The Separation of Dysprosium and Holmium for Production of n.c.a. Ho-166

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1. Introduction

The uses of radiolanthanide series are increasing in these days because of target therapy which does not require surgery. Certain radiolanthanides is very useful since they have the ability of simultaneous diagnosis and therapeutic effect in nuclear medicine. But this conventional therapeutic method has often limited by specific activity which is important things to affect labeling yield such as radiommunoconjugation and peptide labeling.

There are two approaches to produce radiolanthanide in nuclear reactor. One is direct method using (n,γ) reaction and the other is indirect method using (n, γ)β reaction. Among the radiolanthanides, Ho-166 can be produced with two methods.

Direct method :
$^{165}Ho(n, \gamma)^{166}Ho$
Indirect method :
$^{164}Dy(n, \gamma)^{165}Dy(n, \gamma)^{166}Dy \rightarrow {}^{166}Ho + \beta^-$

Indirect method gives a product as carrier free Ho-166. Carrier free Ho-166 can be obtained from β decay of Dy-166 which can be produced by double neutron capture process in reactor.

Ho-166($t_{1/2}$ = 26.6hr) is a potential therapeutic candidate and also used as therapeutic nuclide because it has enough energy ($E_{\beta(av)}$ = 665.7keV) to effect therapy. Dy/Ho pair via indirect production also can be used as *in vivo* generator that mother nuclide is delivered to target tissue and then *in vivo* decay to be a daughter nuclide.

Nowadays, in the medical applications, carrier free Ho-166 is preferred rather than carrier added one. There are some reports on the production and separation of carrier free Ho-166. Dodachova et al have separated n.c.a Ho-166 by using metal free HPLC system with Dowex AG 50 or Aminex cation exchange resin and α-HIBA(α-hydroxyisobutyric aicd) as complexing agents. S. Lahiri et al have also tried and separated them by using Dowex Ag 50x8 or Aminex A-7.

To produce n.c.a Ho-166, detail roots of each state including double (n,γ) reaction can be noted with 5 type pathways. In this research, we will present here the production yield of carrier free Ho-166 considering the reaction root of double (n,γ) reaction. We also present here separation technique and chromatogram of Dy/Ho.

2. Experiments

2.1 Method, reagents and Instruments

The pathway equation and calculation was performed with math lab. All reagents are used ACS grade without metal impurities and purchased from Sigma Aldrich. Ultra High Pressure Constant Pressure Pump was purchased from Chrom Tech, Inc. Metal identification was performed by using AA(Atomic Adsorption spectroscopy, AA-7000, Shimadzu) and ICP-mass(NexIon 300D, PerkinElmer)

2.2 Reaction pathway and calculation

To produce n.c.a ^{166}Ho, the detail routs via double (n,γ) reaction can be shown with 5 type pathways like below. The detail processes show Fig 1.

$^{164}Dy(n, \gamma)^{165}Dy(n, \gamma)^{166}Dy \rightarrow {}^{166}Ho + \beta^-$
$^{164}Dy(n, \gamma)^{165m}Dy(n, \gamma)^{166}Dy \rightarrow {}^{166}Ho + \beta^-$
$^{164}Dy(n, \gamma)^{165m}Dy \rightarrow {}^{165}Dy\ (n, \gamma)^{166}Dy \rightarrow {}^{166}Ho + \beta^-$
$^{164}Dy(n, \gamma)^{165m}Dy \rightarrow {}^{165}Ho\ (n, \gamma)^{166}Ho$
$^{164}Dy(n, \gamma)^{165}Dy(n, \gamma) \rightarrow {}^{165}Ho\ (n, \gamma)^{166}Ho$

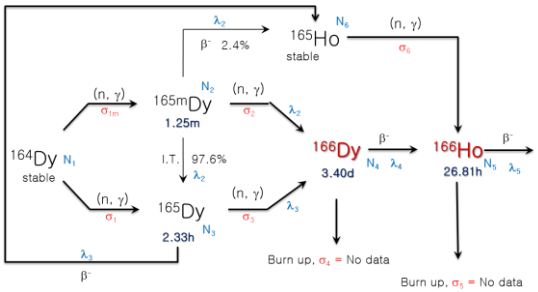

Figure 1 Reaction pathway for production of Ho-166

The differential equations have been established for each state and calculated with math lab. This equation also can be expressed in 6x6 matrix.

With the condition of thermal neutron flux 5.8E13n/cm^2 at the IP5 irradiation port in HANARO, the maximum production time (^{166}Dy) is when neurons irradiate for 343hrs. The maximum time is depended on the neutron flux. When enriched target(10mg [^{164}Dy] Dy_2O_3 , 96.7%) is used, the maximum product amount of ^{166}Dy was calculated as 0.21Ci.

2.3 Separation and Identification with cold materials

Before the hot test, metal separation was performed by using stable metals. Each 1g of metal oxide was dissolved with $HCl_{(aq)}$ (metal free) and the solution was

heated to remove the solvent. 2mg of Ho and 5mg of Dy was taken in stock solution and mixed. The column packed with cation exchange resin was pre-equilibrated and eluted with 0.2M HIBA. Each 8ml of eluents was fractionized to get the separated metals. Identification step was performed AAS and ICP mass. The chromatogram of metal mixtures was shown as Fig 2.

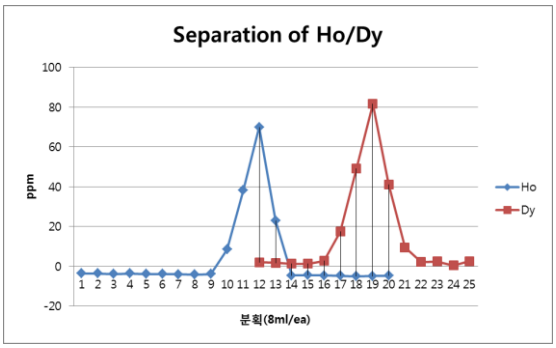

Figure 2 The chromatogram of Ho/Dy

3. Result and discussion

Some radiolanthanides show the good theranostic effect in that they have proper LET (Linear Energy Transfer) to induce apoptosis for cancer treatment and gamma ray to use as a tracer for cancer diagnosis.

The aim of this project based on this view is to get the carrier free radioisotopes for applying the nuclear medicine. Especially, to get the double (n,r) radioisotope(n.c.a Ho-166) is a challenging study which is not attempt in KOREA. After HANARO is re-operated, the study of double (n,γ) reaction and separation using hot nuclide will be done.

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