ADSORPTION OF ^{153}Sm-EDTMP ON HYDROXYAPATITE*

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ABSTRACT

Adsorption of a promising bone tumor therapeutic agent ^{153}Sm-EDTMP (ethylene diamine tetramethylene phosphonic acid) and effects of several coexisting substances on adsorption and desorption were investigated using HA (hydroxyapatite) as an in vitro model. The adsorption is quantitative up to total deposition of 40 μmol/g HA, while nonquantitative when the complex concentration is above 40 μmol/g HA in the medium of pH=7.0±0.2. The uptake increases significantly with the Ca ions added. Desorption of the adsorped complexes is in the sequence of EDTMP≫DTPA > EDTA. Two modes of adsorption of ^{153}Sm-EDTMP on HA are suggested, the first one ($\leq$ 40μmol/g HA) quantitatively covers the available surface and the second, by which, is less efficient, additional complexes are adsorped. Non-quantitative adsorption is attributed to Coulomb repulsion while the complex concentration ranging from 40 to 80 μmol/g HA.

Keywords ^{153}Sm-EDTMP, Bone tumor therapeutic agent, Hydroxyapatite, Adsorption and desorption, Adsorption modes

1 INTRODUCTION

In 1977, Van Langevelde *et al*[1] studied the adsorption of ^{99m}Tc-HEDP (1-hydroxyl ethylidene diphosphonate) on HA (hydroxyapatite) and concluded that the bone affinity of phosphorus-containing ligands complexed to technetium could be justified by using HA as an in vitro model. After that, several ^{99m}Tc-complexes have been studied for understanding their adsorption behaviors on HA. ^{153}Sm-EDTMP, a hopeful bone tumor therapeutic agent, was prepared in our Institute[2–4]. In view of the results on ^{99m}Tc-complex adsorption, we propose that the investigation of adsorption of ^{153}Sm-EDTMP on HA can result in the discovery of its concentrating mechanism on skeleton and the understanding of the structure-activity-relationships (SARs) of different ligands bound to ^{153}Sm. As part of our investigation, we measured the degree of adsorption and desorption behavior of ^{153}Sm-EDTMP using HA as an in vitro model.

2 EXPERIMENTAL

2.1 Materials

EDTMP was synthesized in our laboratory and its structure was confirmed by MS, NMR, IR and element analysis. ^{153}Sm with specific activity of 3 GBq/g Sm_2O_3

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was prepared by irradiating natural Sm_2O_3 in the research reactor of our Institute. HA, chromatographic grade and 50 m^2/g surface, and other reagents with A.R. were purchased commercially and were not purified before use.

2.2 Preparation of ^{153}Sm-EDTMP

To a vial containing EDTMP, 0.5 ml of ^{153}Sm solution was added, and then the pH value was adjusted to about 9.0±0.5. After sealing, the vial was placed in a boiling-water bath for 30 min. The complex yield measured by radio-paper chromatography was above 95%.

2.3 Adsorption of ^{153}Sm-EDTMP on HA

Portions of HA (40±1 mg) were weighed into glass columns (Φ8mm×100mm) with porous glass bed supports and a removable glass stopples, 2.0 ml of the complex solution of different concentrations was added to each column. After covered, the columns were vibrated in a vibrator. The solution was pressed out through the column, some of the solution (0.2 ml) was taken out, and counted under the same conditions as those for the complex reference.

2.4 Influence of EDTMP and Ca ions on the adsorption

Based on the procedure and the results of complex adsorption, non-quantitative adsorption conditions selected are 4.8 μmol of ^{153}Sm-EDTMP, 0~ 30μmol EDTMP, 0~ 30μmol Ca ions, total volume of 2.0 ml; and the adsorption percentage was obtained by counting the activity in both adsorped complex solution in the presence of EDTMP or Ca ions and the complex reference.

2.5 Removal of complex from HA

Columns were prepared with 2.0 ml of ^{153}Sm-EDTMP solution (4.8 μmol of ^{153}Sm-EDTMP) as given in adsorption procedure, each column was then vibrated with 2.0 ml of EDTMP solution (3.0 μmol) and the eluate collected. This was repeated 3 or 4 times for a total of 4 or 5 elutions. The activity in each of the eluates and that remaining on the column were measured. A similar series of experiments were done using DTPA, EDTA as the eluents. Blanks were also run using saline as the eluent.

3 RESULTS AND DISCUSSION

3.1 Influence of equilibrium time

Adsorption yield increases with the increase in vibration time, and the adsorption is in equilibrium state when the time is up to 30 min.

3.2 Adsorption on HA

Fig.1 shows that the adsorption is quantitative when amount of complex is $\leq$ 40μmol/g HA, but non-quantitative when $>$ 40μmol/g HA. The estimated cross section area of either an approximately spherical complex or an elongated free ligand is about 1 nm^2[5]. For a surface area of ~ 50m^2/g HA, a mono-molecule layer saturation of ^{153}Sm-EDTMP adsorped is about 80 μmol. The results represent one complex for each ~ 2nm^2 surface area.

3.3 Influence of EDTMP and Ca ions

As shown in Fig.2, adsorption reduces significantly with the addition of ligand EDTMP, no matter whether the pH value equals 7.0(±0.2) or 9.0(±0.2), because of its competitive adsorption.

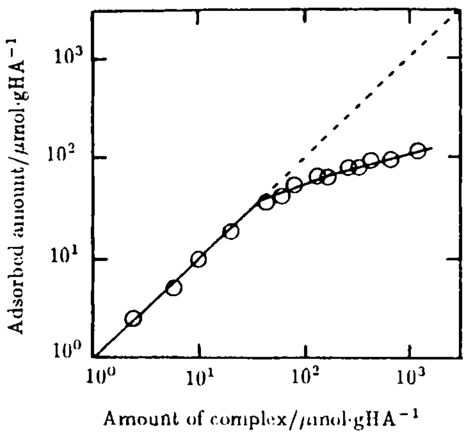

Fig.1 Adsorption of ^{153}Sm-EDTMP on HA (pH=7.0±0.2)

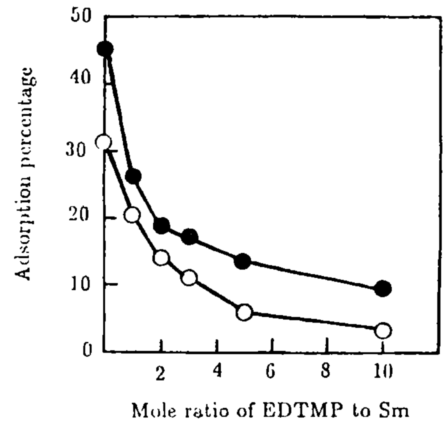

Fig.2 Effect of EDTMP on the adsorption percentage of ^{153}Sm-EDTMP complex

o pH=9.0±0.2, • pH=7.0±0.2

Fig.3 shows that as the Ca ions are added, the complex deposition increases in non-quantitative adsorption conditions and when the mole ratio of Ca ion/complex is 0.5, adsorption is up to 80 μmol/g HA (mono-molecule layer saturation) and it shows to be quantitative by the ratio up to 10. A rational explanation for the acceleration effect may be balance of the negative charges on adsorped complex layer in the presence of Ca(Ⅱ) ions.

3.4 Removal of complex from HA

Results of adsorped complex desorped by solution of EDTMP, DTPA, EDTA are shown in Table 1. Columns were loaded 55 μmol/g HA. EDTMP removes ^{153}Sm adsorped most effectively, about 30% of the activity is eluted after four elutions. The removal is 17% and 11% for DTPA and EDTA, respectively. In comparison with EDTMP and DTPA, the lower stable constant of EDTA complexed to ^{153}Sm (see Table 2) results in lower removal of ^{153}Sm adsorped, this is consistent with the results given in Table 1.

Apparent difference in removal of complex adsorped between EDTMP and DTPA, in despite of their similarity in complexation capability, may be attributed to the competitive adsorption of EDTMP.

3.5 Adsorption modes

Adsorption is non-quantitative when a total of complex is above 40 μmol/g HA (far from mono-molecule layer saturation, 80 μmol/g HA) at pH=7.0±0.2. We have analysed the structure of ^{153}Sm-EDTMP[5] and measured its apparent charges at different pH

Table 1
Desorption percentage of ^{153}Sm-EDTMP from HA

Desorping agents	Times of elution 1	2	3	4	5
Saline	2.0	0.8	0.7	0	0
EDTMP	13.8	5.9	4.2	3.3	2.8
DTPA	7.9	3.1	2.6	2.4	1.3
EDTA	5.6	2.0	1.8	1.0	0.7

*Data were the mean values of three experiments, error were not shown here to save space

Table 2
Stable constants of Sm-complexes

Sm complex	$\lg K_s$
EDTMP	22.4
DTPA	22.8
EDTA	17.1

values, which are shown in Table 3. These results suggest that the accumulation of charges on the surface of HA, as deposition of ^{153}Sm-EDTMP with negative

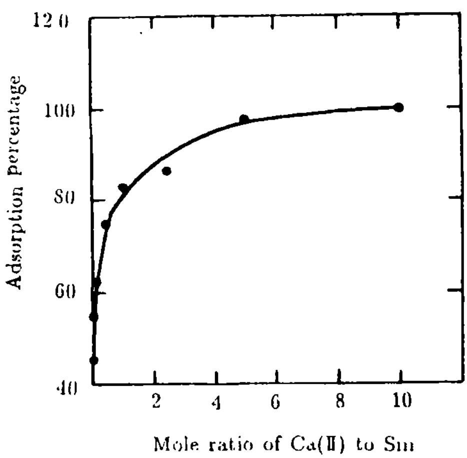

Fig.3 Effect of Ca(II) ions on adsorption of ^{153}Sm-EDTMP

pH=7.0±0.2

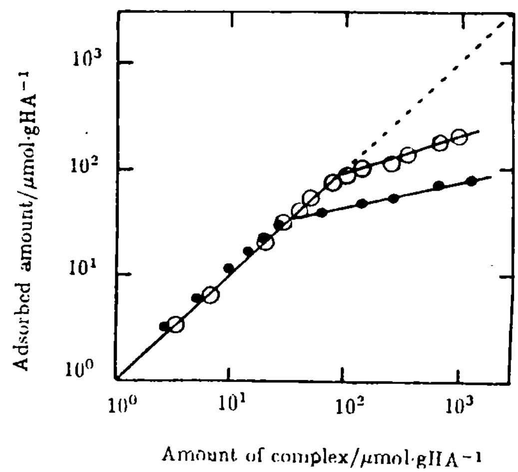

Fig.4 Adsorption of ^{153}Sm-EDTMP on HA

o pH=5.0±0.2, • pH=9.0±0.2

charges increases, brings about the Coulomb repulsion to other complexes with same ones, which causes non-quantitative adsorption meanwhile the complex concentration is between 40 and 80 μmol/g HA. The above suggestion is supported by following facts. a) Quantitative adsorption changes with the change in pH value; as shown in Fig.4, the adsorption is 70 and 15 μmol/g HA at pH=5.0±0.2 and 9.0±0.2, respectively. b) As the Ca(II) ions are added, the complex deposition increases sharply.

Table 3
Apparent charges of ^{153}Sm-EDTMP

pH values	Apparent charges
4.5±0.2	-1.0±0.1
7.0±0.2	-2.0±0.2
9.0±0.2	-3.0±0.2

4 CONCLUSION

In the medium of pH=7.0±0.2, the adsorption of ^{153}Sm-EDTMP on HA is quantitative up to total deposition of 40 μmol/g HA, while non-quantitative when the complex concentration is above 40 μmol/g HA.

Because of its balance of the negative charges on adsorped complex layer, the complex adsorption increases sharply with the addition of Ca(II) ions, while the adsorption reduces for its competitive adsorption, as ligand EDTMP is added. Removal of the adsorped complex is in the sequence of EDTMP$\gg$DTPA>EDTA.

Two modes of the adsorption of ^{153}Sm-EDTMP on HA are suggested, the first one ($\leq$40 μmol/g HA) quantitatively covers the available surface, and the second, by which, is less efficient, additional complexes are adsorped, non-quantitative adsorption is attributed to Coulomb repulsion while the complex concentration ranging from 40 to 80 μmol/g HA.

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