Excitation Functions of Proton-Induced Reactions on \( ^{nat}Sn \) and \(^{nat}Cd\): Relevance to the Production of \(^{111}In\) and \(^{114m}In\) for Medical Applications

F. Tárkányi\(^1\), F. Ditrói\(^1\), S. Takács\(^1\), I. Mahunka\(^1\), J. Csikai\(^1\), M. S. Uddin\(^2\), M. Hagiwara\(^2\), M. Baba\(^2\), T. Ido\(^2\), A. Hermanne\(^3\), Yu. Shubin\(^4\), and A. I. Dityuk\(^4\)

\(^1\) Institute of Nuclear Research of the Hungarian Academy of Sciences, Debrecen, Hungary
\(^2\) Cyclotron and Radioisotope Center, Tohoku University, Sendai, Japan
\(^3\) Cyclotron Laboratory, Vrije Universiteit Brussel, Brussels, Belgium
\(^4\) Institute of Physics and Power Engineering, Obninsk, Russian Federation

Abstract: Excitation functions of proton induced nuclear reactions were measured for application purposes up to 80 MeV proton energies on natural Cd and Sn targets. The measured excitation functions were compared with the experimental results reported in the literature and with the results of theoretical calculations using the ALICE-IPPE code. In the present work we report on the excitation functions, the deduced integral yields and impurity levels related to the production of the medical radioisotopes of indium (\(^{111}In\), \(^{114m}In\)). High energy production routes by using Cd, In and Sn targets are compared.

INTRODUCTION

The \(^{111}In\) (T\(_{1/2}\)=2.8 day) isotope is used both for diagnostic and therapeutic purposes and \(^{114m}In\) (T\(_{1/2}\)=49.5 day) is a therapeutic radioisotope. Some neutron deficient radioisotopes of indium - \(^{110}In\) (T\(_{1/2}\)=69.1 min), \(^{109}In\) (T\(_{1/2}\)=4.2 h) and \(^{108m,9}In\) (T\(_{1/2}\)=39.6 min and T\(_{1/2}\)=58.0 min) - have importance as analogs to follow the bio-distribution of the diagnostic and therapeutic radioisotopes of indium by using high resolution, quantitative PET technology. The \(^{111}In\) and \(^{114m}In\) radioisotopes are on the list of the medical radioisotopes of IAEA for production of which recommended cross section database is required [1, 2].

In the frame of the systematic investigation of the excitation functions of the light ion induced reactions on different targets up to 100 MeV, cross sections of proton induced nuclear reactions on Cd and Sn targets were measured. These newly obtained data have various practical applications. Here we present data for production of medical radioisotopes by using medium energy cyclotrons and targets with natural isotopic composition. The possible advantage of these production routes: no difficulties with commonly used, expensive, highly enriched targets (\(^{111}Cd\), \(^{112}Cd\), \(^{113}Cd\), \(^{114}Cd\)), high production yields due to the high target thickness. For production of \(^{111}In\) and \(^{114m}In\) by using highly penetrating protons up to 100 MeV only stable isotopes of Sn, In and Cd can serve as targets. Out of them the In target results in a not carrier free \(^{114m}In\). Carrier free \(^{111}In\) can only be obtained via a generator method by short irradiation (1-2 h) and separation of the produced Sn isotopes. The \(^{111}Sn\) has short half-life (35.3 min), and completely decays to \(^{111}In\). The other In decay-products of the simultaneously produced Sn radioisotopes are short-lived compared with \(^{111}In\). The cross sections, the targetry and the separation method for In were investigated in detail by the South African group [3, 4]. In this study we determined the excitation functions, production yields and impurity levels for production of the medically used \(^{111}In\) and \(^{114m}In\) via proton irradiiation of Sn and Cd targets.
Earlier Investigations

According to our knowledge no earlier results are available in this energy range in the literature for reactions on Sn targets. In the case of Cd the available cross section data are contradicting. Cross sections on natCd up to 200 MeV protons were measured by Nortier et al. [3], and by Zaitseva et al. [5] up to 63 MeV. By comparing the two results the excitation functions show a significant energy shift. The data of Zaitseva et al. contradict not only those obtained by Nortier et al. on natCd, but also their own results measured on monoisotopic enriched targets of Cd.

EXPERIMENTAL AND DATA EVALUATION

The excitation functions for production of 111,114mIn radioisotopes were measured from the respective thresholds up to 80 MeV by using an activation method, the stacked foil irradiation technique and direct HpGe gamma counting of irradiated samples. The irradiations were done at an external beam line of the Tohoku University (Sendai, Japan) and Vrije Universiteit Brussel (Brussels, Belgium) cyclotrons. The beam intensity and the energy degradation were controlled in the whole energy range by simultaneously measured natAl(p,x)22,24Na and natCu(p,x)56,58Co,62,65Zn monitor reactions [6, 7].

The experimental technique and the data evaluation including the estimation of the uncertainties were similar as described in more details in our earlier reports [7, 8].

THEORETICAL CALCULATIONS

The experimental cross sections measured in this work and found in the literature were compared with a priori theoretical calculation. The used ALICE-IPPE model code [9] is an upgraded version of ALICE-91 code [10], in which the geometry-dependent hybrid model is used to describe the pre-equilibrium particle emission and the statistical model for equilibrium decay.

NEW RESULTS AND COMPARISONS

Excitation Functions

The excitation functions were measured for production of 111In and 114mIn as well as for the possible contaminants. Here we report on the cross section of the main products.

natSn Target

In Figs. 2 and 3 our new experimental results are compared with earlier experimental results and with the theoretical calculations. Our data are in good agreement with the reported values of Nortier et al. [3] and contradict the results of Zaitseva et al. [5].

FIGURE 1. Excitation function of the natSn(p,x)111,114mIn nuclear reactions.

natCd target

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FIGURE 2. Excitation function of the $^{nat}Cd(p,x)^{111}In$ nuclear reaction.

FIGURE 3. Excitation function of the $^{nat}Cd(p,x)^{114m}In$ nuclear reaction.

**Integral Yields**

The integral yields as function of the incident energies for elemental targets were calculated from the measured excitation functions. The calculated integral yields for the different targets are compared on Fig. 4.

**Production of $^{111}In$**

The integral yields of the $^{nat}Sn(p,x)^{111}In$, $^{nat}In(p,x)^{111}Sn$ and $^{nat}Cd(p,x)^{111}In$ nuclear reactions are shown in Fig. 4. For the calculation of the integral yields, our new data and results of Nortier et al. [3] were used. For comparison in the case of an In target only the indirect production rate from the parent $^{111}Sn$ was calculated as upper limit, supposing short irradiations and immediate separation.

**Production of $^{114m}In$**

The integral yields of the $^{nat}Sn(p,x)^{114m}In$ and of the $^{nat}Cd(p,x)^{114m}In$ nuclear reactions are shown in Fig. 4.

**FIGURE 4.** Integral yields for production of $^{111}In$ and $^{114m}In$ on Cd, In and Sn targets by proton bombardment.

**CONCLUSIONS**

The prediction capability of the used theoretical code is acceptably good and very useful to estimate and understand the magnitude of the different contributing processes.

The comparison of the excitation functions for production of $^{111}In$ on different targets shows:

- The cross section of $^{nat}Sn(p,x)^{111}In$ reaction up to 60 MeV is small, around 80-100 MeV the cumulative cross section is about 80 mb. By irradiating Sn targets two options are open for production of $^{111}In$ by separation of In reaction products from the target material. In the first route the separated In is used after a proper cooling time. In the second, generator route, pure $^{111}In$ can be obtained from the separated fraction through the decay of the produced $^{111}Sn$. The cross section for the production of $^{111}Sn$ is around 40 mb, according to the theory. A disadvantage of the first process is that the final product contains significant amounts of $^{114m}In$. In the second case if we do not consider the absolute values of the cross sections, the short half-life of the $^{111}Sn$ limits the production yield (see later by In target). Both processes can be optimized on the basis of the excitation functions.
• The cross section of the $^{nat}\text{In}(p,x)^{111}\text{Sn}^{111}\text{In}$ process is high in the 20-50 MeV energy range (200-300 mb). An advantage compared to the other two routes is that no $^{114m}\text{In}$ is present in the final product. The main disadvantage is the small batch yield due to the short half life of the parent $^{111}\text{Sn}$ (short irradiation time, losses during the separation).
• The $^{nat}\text{Cd}(p,x)^{111}\text{In}$ process has significant production rates in 10-60 MeV, but the yield of $^{114m}\text{In}$ is also high. A minimal contribution can be found with optimization of the incident energy and the target thickness.
• For production of $^{114m}\text{In}$ in carrier free form, only the Sn and Cd targets should be considered:
  • The $^{nat}\text{Cd}(p,x)^{114m}\text{In}$ reaction has high cross sections at energies up to 40 MeV. The $^{111}\text{In}$ occurs as a significant contaminant, but it can be reduced to the required level by a proper cooling time.
  • The production of the high spin $^{114m}\text{In}$ by the $^{nat}\text{Sn}(p,x)^{114}\text{In}$ reactions is more favorable at high energies. The thicker target probably can compensate the lower cross sections (compared to $^{nat}\text{Cd}$).

According to the comparison of the production routes on the investigated natural targets the required high purity $^{111}\text{In}$ can be obtained only through the decay of separated $^{111}\text{Sn}$. For therapy a mixture of $^{111}\text{In}$ and $^{114m}\text{In}$ radioisotopes can be produced effectively by proton induced nuclear reactions on natural cadmium and tin targets, in which the amount of $^{111}\text{In}$ can be reduced with proper cooling time.

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