Adsorption of ^{117m}Sn(IV)-EDTMP on hydroxyapatite and collagen

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Abstract Some organic phosphines labeled with ^{117m}Sn(IV) have been proved promising for imaging and pain palliation of bone tumor. In this paper, a preliminary investigation on the adsorption characteristics of EDTMP (ethelenediaminetetramethylene phosphoric acid) labeled with ^{117m}Sn(IV) on HA(hydroxyapatite) and collagen, and an investigation on the adsorption mechanism of ^{117m}Sn(IV)-EDTMP on HA was presented.

Keywords ^{117m}Sn(IV)-EDTMP, HA, Collagen, Adsorption/Desorption

CLC numbers O615.3, O614.432, R817.8

1 INTRODUCTION

Stannum is one of the necessary elements for life. And some stanniferous organic compounds can resist growth of bacteria, though the mechanism of this action isn't known yet.[1] ^{117m}Sn with or without carrier, which can be produced through such reactions as ^{116}Sn(n,γ)^{117m}Sn, ^{116}Cd(α, 3n)^{117m}Sn and ^{115}In(α, pn+d)^{117m}Sn, [2] has a half life of 13.6 days with the inner converted electron energy of 129 keV and 155 keV. ^{117m}Sn labeled compounds have attracted great attention recently in that they may well break through marrow depression resulted from ^{89}Sr while maintaining, even surpassing, its high uptake in abnormal bone with a brand new way—moderate energy inner converted electron.[3] Researches of ^{117m}Sn in recent years have focused on ^{117m}Sn-DTPA[4-8], on the properties *in vivo* or *vitro* and on the mechanism of bone adsorption and bone uptake. DTPA itself isn't osteophilic so that ^{153}Sm-DTPA with high conjugation constant can't concentrate in bone while being rapidly removed from blood. In comparison, EDTMP has high bone affinity so that ^{153}Sm-EDTMP shows favorable effects in bone imaging and therapy. With respect to the high osteophilicity of ^{117m}Sn as well as ^{153}Sm, ^{117m}Sn-EDTMP may well show the same or better application prospects than those of ^{153}Sm-EDTMP and ^{117m}Sn-DTPA. Therefore, we gave a preliminary investigation on the adsorption characteristics and adsorption mechanism of ^{117m}Sn-EDTMP on bone model including HA and collagen.

2 EXPERIMENTAL

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2.1 Materials

^{117m}Sn was supplied by the Chinese Institute of Isotopes, ^{117m}Sn-EDTMP was prepared in our laboratory with 99 percent plus of radioactive purity. Collagen was supplied by Sigma and HA with specific area of 87.6m^2/g by Shanghai Biochemical Company. Other agents were of reagent grade.

2.2 Adsorption of complex on HA and collagen

Portions of HA and collagen were weighed into centrifugal tubes, where aqueous solution of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP with given pH values were added. Then the tubes were placed in oscillator at a certain temperature for a given range of time. The oscillated mixture was then centrifuged till the upper solution became transparent. The measurement method was the same as that for adsorption of ^{153}Sm-EDTMP on HA.[9]

2.3 Adsorption of EDTMP on HA

The adsorption quantity of EDTMP on HA had been researched through ^{14}C labeled EDTMP.[10] Another method for calculating the adsorption quantity of EDTMP on HA was created here. In K gram HA which had been saturated with B mole of ^{117m}Sn(IV)-EDTMP, A gram of control HA was added in, where aqueous solution of C mole of EDTMP was then added. When adsorption equilibrium was reached, the desorption quantity could be calculated as D mole with the same method as that for desorption of ^{153}Sm-EDTMP from HA.

Then x mole, the adsorption quantity of EDTMP on HA could be calculated through the following equation:

$$D/K = \{C + B - (A + K)x\}/(A + K)$$

2.4 Extraction of complex from preloaded HA and collagen

After ^{117m}Sn(IV)-EDTMP has adsorbed on HA and collagen, the upper solution was totally removed from the centrifugal tubes, where saline and aqueous solution of EDTMP were added. Then the same procedure as in adsorption was conducted. The desorption percentage could be calculated with the same method as that for desorption of ^{153}Sm-EDTMP from HA.[9]

3 RESULTS AND DISCUSSION

3.1 Adsorption of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on HA

The adsorption of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on HA under the condition of pH=7 and at 37±0.5°C was investigated. The adsorption equilibrium and the adsorption quantity are illustrated in Fig.1 and Fig.2. It shows that ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP adsorb on HA very rapidly, and the adsorption percentage reach 95

percent in 2 min. ^{117m}Sn(IV) adsorbs more rapidly and the adsorption is linear in a wide range of concentration. ^{117m}Sn(IV)-EDTMP adsorbs linearly when the concentration is less than 60 μmol/gHA. Then the adsorption deviated from linear one, but still increase significantly with increase in the concentration. Adsorption of EDTMP on HA shows the remarkable Langmur type. According to mono-layer adsorption model, the average surface area of HA for a single molecular of ^{117m}Sn(IV)-EDTMP was about 2.4 nm^2 before the deviation, while decreased to 0.3 nm^2 when the concentration was far beyond the deviation point. With respect to the molecular section area of EDTMP[9,10], which had been considered as 1 nm^2, it could be concluded as follows: In the linear stage, what's adsorbed was the whole labeled complex. In the deviation stage, there was a contradiction between limited surface area and high bone affinity of ^{117m}Sn(IV). When the surface area has been saturated with a monolayer of ^{117m}Sn(IV)-EDTMP, later-reached ^{117m}Sn(IV)-EDTMP probably transconjugated with HA. In the deviation stage, therefore, what's adsorbed might well include both the labeled complex and free ^{117m}Sn(IV) dissociated from complex. In fact, inorganic crystal of human bone has very large specific surface area from 64 m^2/g to 200 m^2/g so that the total surface area of inorganic bone crystal for a man weighing 70 kg surpasses 100 acres.[11] Though the existence of organic collagen will greatly decrease the effective surface, several liters of body fluid will still cover several acres of bone crystal. The average dosage of ^{117m}Sn(IV)-EDTMP for a man is about 22×10^7 Bq, which will be diluted by large amount of body fluid, so it could be considered that the adsorption of ^{117m}Sn(IV)-EDTMP on inorganic crystal of human bone is in the linear stage.

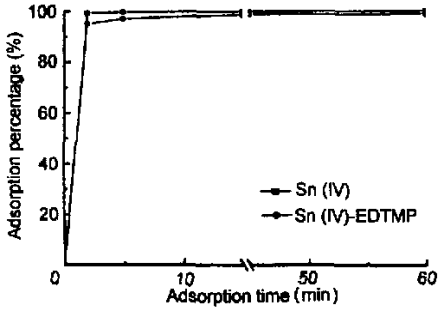

Fig.1 The adsorption equilibrium of ^{117m}Sn(IV) and ^{117m}Sn-EDTMP on HA

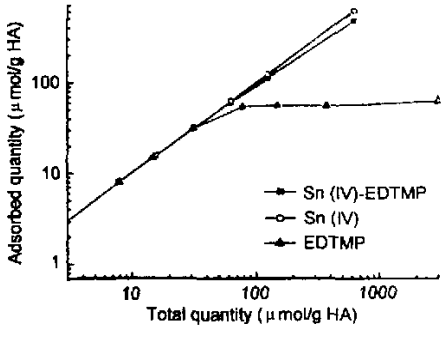

Fig.2 The adsorption quantity of EDTMP. ^{117m}Sn(IV)and ^{117m}Sn-IV-EDTMP on HA

3.2 Adsorption of ^{117m}Sn(IV)-EDTMP on HA under different pH

The effect of pH on adsorption of ^{117m}Sn(IV)-EDTMP on HA under the condition of 480μmol/gHA at 37±0.5°C is shown in Fig.3. It could be explained that the adsorption of ^{117m}Sn(IV)-EDTMP on HA has close relationship with electric attraction. HA, whose point of zero charge stands at pH=8.6,[11] take positive charge in acidic environment. The more acidic the solution is, the more positive charge HA takes, and the stronger the attraction between HA and ^{117m}Sn(IV)-EDTMP, the larger adsorption quantity becomes. When pH stands at about 8, little adsorption takes place. Because the micro-environment around abnormal bone was reported acidic[12], this is a very favorable property for enhancing the target orientation. It needs further investigation why adsorption quantity in basic solution is larger than that at about zero charge point.

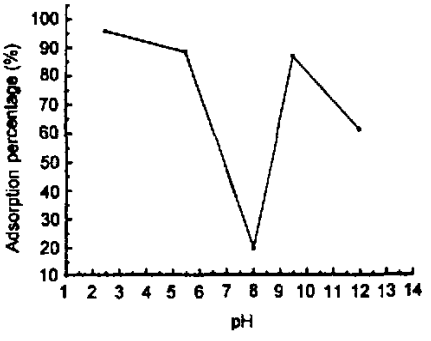

Fig.3 The effect of pH on the adsorption of ^{117m}Sn(IV)-EDTMP on HA

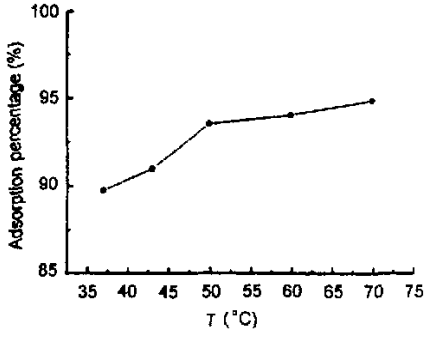

Fig.4 The effect of temperature on the adsorption of ^{117m}S(IV)-EDTMP on HA

3.3 Adsorption of ^{117m}Sn(IV)-EDTMP on HA under different temperature

The effect of temperature on adsorption of ^{117m}Sn(IV)-EDTMP on HA under the condition of 120 μmol/g HA at pH=7 is shown in Fig.4. Increase in temperature effects slightly the adsorption of ^{117m}Sn(IV)-EDTMP on HA. Within the body temperature range between 37°C and 39°C, temperature has no effect on the adsorption.

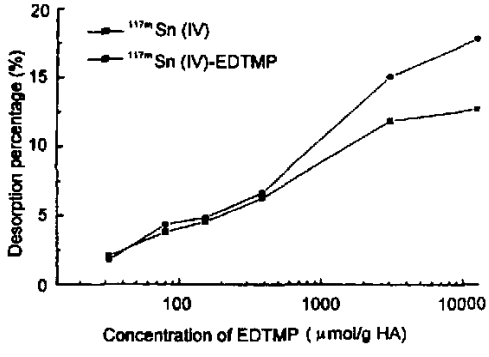

Fig.5 The desorption of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP from HA with EDTMP

3.4 Extraction of complex from preloaded HA

Extraction of complex with EDTMP from preloaded HA is shown in Fig.5. Desorption percentage with concentrated solution of EDTMP could reach 17.7 and 12.6 for ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP respectively. Extraction of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP from HA with saline is very difficult, and the desorption percentage is 2.75 and 3.01 for ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP respectively. Generally, the adsorbed ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on HA are comparatively stable, which ensures a long retention time and high uptake of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on bone.

3.5 Adsorption of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on collagen

Collagen, existing extensively in bone and on bone surface, constitutes the main organic material of bone, especially the primary material of periosteum. Therefore, collagen naturally plays an important role in ion exchange and adsorption on bone. Though it's well known that collagen affects adsorption on bone, previous researches just took HA as the only material of bone model. In this work, the adsorption of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on collagen was also investigated. Adsorption equilibrium and adsorption quantity of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on collagen under the condition of pH=2 and at 37±0.5°C are shown in Fig.6 and Fig.7. They illustrate different adsorption characteristics of ^{117m}Sn(IV) from those of ^{117m}Sn(IV)-EDTMP on collagen. Firstly, ^{117m}Sn(IV) adsorbs rapidly while ^{117m}Sn(IV)-EDTMP rather slowly. Secondly, the adsorption percentage for ^{117m}Sn(IV) could be no more than 40 percent, even after adsorbing for 16 hours, while that for ^{117m}Sn(IV)-EDTMP could reach 90 percent. Thirdly, adsorption of ^{117m}Sn(IV)-EDTMP on collagen is linear in the studied concentration range, while that of ^{117m}Sn(IV) deviated obviously from linear one in high concentration. All the above three characteristics of adsorption on collagen are contrary to those on HA.

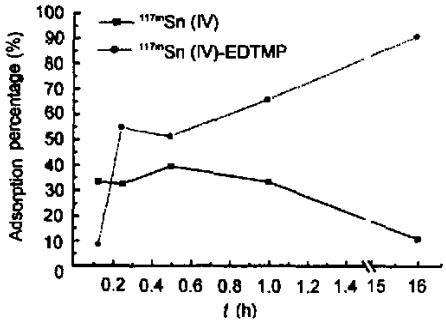

Fig.6 The adsorption equilibrium of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on collagen

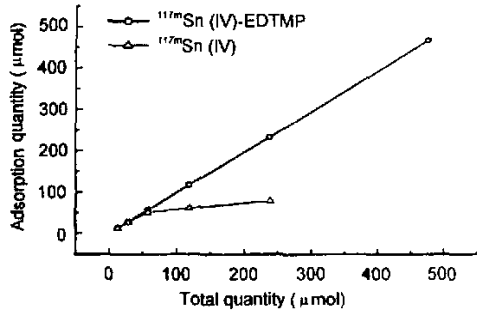

Fig.7 The adsorption quantity of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on collagen

3.6 Adsorption of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on collagen under different pH

The effect of pH on adsorption of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on collagen under the condition of 120 μmol/g collagen at 37±0.5°C for 45 min is shown in Fig.7. With similarity to adsorption on HA, pH greatly affects adsorption on collagen and acidic environment is more favorable for adsorption than basic one. When the pH value is above 10, almost no adsorption takes place. This property is also favorable with regards to the reported acidic micro-environment around abnormal bone.[12]

3.7 Adsorption of ^{117m}Sn(IV)-EDTMP on collagen under different temperature

The effect of temperature on adsorption of ^{117m}Sn(IV)-EDTMP on collagen under the condition of 30 μmol/g collagen at pH=7 is shown in Fig.8. Increase in temperature effects slightly the adsorption of ^{117m}Sn(IV)-EDTMP on collagen.

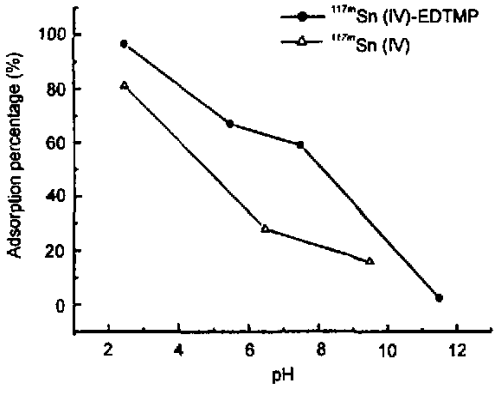

Fig.8 The effect of pH on the adsorption of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on collagen

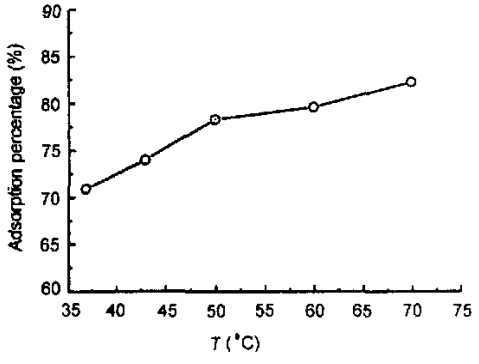

Fig.9 The effect of temperature on the adsorption of ^{117m}Sn(IV)-EDTMP on collagen

3.8 Extraction of complex from preloaded collagen

The comparison of desorption percentage of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP from collagen and from HA with saline and solution of EDTMP is shown in Tab.1. ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP adsorbed on collagen are much more stable than those on HA, and little of them could be extracted from collagen, especially for ^{117m}Sn(IV)-EDTMP. Therefore, it could be estimated that adsorption of ^{117m}Sn(IV) and ^{117m}Sn(IV)-EDTMP on collagen should be a rate-controlling and quantity-limiting procedure for the whole process of adsorption on bone.

Table 1 The comparison of desorption from HA and collagen

Desorption system	Desorption percentage(%)	
	^{117m}Sn(IV)	^{117m}Sn(IV)-EDTMP
6.25×10^{-4} mol EDTMP/g HA	7.3	8.2
6.25×10^{-4} mol EDTMP/g collagen	1.58	0.08
9% NaCl-HA	2.75	3.01
9% NaCl-collagen	0.85	0.16

4 CONCLUSION

Our studies about the adsorption of ^{117m}Sn(IV)-EDTMP on HA and collagen will be rendered to further investigation on the mechanism of its bone uptake.

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