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Accurate Formulae for the Cross-Section Data for the Radio-Halogen I-123 from Cyclotron Production

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Abstract

123I is the most widely used cyclotron-produced radio-halogen in medical research. In this paper, excitation function formulae for the nuclear reactions of 123I production are introduced. 124Te (p, 2n)123I and 127I (p, 5n)123Xe → 123I nuclear reactions have been studied as a function of the energy of the neutrons. Both two formulae were created using the least squares regression of the experimental cross sections data, which were obtained from the Experimental Nuclear Reaction Data EXFOR Database version of 2023. The proposed formulae were evaluated using two statistical indicators for goodness-of-fit. High agreement was observed between the empirical and experimental results for both nuclear processes.

Keywords

Cross Section, Radioisotope Production, PET, SPECT and Radio-Halogens

1. Introduction

The family of chemical elements in group 7A of the periodic table is composed of fluorine, chlorine, bromine, iodine, and astatine, these chemical elements are called the halogens, and they are not found in nature as free chemicals. However, it is documented as a halide (X−) ion in the majority of minerals. The radioisotopes of chlorine or astatine are of no concern to radiography. Additionally, radioisotopes of bromine are not typically employed in clinical settings. Among the halogens, iodine is the most powerful agent for reducing [1] [2].

Among the isotopes of iodine that are radio chemically active, 123I, 124I, and

131I have physical properties that are conducive to the development of molecular imaging radiopharmaceuticals for both PET and SPECT, but the most popular of these is probably 123I. 123I has overtaken 131I as the isotope of choice for pharmaceuticals that contain radio-iodine for diagnosis and treatment. It decreases the radiation dose to the patient by approximately 80%, the gamma ray energy of 159 keV is most ideal for incorporation into a gamma camera. The gamma-ray will have a strong effect on tissue that is not excessive in its radiation dose. As a result, it has frequently been supplanted by 131I produced by the reactor. Many radiopharmaceuticals have been identified using 123I [3].

In cyclotrons, multiple nuclear reactions can be employed to create 123I depending on both the material of the target and the energy of the charged particle used. It decays by electron capture mode with 100% branching, with two main gamma rays 0.028 and 0.160 MeV. There are two main ways to produce a 123I: The first is the direct method as shown in Equation (1), while the second is through the production of 123Xe, which in turn is left to decompose to 123I shown in Equation (2). The second method has the advantage of easily separating the xenon from the original target material and allowing it to decay separately, giving I-123 very little contamination from other radioactive isotopes of iodine [4] [5].

$$\text{124Te (p, 2n) 123I} \tag{1}$$

$$\text{127I (p, 5n) 123Xe} \xrightarrow{T_{1/2}=2.08\text{ h}} \text{123I} \tag{2}$$

Table 1 highlights some of the significant physical properties of iodine that are different from hydrogen, additionally, **Table 2** states the nuclear properties of 123I, 124I, and 131I isotopes that are used in the development of molecular imaging [6].

Table 1. Physical properties of Iodine.

Atomic number	Atomic radius	Ionic radius	Electron structure	Electronegativity	Oxidation state	First ionization potential
53	139 pm	216 pm	[Kr], 4d10, 5s**2**, 5p**5**	2.66	−1, +1, +5, +7	10.44 eV
1	31 pm	154 pm	$1s^1$	2.2	−1, +1	13.12 eV

Table 2. Nuclear properties of Iodine radionuclides that are useful for radio imaging.

Nuclide	Decay Type	Branching	$T_{1/2}$	Energy of γ ray MeV	Energy of β particles MeV	
					Emax	Emean
123I	EC	100	13.2 h	0.159	---	---
	γ	84				
124I	β+	25	4.176 d	0.602 0.722 1.69	2.137	0.82
	Ec	75				
	γ	75				
131I	β-	87	8.025 d	0.364	0.6	0.189
	γ	82				

The majority of the radionuclides derived from the cyclotron is neutron-poor and primarily decay via electron capture (EC) or the release of positrons (β+). It's particularly beneficial for medical research. It is important to recognize that, according to the ICRC, there were over 1500 cyclotron devices worldwide, which were owned or affiliated with 95 different countries [7]. Many institutions, such as hospitals, create short-lived nuclear weapons for medical purposes. As a result, the science and technology involved in creating radionuclides in cyclones has become paramount to the modern nuclear medicine field [8].

The use of radioisotopes in medicine is constantly increasing and there is a need for cyclotron-produced radionuclides. In addition to the availability of radionuclides, radiopharmaceutical chemistry and medical imaging devices are among the most important factors in the production of radioisotopes for use in medical fields. Therefore rapid, high-resolution imaging devices such as SPECT and PET, currently are commonly available for diagnostic studies [9].

Also, CT data for nuclear reaction in radioisotope production programs are mainly necessary to improve production methods, *i.e.* maximize the yield of the desired product and minimize the yield of radioactive impurities, where cross-section reaction data play a very important role as noted by many researches such as [10] [11]. The production of cyclotron radionuclides requires complete and accurate knowledge of the transversals of nuclear reactions at all energies, in order to calculate the outputs with high accuracy [12].

Such reactions need to be better known in order to obtain more accurate radioisotope production calculations. Cyclotrons require a complete dataset of charged particles induced reactions. Therefore, these cross-section calculations play an important role due to the limited experimental data in literature.

The Nuclear Reaction Data base EXFOR experimental database of nuclear reactions was established in 1967 with the cooperation of a group of the largest nuclear data centers in the world, under the auspices of the International Atomic Energy Agency. The EXFOR library contains an extensive compilation of experimental nuclear reaction data and it contains data from 24,649 experiments [13] [14].

Neutron interactions nuclear data have been grouped systematically since the discovery of the neutron, while interactions of charged particles have been covered less frequently. From here, especially since the cyclotron needs nuclear data of the interactions of charged particles, an urgent need has arisen to convert some experimental data into equations (fitting) that are easy to use in programming and radioisotope production calculations using the cyclotron. The most important of these data is the excitation function, which represents the relationship between the cross-section of a nuclear reaction versus the energy of an induced charged particle. Also as indicated in ref [15], the more accurate the nuclear data, the easier it is to identify the type of targets used to produce I-123 as either solid, liquid, molten, or gaseous.

2. Methodology

The least square method is one of the most important techniques of curve fitting. The easily applied measures of error are those that involve minimizing the total squared error between the observed and estimated data [16] [17].

By assuming that the experimental data are composed of pairs (x_i, y_i) and that the estimated function is a straight line with parameters a and b is:

$$Y = a * X + b \tag{1}$$

For certain value x_i of experimental data, we can define $\hat{Y}_i$ as:

$$\hat{Y}_i = a * x_i + b \tag{2}$$

The error associated with estimating e_i is then

$$e_i = y_i - \hat{Y}_i = y_i - a - bx_i \tag{3}$$

The total squared error can be defined as in Equation (4):

$$E_1 = \sum_{i=1}^{N} e_i^2 = \sum_{i=1}^{N} \left(y_i - a - bX_i \right)^2 \tag{4}$$

where the observed pairs of data are represented by the variable "N". Meanwhile, the subscript for the solution's order is denoted by "E".

As the value of E_1 decreases, the proximity of the proposed solution to the observed data increases. In order to calculate the constants a and b, E_1 must be reduced to a very small value. To determine the values of a and b, the Equation (4) must be partially derived with respect to a and b twice, and the resulting derivatives must be equated to zero. This will lead to the deduction of the constants a and b.

$$\frac{\partial}{\partial a} E_1 = \frac{\partial}{\partial b} E_1 = 0 \tag{5}$$

$$\frac{\partial}{\partial a} E_1 = \frac{\partial}{\partial a} \sum_{i=1}^{N} \left(y_i - a - bX_i \right)^2 = 0 \tag{6}$$

$$\frac{\partial 2}{\partial b} E_1 = -2 * \sum_{i=1}^{N} y_i - a - bX_i = 0 \tag{7}$$

So

$$\sum_{i=1}^{N} y_i = a * N + b * \sum_{i=1}^{N} E_i \tag{8}$$

$$\sum_{i=1}^{N} y_i * E_i = a * \sum_{i=1}^{N} E_i + b * \sum_{i=1}^{N} E_i^2 \tag{9}$$

where the values of parameters a and b are determined by solving Equations (8) and (9).

When it comes to typical situations, the least-squares method is implemented in order to obtain optimal solutions by discovering the most suitable values for a set of parameters.

In order to determine whether an estimated formula accurately describes experimental data, a goodness-of-fit test is conducted using statistical analysis. The Nash-Sutcliffe efficiency (NSE) and the root mean square error (RMSE) are two widely used indicators to evaluate the goodness of fit, as recognized within the field [18].

The definition of RMSE, or Root Mean Square Error, can be expressed as follows when there are "N" points of observation [18]:

$$\mathrm{RMSE} = \frac{1}{N}\sum_{1}^{N}\left(y_i - Y_i\right)^2 \tag{10}$$

The range of value for this particular metric spans from zero to infinity, with a value of zero denoting the optimal fit.

The NSE serves as the second indicator of goodness-of-fit, and is a dimensionless quantity that can be computed as:

$$\mathrm{NSE} = 1 - \left[\sum_{1}^{N}\left(y_i - Y_i\right)^2 \Big/ \sum_{1}^{N}\left(y_i - Y_{mean}\right)^2\right] \tag{11}$$

where the variable, y_{mean}, denotes the average value of the estimated or fitted values in the cross-sectional analysis and the range of NSE extends from negative infinity to one, with NSE of one representing the optimal fit [19].

3. Experimental Data

3.1. Experimental Data of 124Te (p, 2n)123I Reaction

By using thin films of substantially enriched 124Te, researchers were able to determine the cross sections within the 9.95 - 28.19 MeV proton energy range for the 124Te(p, 2n)123I reaction. Through experimentation, production rates were established, as were the optimal fractions of excitation functions necessary for achieving the highest level of 123I radiochemical purity with various isotopic enrichments of 124Te [20]. Furthermore, the cross sections for (p, 2n) reactions on highly enriched 124Te were measured using the stacked-foil technique in the proton energy range of 6 - 31 MeV [21].

3.2. Experimental Data of 127I (p, 5n)123Xe ⟶ 123I Reaction

In 1975, an experimental study was conducted at the Crocker Nuclear Laboratory to describe the yields and excitation functions involved in the production of 123I through the 127I (p, 5n)123Xe ⟶ 123I reaction. The study was conducted in the proton energy range of 45 - 62 MeV [22]. In the following year, the University of Groningen conducted additional excitation function studies in the proton energy range of 43 - 66 MeV [23]. Further research continued to be conducted to obtain more precise results for the excitation function involved in the production of 123I from the 127I (p, 5n) reaction. Medical cyclotrons were utilized to carry out these experimental studies in order to obtain the most accurate results. The latest experimental study, conducted by Zaitseva in 1991, focused on the proton energy range of 48 - 100 MeV [24].

4. Results and Discussion

The data regarding the cross section of nuclear reactions involving 124Te (p, 2n)123I and 127I (p, 5n)123Xe leading to the production of radio-halogen I-123 through cyclotrons was taken from the EXFOR database of experimental nuclear reaction data, version 2023.

Systematic analysis showed that the most appropriate match for the initial nuclear reaction of 24Te (p, 2n) 123I is Fourier with a second order approximation as the follows:

$$f(E) = a_0 + a_1 * \cos(wE) + b_1 * \sin(wE) + a_2 * \cos(2wE) + b_2 * \sin(2wE) \quad (12)$$

where, $a_0 = 0.564$, $a_1 = 0.159$, $b_1 = 0.3781$, $a_2 = -0.01336$, $b_2 = -0.124$, and $w = 0.3349$.

And the best fit for the 2nd nuclear reaction 127I (p, 5n) 123Xe ⟶ 123I is Gaussian with 2nd order as:

$$f(E) = a_1 * \mathrm{e}^{-\left(\frac{E-b_1}{c_1}\right)^2} + a_2 * \mathrm{e}^{-\left(\frac{E-b_2}{c_2}\right)^2} \quad (13)$$

where, $a_1 = 0.2968$, $b_1 = 55.65$, $c_1 = 8.767$, $a_2 = 0.1364$, $b_2 = 72.26$, and $c_2 = 18.46$.

The two equations, Equation (12) and Equation (13), offer novel empirical formulas for the cross section (in millibars) as a function of the energy (in mega-electronvolts) of the charged particle that is incoming. The data that corresponds to each formula is depicted in **Figure 1** and **Figure 2**, respectively. These figures illustrate the graphic coupling of the observed data with the corresponding formula.

One of the most critical tests after inferring regression models is to assess the quality of the model's suitability as it is necessary to verify the appropriateness of the derived equations for experimental data.

The root mean square error (RMSE) serves as an effective tool to approximate the standard deviation of an ordinary observed value from the model's prediction. It is capable of informing us about the mean difference between the model's fitted values and the factual experimental values within the dataset. A regression equation is considered to be more effective when the RMSE value is smaller.

An additional significant metric to examine is the R-square. In the context of linear regression models, the R-squared value gauges the goodness-of-fit. This numerical value demonstrates the percentage of the variation in the response variable that can be accounted for by the independent variables collectively. Represented on a scale of 0 to 1, the R-squared metric evaluates the potency of the correlation between the model and the response variable. **Table 3** shows the values of the indicators to measure the goodness-of-fit for each case.

Table 3. Statistical indicators for goodness-of-fit for each case.

Nuclear Reaction	Goodness of fit indicators		
	SSE	RMSE	R^2
124Te (p, 2n)123I	0.6363	0.1311	0.8646
127I (p, 5n)123Xe ⟶ 123I	0.1747	0.04357	0.8734

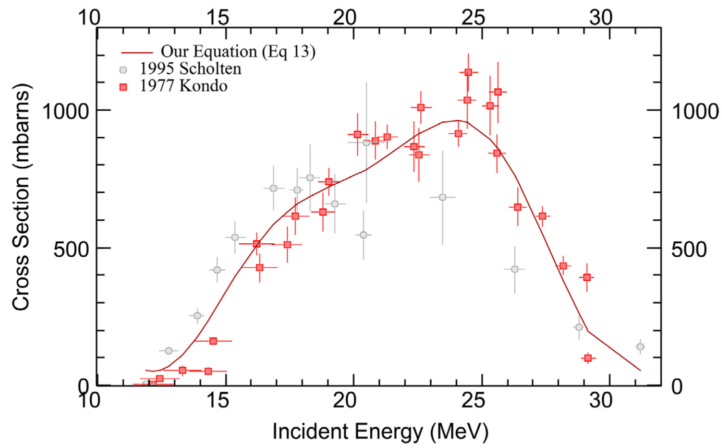

Figure 1. The Excitation Function of 124Te (p, 2n)123I Nuclear Reaction.

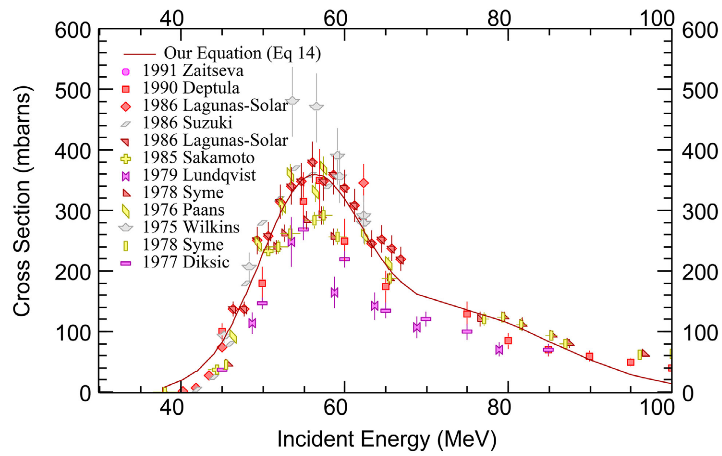

Figure 2. The Excitation Function of 127I (p, 5n)123Xe ⟶ 123I Nuclear Reaction.

5. Conclusion

Experimental cross section data for the radio-halogen 131I produced from the two nuclear reactions 124Te (p, 2n)123I and 127I (p, 5n)123Xe ⟶ 123I in the cyclotron were used in the present work and extracted from EXFOR V2023. A least square regression with three indicators (SSE, RMSE and R^2) was also used to measure the goodness-of-fit. The least square regression showed that the best fit for the cross section data versus the energy for the two above-mentioned reactions was, Fourier and Gaussian functions of second order, respectively. Moreover, the best fit was verified by the tabulated data in **Table 3**. Therefore, the present model of regression can be of great assistant in the prediction of the excitation energies for the radio-halogens that are produced for medical uses.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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