ELSEVIER

Journal of Alloys and Compounds 271–273 (1998) 112–115

Journal of ALLOYS AND COMPOUNDS

Computer modelling of the chemical speciation of lanthanide and actinide elements in the human gastrointestinal tract

L.M. Webb*, D.M. Taylor, D.R. Williams

University of Wales, Cardiff, Department of Chemistry, P.O. Box 912, Cardiff CF1 3TB, UK

Abstract

Joint Expert Speciation System (JESS) computer modelling is used to produce biokinetic models of the gastrointestinal tract, for the radiation dose from internally deposited radionuclides to be calculated. Preliminary estimations of the interactions of Gd and Cm with all the metal binding species present in the small intestine, i.e. bile and pancreatic fluid, over a pH range of pH 5.0–9.0, have been made. The development of the models and these initial validation results for the use of Gd as a surrogate for Cm, will be presented and discussed. From these aqueous studies it appears that the use of Gd as a surrogate for Cm in bile or pancreatic fluid is doubtful. However, further speciation modelling, incorporating solids, is in process to confirm these findings. © 1998 Published by Elsevier Science S.A.

Keywords: Computer modelling; Chemical speciation; Lanthanide; Actinide; Human gastrointestinal tract

1. Introduction

The calculation of radiation dose from internally deposited radionuclides requires physiologically realistic biokinetic models to describe the behaviour of the element in the body. One important parameter is the fractional absorption from the gastrointestinal tract. It is therefore necessary to use either indirect data such as animal data for the element of interest, or a chemical analogue, or human information for a chemically related surrogate element. Computer speciation modelling allows the validation of the use of stable isotopes of lanthanide elements as surrogates for the highly toxic actinides for the measurement of absorption from the gastrointestinal tract. The Joint Expert Speciation System [1–3] has been used to develop and test the computer models, to identify any important variations in the biological behaviour of the element of interest and its surrogate. JESS can effectively estimate interactions of the selected elements with all the metal binding species present in the gastrointestinal system. This contribution describes models for the important fluids in the small intestine, which are bile and pancreatic fluid. The development of aqueous models for bile and pancreatic fluid, for an average healthy adult, and the initial results of modelling Gd and Cm are discussed.

Table 1
Total concentrations of the bio-fluid components used to create chemical speciation models for bile and pancreatic fluid in JESS [4]

Bio-fluid components	Bile (mol dm^{-3})	Pancreatic fluid (mol dm^{-3})
Ligands		
CO_3^{2-}	1.90×10^{-2}	1.90×10^{-2}
PO_4^{3-}	4.50×10^{-2}	8.00×10^{-4}
SO_4^{2-}		4.20×10^{-3}
Cl^-	3.10×10^{-2}	7.66×10^{-2}
F^-	7.27×10^{-6}	
Lactate	4.10×10^{-3}	
Urea	5.40×10^{-3}	1.78×10^{-3}
Metals		
Ca^{2+}	7.70×10^{-3}	1.70×10^{-3}
Mg^{2+}		5.00×10^{-4}
Zn^{2+}		1.85×10^{-5}
Fe^{3+}	1.00×10^{-4}	
K^+	1.35×10^{-2}	4.60×10^{-3}

2. Experimental details

JESS (the Joint Expert Speciation System) is a computer program which is capable of modelling chemical speciation in complex environments. By doing so, the different chemical species within a biological system can be identified and the relative abundance of these species, that are

*Corresponding author. Tel.: +44 1222 874000; fax: +44 1222 874030.

0925-8388/98/$19.00
PII: S0925-8388(98)00036-X

Table 2
Equilibrium constants (log K) calculated by JESS for gadolinium and curium in bile and pancreatic fluid at 37°C and an ionic strength of 0.15 mol dm^{-3}

Gadolinium species	log K (37°C, I=0.15 mol dm^{-3})	Curium species	log K (37°C, I=0.15 mol dm^{-3})
$GdHPO_4^+$	4.22	$CmLactate^{2+}$	2.65
$GdH_2PO_4^{2+}$	8.59	$Cm(Lactate)_2^+$	4.39
$GdH_2(PO_4)_2^-$	6.37	$Cm(Lactate)_3$	6.16
$GdLactate^{2+}$	2.91	$CmOH^{2+}$	−5.72
$Gd(Lactate)_2^+$	5.18	$CmCl^{2+}$	0.30
$GdCO_3^+$	−4.25	CmF^{2+}	3.60
$Gd(CO_3)_2^-$	−9.98	$CmSO_4^+$	
$GdHCO_3^{2+}$	1.94	$Cm(SO_4)_2^-$	
$GdSO_4^+$	2.14		
$Gd(SO_4)_2^-$	3.40		
$GdCl^{2+}$	−0.23		

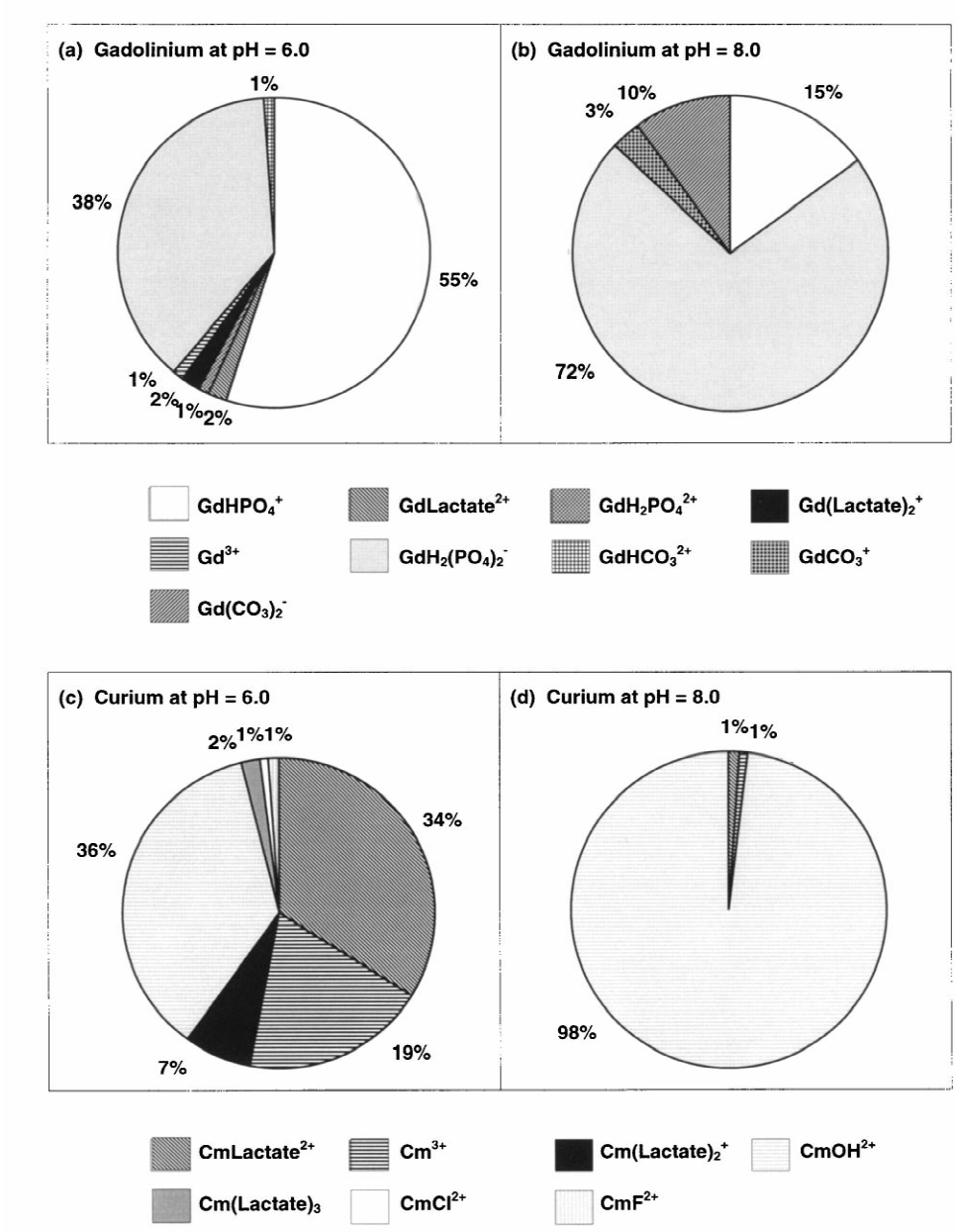

Fig. 1. Chemical speciation of Gd^{3+} (a,b) and Cm^{3+} (c,d) at 5.00×10^{-7} mol dm^{-3} in bile. Percentage distributions of Gd^{3+} and Cm^{3+} with lmm ligands, at two points over the pH scan (pH 6.0 and 7.0).

dependent on the thermodynamic equilibria and the kinetics of competitive reactions, can also be determined. For the bile and pancreatic fluid systems, the behaviour of Gd^{3+} and Cm^{3+} in these can easily be modelled and compared. This is done using the relevant reactions and constants from the 58 000 reactions and 145 000 critically assessed thermodynamic constants (i.e. complex formation and protonation constants) that are available in the JESS Thermodynamic Database.

Fixed total concentration values for all the metal ions and lmm ligands involved in the bile and pancreatic systems (Table 1 [4]) are assumed for the separate models, along with either Gd^{3+} or Cm^{3+} at 5.00×10^{-7} mol dm^{-3}. Both the bile and pancreatic models were set at 37.0°C and an ionic strength of 0.15 mol dm^{-3} in order to be biologically realistic. A pH scan for each model was run from pH 5.0–9.0, to give a wider view of the chemical speciation occurring as Gd^{3+} or Cm^{3+} enters the bile and pancreatic systems from the gastric compartment, before reaching the large intestine. At this stage all modelling was carried out using an aqueous system with no solids present. Table 2 contains the equilibrium constants calculated by JESS, under these conditions, for the resultant Gd and Cm species.

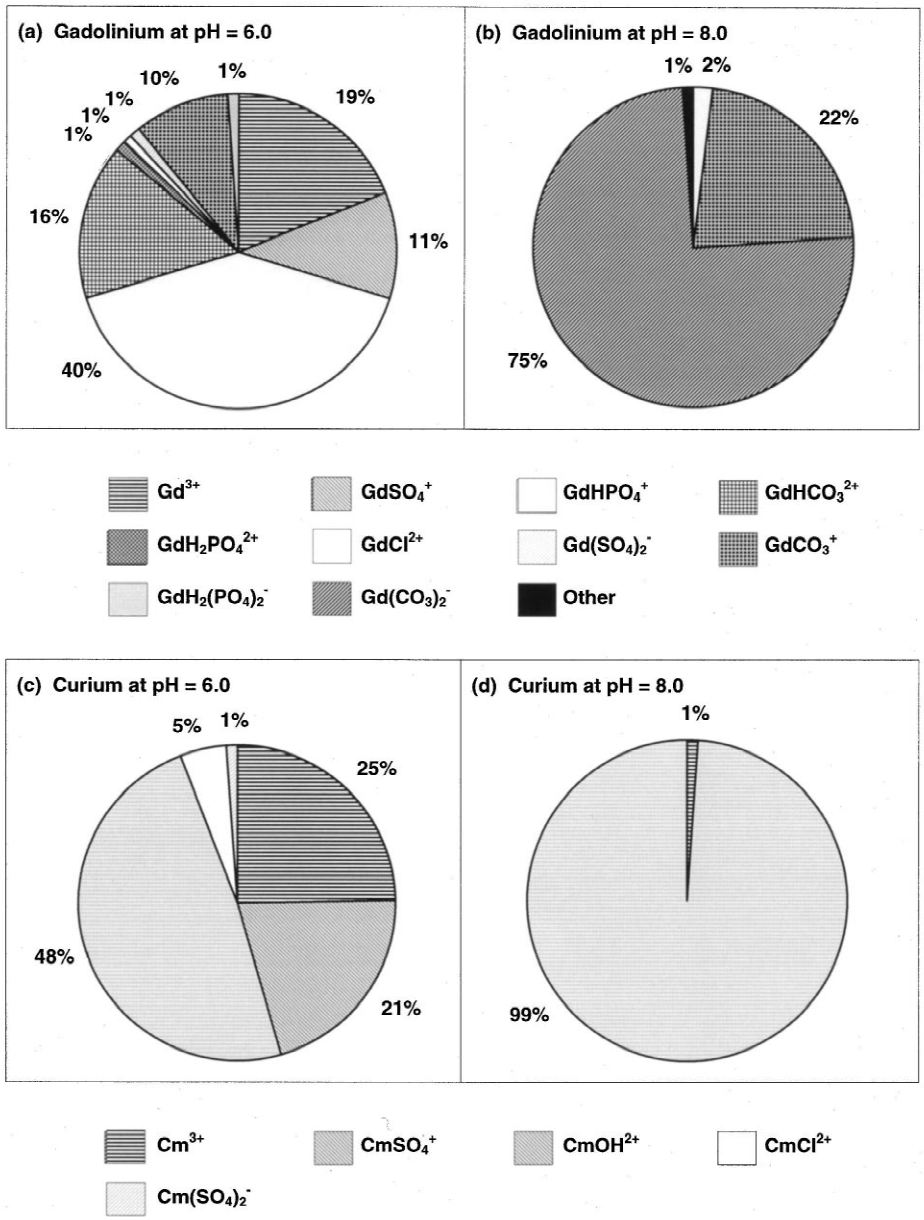

Fig. 2. Chemical speciation of Gd^{3+} (a,b) and Cm^{3+} (c,d) at 5.00×10^{-7} mol dm^{-3} in pancreatic fluid. Percentage distributions of Gd^{3+} and Cm^{3+} with lmm ligands, at two points over the pH scan (pH 6.0 and 7.0).

3. Results

3.1. Gd^{3+} and Cm^{3+} distribution in bile

Table 1 shows the metal ion and ligand concentrations used in the bile and pancreatic fluid models. Fig. 1 shows the chemical speciation results at pH 6.0 and 8.0, expressed as percentages of the total concentration of Gd^{3+} and Cm^{3+} (5.00×10^{-7} mol dm^{-3}) added.

The pH appears to have a significant effect on the speciation of Gd^{3+} and Cm^{3+}. Fig. 1 shows that Gd^{3+} is distributed between seven species at pH 6.0, the major species being $GdHPO_4^+$ (55%) and $GdH_2(PO_4)_2^-$ (38%). At pH 8.0, the Gd^{3+} redistributes itself, with $GdHPO_4^+$ decreasing in concentration (15%) and carbonate species starting to occur, although the $GdH_2(PO_4)_2^-$ remains the predominant species at 72% of the total concentration of Gd^{3+} present. In bile at pH 6.0, Cm^{3+} is also distributed between seven species (Fig. 1), however, both the concentration and the type of species formed generally differ to those observed for Gd^{3+}. The free metal ion concentration for Cm^{3+} was greater, 19 compared to 1% for Gd^{3+}. The two major species at this pH are $CmLactate^{2+}$ (34%) and $CmOH^{2+}$ (36%). At pH 8.0, the number of species decreases, with $CmOH^{2+}$ remaining the predominant species at 98% of the total concentration of Cm^{3+} and reaching 100% at pH 8.5.

3.2. Gd^{3+} and Cm^{3+} distribution in pancreatic fluid

Fig. 2 shows the chemical speciation results for pancreatic fluid in terms of the percentage distribution of the total concentration of Gd^{3+} and Cm^{3+} (5.00×10^{-7} mol dm^{-3}).

Again pH appears to significantly effect the speciation of Gd^{3+} and Cm^{3+}. Fig. 2 shows that, at pH 6.0, the Gd^{3+} is distributed between nine species, the predominant species being $GdHPO_4^+$ (40%) and Gd^{3+} (19%). At pH 8.0 the majority of Gd^{3+} is complexed with carbonate ligands as $Gd(CO_3)_2^-$ (75%) and $GdCO_3^+$ (22%), leaving only 2% as $GdHPO_4^+$. However, in pancreatic fluid (Fig. 2) at pH 6.0, Cm^{3+} distributes itself between only five species, the predominant species being $CmOH^{2+}$ (48%), but there are also significant concentrations of Cm^{3+} (25%) and $CmSO_4^+$ (21%). The $CmOH^{2+}$ concentration increases to 99% of the total concentration of Cm^{3+} at pH 8.0 and, as was observed for Cm^{3+} in bile, it reaches 100% at pH 8.5.

4. Conclusions

The chemical speciation profiles for Gd^{3+} and Cm^{3+}, at 5.00×10^{-7} mol dm^{-3}, in bile and pancreatic fluid, with the absence of solids, are quite different. These initial findings suggest that the use of Gd^{3+} as a surrogate for Cm^{3+} in bile or pancreatic fluid studies is dubious. Gd^{3+} prefers to form complexes with phosphate and carbonate under these conditions, and Cm^{3+} predominantly forms $CmOH^{2+}$.

However, the introduction of solids into the modelling may alter these results and requires investigation.

Acknowledgements

This research project is funded by Contract FI4P-CT95-0011 with the CEC Fourth Framework Programme in Radiation Protection and Nuclear Fission Safety.

References

[1] P.M. May, K. Murray, Talanta 38(12) (1991) 1409–1417.
[2] P.M. May, K. Murray, Talanta 38(12) (1991) 1419–1426.
[3] P.M. May, K. Murray, Talanta 40(6) (1993) 819–825.
[4] J.R. Geigy S.A., Documenta Geigy Scientific Tables, 7th ed., K. Diem, C. Lentner (Eds.), Published by J.R. Geigy S.A., Basle, Switzerland, 1970.