of [Am] on the speciation of Am(III) in interstitial fluid

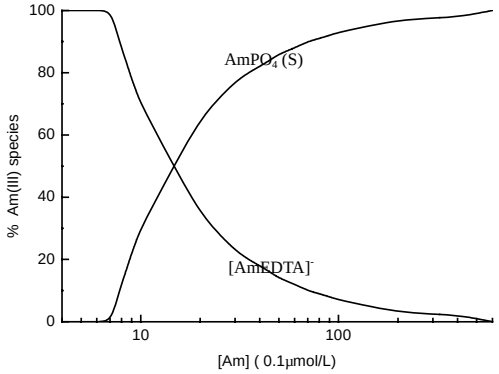

Fig.6 Influence of EDTA on the speciation of Am(III) in interstitial fluid

3.4 Speciation of Am^{3+} in intracellular fluid

Interstitial fluid was the outer environment of cell. Am(III) in interstitial fluid may enter intracellular fluid by getting cross plasma membrane to injure the DNA and RNA of cell. Fig.7 showed the speciation of Am(III) in intracellular fluid when Am(III) was 0.1nmol/L. Fig.7 told us high percentage of solid $AmPO_4$ existed in all normal intracellular fluid pH range (pH6.0~pH7.4) which indicated that Am(III) behaved strong toxicity to cell. The pH value of the intracellular fluid of macrophage could be as lower as 4.5. Fig.7 illustrated that the Am(III) granule ingested by macrophage in the form of aerosol could dissolve in intracellular fluid, and then came out to interstitial fluid. Fig.8 showed the speciation of Am(III) in intracellular fluid when Am(III) was as low as 0.004nmol/L. Fig.8 supported that Am(III) behaved strong cell toxicity even if the concentration of Am(III) was low to 0.004nmol/L.

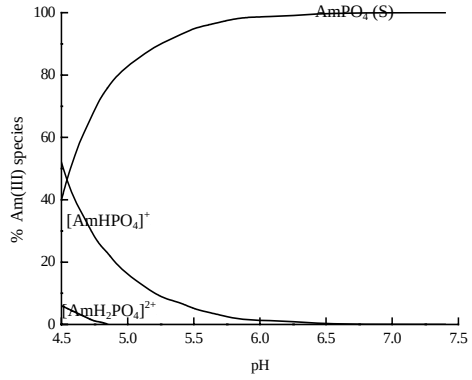

Fig.7 Influence of pH on the speciation of Am(III) in intracellular fluid

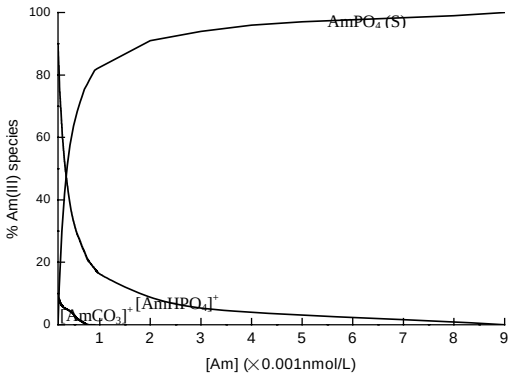

Fig.8 Influence of [Am] on the speciation of Am(III) in intracellular fluid

3.5 Speciation of Am^{3+} in urine

It was favorable to take alkaline material such as $NaHCO_3$ to reduce the toxicity of U(VI) to kidney by increasing the solubility of U(VI) complexes in urine. Fig.9 showed the speciation of Am(III) in urine when its concentration was 0.1nmol/L.Fig.9 indicated that soluble Am(III) species such as $[AmHPO_4]^+$, $[AmSO_4]^+$ and $[AmH_2PO_4]^{2+}$ were dominant only when pH value was as lower as 4.5. whereas, the solid $AmPO_4$ was the major species of Am(III) when pH value was more than 4.5. So, it was not favorable to take alkaline material to egested Am(III) from kidney.

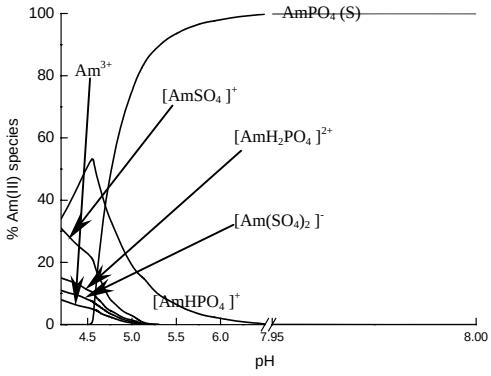

Fig. 9 Speciation of Am(III) in urine

4 Conclusions

1) In gastric juice, the major Am(III) species were Am^{3+}, $[AmCl]^{2+}$ and $[AmH_2PO4]^{2+}$ at pH <2.9 and the solid phase $AmPO_4$ became dominant with higher pH value when Am(III) was 0.1mmol/L.2) In sweat, Am(III) existed with soluble species at pH4.2~pH7.5 when Am(III) was 0.1mmol/L , and Am(III) existed with Am^{3+} and $[AmOH]^{2+}$ at pH6.5 when Am(III) was lower than 0.3nmol/L or more

than 50nmol/L.3) In interstitial fluid, with addition of 1mmol/L of EDTA, the Am(III) existed with soluble $[AmEDTA]^-$ whereas the Am(III) existed with insoluble $AmPO_4$ when [Am] > 0.001nmol/L.4) In intracellular fluid, the major Am(III) species was $AmPO_4$ at pH7.0 when Am(III) was as lower as 0.004nmol/L, which implied Am(III) presented strong cell toxicity. The percentage of Am(III) soluble species increased at lower pH hinted that the Am(III), in the form of aerosol, ingested by macrophage, could released into interstitial fluid.5) The soluble Am(III) species was dominant when pH<4.5 whereas the solid $AmPO_4$ was major species with higher pH when Am(III) was 0.1nmol/L in human urine. So it was favorable to excrete Am(III) from kidney by taking acid materials.

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