A Critical Literature Assessment of the Production of Alpha Emitting Medical Radioisotopes

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Received: 12-05-23
Accepted: 09-06-23
Published: 17-08-23

Abstract

The use of radionuclides for medical application has eased the treatment of complicated diseases especially cancerous diseases. This is due to their seamless application especially with the use of targeting molecules. Alpha particles have interesting properties of destroying the cancerous cells due to their short penetration and high linear energy transfer hence the use of the alpha emitting radionuclides allows for targeting specific cancerous cells and killing of the individual cells while minimizing the toxicity to the surrounding healthy cells. This has increased the need for the radionuclide and therefore, the need for more production of the radionuclide with high quality and quantity to meet the world need. Astatine (^{211}At) and Bismuth (^{213}Bi) are promising alpha emitting radionuclides for Targeted Alpha Therapy (TAT) for the destruction of cancerous cells. This prompted the review and assessment of their measured production cross-sections to ascertain the level of the update of the production cross-sections, the material used and the theoretical models used for the calculation and evaluation of the production cross-section with the aim to increase their production yield. ^{211}At ($T_{1/2}$ = 7.2-hour) having the advantage of longer half-life is produced via accelerator while ^{213}Bi ($T_{1/2}$ = 46 min) with short half-life is produced by generator through the Actinium parent (^{225}Ac/^{213}Bi). The experimental data from the nuclear data EXchange FORmat in the Nuclear Data section of the International Atomic Energy Agency were retrieved for the analysis. Most of the cross-section data were cumulative and they were measured long ago. ^{209}Bi and ^{208,209}Pb bombarded with alpha particle or Healium-6 beam and Lithium beam respectively are the most promising candidate materials for the production of ^{211}At and ^{232}Th and ^{226}Ra bombarded with spallation energy proton beam and low energy proton beam respectively are the most promising candidate material for the production of ^{225}Ac/^{213}Bi. The production energies were found to be sparse and most of the evaluations were not done with modular codes. Therefore, there is need for the update of the data and the evaluation, with modular codes, of the production routes to ascertain the direct production cross sections for the purpose of maximizing the production yield.

Keywords: Cross-section, Radioisotopes, Radiotherapy. Targeting Alpha Therapy, Astatine-211 and Bismuth-213.

1.0 INTRODUCTION

The need for medical radioisotopes is on the increase following the discovery of their importance in simplification of medical services such as diagnosis and treatment of complicated diseases especially cancer. There are many natural radionuclides that are known. Many of such nuclides are isotopes of heavy elements. Heavy nuclides have the advantage of emitting alpha particles because of the abundance of protons and neutrons. While some of the radionuclides live for short time, in nano-seconds, most of the heavy nuclides have very long half-life where some live for billions of years. As they decay, the emit particles such as neutron, proton, beta or alpha particles, which are usually accompanied by gamma radiation. These radiations have properties that are utilized in several applications including medicine. Among the radiations, alpha has advantage of high Linear Energy Transfer (LET) and short distance travel in human tissue. These make it easier to be used in targeted therapy with high precision, high cytotoxicity and specificity to destroy targeted cells without harming the nearby healthy tissues (Christopher, 2018; Miederer et al., 2018). Due to these potentials, the development of alpha-emitting radiopharmaceuticals for Targeted Alpha Therapy (TAT) has become an interested area of research for both commercial and academic fields worldwide.

The candidate radionuclides for TAT include Astatine-211 (^{211}At) and Bismuth-213 (^{213}Bi). ^{211}At is a promising radionuclide with specific favorable characteristics for α-particle therapy of cancer. Its half-life is 7.2 hours suitable to the kinetics of full antibodies or other biomolecules that require several hours to reach an optimal tumor-to-blood dose ratio (Zalutsky et al., 2008).

Bismuth-213 is an isotope with high LET, though it has short half-life of 46min. Several clinical trials have demonstrated the potentials of ^{213}Bi radiopharmaceuticals to treat advanced cancers (Allen et al., 2011; Jurcic & Rosenblat, 2014; Kratchowil et al., 2014; Kratochwil et al, 2016;). However, the introduction of ^{211}At and ^{213}Bi-based radiopharmaceuticals into clinics has been slowed by several difficulties including the production and the availability of the radionuclides. Radioisotopes with the properties required for medical applications are mostly not found naturally, and are not in abundance, hence the need to produce them to meet the required needs both in quantity and quality.

It is against this backdrop that this paper reviewed the production cross-section data of the production routes of ^{211}At and ^{213}Bi to ascertaining the level of the update of the cross-section data available, the materials involve, and the theoretical models for the calculation of the cross-section data.

The experimental data were sourced from the internet through the experimental nuclear reaction data EXchange FORmat (EXFOR) library contained in the Nuclear Data Section (NDS) of the International Atomic Energy Agency (IAEA) through the website: https://www-nds.iaea.org/exfor/. The retrieval of the data was done by inputting the product and the quantity (All cross section). This retrieves all the measurements that contain the cross-sections of the reactions that resulted to the product.

After a brief introduction of the alpha emitting radionuclides for radiotherapy, the review of the production cross-section of ^{211}At induced by beams of light and heavy ion projectiles is presented. The cross-section data for the production of ^{213}Bi are reviewed and the overview of the theoretical models for the calculation and evaluation of the cross-section data is presented. Finally, the conclusion drawn from the review is presented.

2.0 LITERATURE FINDINGS

2.1 Brief Introduction of Alpha Emitting Radionuclides for Radiotherapy.

The alpha emitting radioisotopes used in medical applications are considered for therapeutic purposes. Alpha particles have energy in the range 4-10 MeV which is a range of high energy (Jean-Pierre & Julie, 2021; Scott, 2014) and traveled in a short distance below 0.1 mm in human tissues. Because of their double positive charges, they deposit large ionization energy along their path. Hence, the use of alpha emitters allows for the killing of specific targeted individual cancerous cells, while reducing the risk of destroying the surrounding healthy cells, as compared to beta particles and gamma rays (Jean-Pierre, & Julie, 2021).

Only a handful of the many known α-emitters can be explored in the clinical setting because of their inherent physical characteristics. Among these are the shorter-lived α-particle-emitting radionuclides: ^{213}Bi ($T_{1/2}$ = 45.59 min), and ^{211}At ($T_{1/2}$ = 7.2 h), as well as the atomic in vivo nano-generators ^{227}Th ($T_{1/2}$ = 18.7 d), ^{225}Ac ($T_{1/2}$ = 9.9 d), and $^{224/223}$Ra ($T_{1/2}$ = 3.6 d/11.4 d) which decay by several α-emissions (De Kruijff, et al., 2015; Parker et al., 2018; Sgouros, 2019). There are many other α-emitters that are been considered for targeted therapy. These include ^{149}Tb, ^{212}Bi, ^{212}Pb, ^{223}Ra, ^{224}Ra, and ^{227}Th (Andrew et al., 2018).

TAT is based on attaching α-emitting radioisotopes to cancerous cells selective carrier molecules. The molecules can target cancerous cells selectively even if they are not clustered in a particular spot. They recognize the cancer cells through their antigens which are expressed on the cell surface and bind to the cells selectively. The carrier molecules serve as means of transportation for the α- emitting radioisotopes to the cancerous cells (Christopher, 2018).

2.2 Production of ^{211}At through Light Ion Induced Reaction

There are different production routes of ^{211}At by light ion induced reaction. The light ion reaction projectile beams used so far in the production are proton, deuteron, helium, and alpha. Table 1 contains the experimental data with high cross sections for the reactions as extracted from the EXFOR library. It shows the reactions, the targets, and the maximum cross sections recorded in the library. There are only few reactions explored with proton beam for the production. The reactions are ^{208}Pb(p,x)^{211}At, ^{209}Pb(p,x)^{211}At, ^{208}Bi(p,x)^{211}At, ^{209}Bi(p,x)^{211}At and ^{232}Th(p,x)^{211}At. The measurement started in 1958 with ^{209}Bi as the target. In the measurement, cross-section values less than 1mb were recorded using 180 MeV and 480 MeV proton beam energy (Kurchatov et al., 1958).

Table 1. The Light ion induced reaction Experimental Available Data in the EXFOR Library for ^{211}At Production Reactions.

Reaction	Target Nucleus	Energy Range (MeV)	Maximum Cross Section (mb)	Energy of Maximum Cross Section (MeV)
(p,x)	^{208}Pb	80	1E-05	80 (Wang et al., 1960)
	^{209}Pb	3000, 6000, 10000	0.01	10000 (Mal`tseva et al., 1963)
	^{208}Bi	3000, 6000, 10000	0.2	6000 (Mal`tseva et al., 1963)
	^{209}Bi	120 – 10000	8.5	152.5 (Gauvin et al., 1962)
	^{232}Th	82,155	2.5	155 (Tarrago, 1962)
(d,x)	^{208}Pb	88.87, 222.76, 372.06	3.662E-05	3372.06 (Wang et al., 1960)
(^{3}He,n)	^{209}Bi	19.14 – 64.45	0.8863	43.23 (Nagame et al., 1988)
(^{3}He,π)	^{208}Pb	130	5E-07	130 (Ward et al., 1987)
(^{6}He,4n)	^{209}Bi	24 – 47.114	1724.13	31.5699 (Deyoung et al, 1998)
(^{238}U,x)	^{1}H	238000	0.606	238000 (Casarejos et al., 2006)
(α,2n)	^{209}Bi	21.1 – 99.445	970	31 (Hermanne et al., 2005)

In 1960, Two groups in their separate measurements, using the same target with beam energy ranging from 130 to 660 MeV, did not get up to 1mb of the production cross-section (Lefort et al., 1960; Wang et al., 1960). Later in 1962, 8.5 mb was recorded at 152.5 MeV which is the highest cross-section values recorded for the production of ^{211}At using ^{209}Bi(p,x)^{211}At reaction (See Table 1). In 1963, Lefort and Tarrago measured lower values in a three-point measurement with 240, 420 and 550 MeV proton beam energy (Lefort & Tarrago, 1963). There was no measurement of ^{209}Bi with proton beam after the 1963 measurement until 1985 when Dombsky and group also measured values less than

1mb (Dombsky et al., 1985). Their cross-section values for the beam energies from 120 MeV to 481 MeV were of the order of 10E-3 mb and the value for 800 MeV is 0.1mb. Generally, the values measured were very low which suggest that bombarding Bismuth-209 (^{209}Bi) with proton beam could not produce enough yield for medical application though the most recent of the measurements was done in 1985, that the data requires update.

Wang and group in their experiment in 1960 used lead-208 (^{208}Pb) as target with 80 MeV proton beam and got 1E-05 mb production cross-section (Wang et al., 1960). They also used deuteron beam of 80.87 MeV, 222.76 MeV, and 372.06 MeV on ^{208}Pb target and got low values of 4E-06 mb, 2.514E-05 mb and 3.662E-05 mb respectively (Table 1). Since then, these have been the only measurements done for the production of ^{211}At with lead-208 target using proton and deuteron beams.

In 1963, Lead-209 (^{209}Pb) and (^{208}Bi) were used as targets at three-point spallation proton energy of 3000 MeV, 6000 MeV and 10000 MeV by Mal`tseva et al. (1963). The cross-section values recorded were not up to 1 mb (See Table 1) and those were the only measurements conducted with the Lead-209 and Bismuth-208 using proton beam. Thorium-232 (^{232}Th) was also used as a target in the production of the ^{211}At with proton beam. In 1962, Tarrago measured the production cross section of 2.5 mb using ^{232}Th target with proton beam of 155 MeV (Tarrago, 1962). Gauvin and his group also carried out similar measurement but could not get up to 1mb at 82 MeV (See Table 1). These were the only data recorded for ^{232}Th target bombarded with proton beam. No such measurement was recorded since 1962.

In using Helium beam as a projectile in the production of ^{211}At, Ward and group in 1987 conducted a measurement and recorded very low cross-section value of 5E-07 mb at 130 MeV Helium-3 (^{3}He) beam energy in $^{208}Pb(^{3}He,\pi-)^{211}At$ reaction (Ward et al., 1987). A year later, Nagame et al. (1988) recorded low cross-section values of the order of 1E-1 mb with ^{3}He beam energy range of 19.14- 64.45 MeV using $^{209}Bi(^{3}He,n)^{211}At$ reaction. However, higher values were recorded with Helium-6 (^{6}He) beam. Using $^{209}Bi(^{6}He,4n)^{211}At$ reaction, significant values in order of hundreds were recorded with ^{6}He beam. In 1988, Deyoung and group measured 1724.13 mb at 31.5699 MeV ^{6}He beam energy and in 1994, Formichev and group recorded 925 mb at 31.2727 MeV in an experiment with beam energy range of 24-47 MeV (Formichev et al., 1994). In 2006, Hassan and group recorded lower values than those recorded by Deyoung and group (Hassan et al., 2006). The data of $^{209}Bi(^{6}He,4n)^{211}At$ reduces as they are been updated. Recent values are lower than the values of the previous measurements. Generally, helium-6 beam produced higher cross section with Bismuth-209 target as recorded in Table 1.

Lower values were recorded with alpha beam and Bismuth-209 target. The energy range studied is 21.1 – 99.445 MeV. Kelly and Segre measured 910 mb at 31 MeV (Kelly & Segre, 1949) while Ramler et al. (1959) measured 908 mb at 31 MeV alpha beam energy, 2 mb lower from the value of Kelly and Segre which is within the experimental error. In 1974, Hofstetter and Stickler recorded lower values in a three-point energy of 24 MeV, 29.8 MeV and 33.9 MeV (Hofstetter and Stickler, 1974). Though they did not take measurement at 31 MeV, their values are lower than the values recorded by Ramler and group also the values of Hofstetter and Stickler. Similarly, the values measured by Deconninck and Longree with beam energy from 40.107 MeV to 99.445 MeV were also low (Deconninck & Longree, 1994). In 2005, Hermanne and group recorded 970mb at 31 MeV (Hermanne et al., 2005), which is similar to the value of Kelly and Segre also the value of Ramler and group. This is a confirmation that $^{209}Bi(\alpha,2n)^{211}At$ is the most common production route of ^{211}At (Valery et al., 2021) that produce reasonable yield (Michael and Marek, 2011). The production route has been relatively simple and there are significantly high number of available facilities (Sture et al., 2020), otherwise $^{209}Bi(^{6}He,4n)^{211}At$ reaction has higher cross section value as measured by Deyoung and group.

In spallation reaction, Taieb et al. (2003) measured a cross section of 0.49 mb in an experiment to measure the nuclide cross section of spallation residues in 1A GeV Uranium-238 + Proton collisions at 238000 MeV beam energy. Casarejos et al. (2006) measured 0.606 mb at the same beam energy in similar experiment.

2.3 Production of ^{211}At through Heavy Ion Induced Reaction

In the production of ^{211}At using heavy ion induced reactions, most of the experimental works recorded in EXFOR were not purposely conducted to produce ^{211}At, but some cross sections were measured and recorded.

Table 2. The Heavy ion induced reaction Experimental Available Data in the EXFOR Library for ^{211}At Production Reactions.

Reaction	Target Nucleus	Energy Range (MeV)	Maximum Cross Section (mb)	Energy of Maximum Cross Section (MeV)
(^{238}U,x)	^{0}Cu	226100	0.71	226100 (Junghans et al., 1998)
(^{7}Li,x)	^{0}Pb	35.3 – 56.9, 245	366	40.7 (Nishinaka et al., 2015)
(^{6}Li,x)	^{209}Bi	28.8 – 47.9	173.3	47.9 (Dasgupta et al., 2004)
(^{7}Li,x)	^{209}Bi	35.8 – 51.9	83	51.9 (Dasgupta et al., 2004)
(^{84}Kr,x)	^{209}Bi	432 – 490	15.7	490 (Bimbot and Rivet, 1973)
(^{14}N,x)	^{209}Bi	61 – 159	13	129 (Gardes et al., 1978)
(^{16}O,x)	^{209}Bi	58 – 99	34.5	94 (Gardes et al., 1978)
(^{19}F,x)	‘’	78.7 – 185.5	26.4	169.5 “ “
(^{20}Ne,x)	‘’	97 – 203	38.4	141 “ “
(^{40}Ar,x)	“	181 – 294	27.5	249 “ “
(^{40}Ca,x)	“	174, 180	0.009	180 “ “
(^{56}Fe,x)	“	263 – 396	12	396 “ “
(^{63}Cu,x)	“	296 – 410	10.4	377 “ “
(^{19}F,x)	^{205}Tl	178	0.092	178 “ “
(^{20}Ne,x)	“	193.5	0.15	193.5 “ “
(^{40}Ar,x)	“	197 – 284	1.48	262 “ “
(^{12}C,x)	^{209}Bi	62.5 – 88	49	87 (Bimbot et al., 1972)
(^{9}Li,x)	^{208}Pb	42.38, 44.89	182	44.89 (Vinodkumar et al., 2009)
(^{8}Li,x)	“	33.33 – 38.94	253.9	38.94 (Aguilera et al., 2009)
(^{7}Li,x)	“	28.8 - 67	760	52.4 (Hassan et al., 2006)
(^{6}Li,x)	“	24.96 – 39.36	171.23	35.328 (Wu et al., 2003)
(^{136}Xe,x)	“	744.231	0.467	744.231 (Barrett et al., 2015)
(^{58}Ni,x)	“	345	1.7	345 (Krolas et al., 2010)
(^{48}Ca,x)	^{248}Cm	267	0.13	267 (Hulet et al., 1977)
	^{254}Es	240, 249	0.0011	249 (Lougheed et al., 1985)

Table 2 contains the reactions, targets and the highest cross-sections with the projectile’s energies from the EXFOR library. From Table 1 and 2, the values of the cross sections of heavy ions reactions for the production of ^{211}At are higher than those investigated with proton beam.

Junghans and group in 1998 measured the cross section of $^{0}Cu(^{238}U,x)^{211}At$ reaction as 0.71 mb at 226100 MeV in an experiment to measure the production cross sections of nuclei produced in the fragmentation of uranium projectile (Junghans et al., 1998). Dasgupta and group in 2004 measured 173.3 mb at 47.9172 MeV using $^{209}Bi(^{6}Li,x)^{211}At$ reaction and 83mb at 51.9123 MeV in $^{209}Bi(^{7}Li,x)^{211}At$ reaction (Dasgupta et al., 2004). The data constantly increase with increase in energy showing that higher cross section values can be recorded with higher projectile energies. The data shows that ^{209}Bi bombarded with ^{6}Li or ^{7}Li beams can be used to produced ^{211}Ac.

Later in 2005 in searching for the properties of the products from the interaction of Lithium ions with Lead nuclei, Demekhina and group recorded 0.4 mb at 245 MeV using $^{0}Pb(^{7}Li,x)^{211}At$ reaction. 10 years later, Nishinaka and group in measuring the production of astatine isotopes with natural Lead using $^{0}Pb(^{7}Li,x)^{211}At$ reaction within ^{7}Li beam energy from 35.3 MeV to 56.9 MeV recorded a maximum value of 366 mb at 40.7 MeV (Nishinaka et al., 2015). The value is the latest and the maximum for the heavy ions induced reactions (See Table 2).

In some earlier measurements, Bimbot and Rivet in 1973 conducted an experiment on $^{209}Bi(^{84}Kr,x)^{211}At$ reaction and measured the production cross section of 15.7 mb at 490 MeV Krypton-84 (^{84}Kr) beam energy (Bimbot and Rivet, 1973). Meanwhile Gardes and group did an intensive work in 1978. They measured the cross section using different heavy ion projectiles with ^{209}Bi and Thalium-205 (^{205}Tl) as targets (Gardes et al., 1978). Using ^{205}Tl as target, they measured 0.15 mb at 193.5 MeV in a one-point measurement with Neon-20 (^{20}Ne) beam as the projectile and 0.092 mb at 178 MeV with Flourine-19 (^{19}F) beam as the projectile. Using Argon-40 (^{40}Ar) beam as the projectile, they recorded a maximum value of 1.48 mb at 262 MeV in a measurement with beam energy range of 197-284 MeV. This is the highest value they recorded with ^{205}Tl target (See Table 2).

In their experiment with ^{209}Bi target and other projectiles, Gardes and group recorded the highest value of 38.4 mb at 141 MeV with Neon-20 (^{20}Ne) projectile beam. Though other projectiles they used produced lower values, the highest values for Calcium-40 (^{40}Ca) and Flourin-56 (^{56}Fe) are at their highest beam energies used which shows that there can be higher values with higher beam energies (See Table 2).

Guo and group also used ^{209}Bi as target in their measurement in 1978. Using $^{209}Bi(^{12}C,x)^{211}At$ reaction they measured 35.5 mb at 69.9 MeV (Guo et al., 1978). They recorded lower value at 72.5 MeV. Meanwhile Bimbot and group had measured 49 mb at 87 MeV earlier in 1972 (Bimbot et al., 1972) which is the highest with ^{12}C projectile beam. Using ^{208}Pb as a target with some Lithium isotopes ($^{9,8,7,6}Li$), Xenon-136(^{136}Xe), and Nickel-58 (^{58}Ni) as the projectile beam, the highest cross section value obtained is 760 mb with ^{7}Li beam (See Table 2). Curium-248 (^{248}Cm) target in $^{248}Cm(^{48}Ca,x)^{211}$ At reaction and Einsteinium-254 (^{254}Es) target in $^{254}Es(^{48}Ca,x)^{211}At$ reaction both with Calcium-48 (^{48}Ca) projectile could not produce up to 1mb as shown in Table 2. The cross sections are generally low and the measurements have been very long ago, they require update.

Generally, it can be seen that some of the heavy-ion induced reactions measured so far can produced significant cross-section values that can be used for medical application. Meanwhile the measurements are sparse both in terms of projective beam energy and in terms of the materials used especially as the targets.

2.4 Production of ^{213}Bi

Bismuth – 213 is a synthetic radioisotope with half-life of 46 min. Because of its short half-life, the production of ^{213}Bi is preferably through generator rather than reactor or accelerator. Though using accelerator in 1977, Hulet and group in searching for super heavy elements in the bombardment of ^{248}Cm with ^{48}Ca measured the cross section of the production of ^{213}Bi as 0.13 mb at 267 MeV calcium energy even though they could not find the super heavy elements. Later in 1984, Eskola and group in an experiment to produce neutron-rich Bismuth isotopes, separated ^{213}Bi in $^{204}Hg(^{18}O,x)^{213}Bi$, $^{205}Tl(^{18}O,x)^{213}Bi$ and $^{208}Pb(^{18}O,x)^{213}Bi$ reactions, but none of the reactions produced a cross sections value up to 1mb (Ekola et al., 1984).

The short-lived α-emitting radionuclides such as ^{213}Bi are best produced by radioactive generators. It is the simplest and most efficient means of the production. The generator for the production of Bismuth is $^{225}Ac/^{213}Bi$. ^{213}Bi which produces ^{213}Bi through the decay of ^{225}Ac. Because of this, attention is drowned to the production of ^{225}Ac rather than the ^{213}Bi itself.

The current main source of ^{225}Ac is ^{229}Th generators, which allow the separation of ^{225}Ra and ^{225}Ac. The shortage of ^{225}Ac limits the production of ^{213}Bi. The possible pathways toward increasing the production of ^{225}Ac include spallation reaction of ^{232}Th with high-energy proton beam.

In the early 1960s, Lefort and group measured the production cross sections of ^{225}Ac and ^{223}Ra from ^{232}Th at a proton beam energy of 150 MeV (Lefort et al., 1961). They recorded 14 mb for the $^{232}Th(p,x)^{225}Ac$ reaction. Pate and Poskanzer measured 5 mb at 680 MeV proton beam energy

(Pate & Poskanzer, 1961) while Gauvin and group measured 2.6 mb at 82 MeV (Gauvin et al., 1962). In a year later, Gauvin in an experiment with 42-115 MeV proton beam measured 5.8 mb at 115 MeV (Gauvin, 1963). In 1999, Titarenko and group conducted a three-point measurement at 200 MeV, 1200 MeV and 1600 MeV and recorded very close values of 19.4 mb, 19.5 mb and 18.5 mb respectively (Titarenko et al., 1999a). They also measured 20.3 mb at 800 MeV in another separate measurement. In 2011, Zhuikov and group measured 13.9 mb at 135 MeV (Zhuikov et al., 2011) while Ermolaev and group in a year later measured 9.7 mb at 54.4 MeV proton beam within energy in a range of 21 – 141.3 MeV (Ermolaev et al., 2012). In that year, Weidner and group measured 14 mb at 800 MeV and 17.5 mb at 78.77 MeV and 94.57 MeV within proton energy range of 56.37 – 194.57 MeV (Weidner et al., 2012a; Weidner et al., 2012b). In 2016, Griswold and group measured 16.7 mb at 170.7 MeV in an experiment within proton energy range of 77.8-191.8 MeV (Griswold et al., 2016). Using high energy proton beam, Robertson et al. (2020) measured 13.3 mb at 438 MeV in 2020 and later in 2021 Steyn and group measured 6.55 mb at 55.4 MeV in an experiment within proton energy range of 39.72 – 66.97 MeV (Steyn et al., 2021). The bombardment of ^{232}Th with proton beam for the production of ^{225}Ac produced some interested results.

Thorium - 232 was also explored with some other projectiles too. In 1963, The cross section values of ^{232}Th(^{22}Ne,x) ^{225}Ac reaction for 111.97 – 154 MeV was measured and recorded by Kumpf and Donets and the value of the cross-section was not up to 1 mb (Kumpf & Donets, 1963). In 1979 Glascock and group measured used alpha particle beam as the projectile at 140 MeV. The production cross section was 8.5 mb (Glascock et al., 1979) which is higher than the data obtained by most of the measurements with ^{232}Th.

In the exploration of Radium, Apostolidis and group carried out some measurements at lower proton beam energies with Radium-226 (^{226}Ra) and recorded 710 mb at 16.8 MeV with 8.8 – 24.8 MeV proton energy in ^{226}Ra(p,2n)^{225}Ac reaction (Apostolidis et al., 2005). The measurement was done in 2005 and it is the only record on the exploration of Radium for the production of ^{225}Ac as recorded in EXFOR and the cross-section is high enough though Radium is difficult to handle because it is radioactive.

Working with uranium, Pate and Poskanzer in 1961 measured the cross section of ^{235}U(p,x)^{225}Ac reaction and recorded 1.1 mb at 680 MeV and 1.8 mb at 1800 MeV (Pate & Poskanzer, 1961). They also used ^{238}U target and measured 1.4 mb at 1800 MeV. Long after that, there was no such measurement until 1998 when Junghans and group using a heavy ion induced reaction ^{0}Cu(^{238}U,x)^{225}Ac measured 2.33 mb at 226100 MeV (Junghans et al., 1998). The cross-section is not high enough for medical application. Titarenko and group in 1999, measured a cross section value of 3.31 mb at 800 MeV using natural uranium target (Titarenko et al., 1999b). In 2001, the group took the measurement at 800 MeV and 1200 MeV proton beam energy and obtain the cross-section values of 3.31 mb and 2.99 mb respectively (Titarenko, 2001). Taieb and group in 2003 measured the production cross section of ^{225}Ac as1.77 mb at spallation energy of 238000 MeV in ^{1}H(^{238}U,x)^{225}Ac reaction (Taieb et al., 2003). The result is also low. In 2006, Casarejos measured higher value of 2.251 mb at the same proton beam energy and same reaction (Casarejos et al., 2006). The result is similar to the result obtained by Junghans and group in 1998 and it is the latest of the measurements thus all the cross-section data obtained are not high enough for medical application.

On a production of cold target-like fragments in ^{248}Cm(^{48}Ca,x)^{225}Ac reaction, Gaggeler and group measured 0.185 mb at 2.59523E+07 MeV (Gaggeler et al., 1986). There is no such measurement since 1986.

2.5 An Overview of the Theoretical Models for the Calculation and Evaluation of the Production Cross Section.

Nuclear reaction models are required in theoretical calculation and the evaluation of the nuclear data for the understanding of the processes involve during the nuclear reaction. As part of their predictive capacity, they are necessary to produce nuclear data for various applications. Hence the review of the models used in the production cross section of ^{211}Ac and ^{225}Ac/^{213}B.

From the review, most of the codes used in the computation of the reactions were not modular codes that are well known as all-in-one such as ALICE, GNASH, EMPIRE and STAPRE. Code such as PACE-4 and a couple channel code CCFULL were use in simulation of $^{4,6}He$ and ^{7}Li on ^{208}Pb and ^{208}Bi nuclei by Hassan et al. (Hassan et al., 2006). COMPLET code was used in the evaluation of $^{209}Bi(a,2n)^{211}At$ by Yihunie, et al. (Yihunie, et al., 2019). Robertson et al. used FLUKA and GEANT4 to simulate the measurement of ^{225}Ac in an experiment of $^{232}Th(p,x)^{225}Ac$ reaction (Roberson, 2020). Hermanne et al. used EMPIRE and other codes as ALIVE-IPPE and GNASH in evaluation of $^{209}Bi(a,2n)^{211}At$ reaction (Hermanne et al., 2005) and it is the reaction recommended by IAEA for the production of ^{211}At. The ENDF data are mostly from the Talys Evaluated Data Library (TENDL) for different years such as TENDL-2019 (Koning, et al., 2019).

3.0 CONCLUSION

In the production of ^{211}At, it is found that most of the light ion induced reaction could not produce high cross-sections as the heavy ion induced reactions. Only the reaction of Bismuth-209 with alpha particle beam and Helium-6 beam produced high cross-sections with Helium-6 producing the highest cross-section among the light ion beams. The cross-section is the overall highest cross-section for the production of ^{211}At.

In the heavy ion induced reaction, Lithium beam produced higher cross-sections with Lead and Bismuth-209 than other heavy ion induced reactions. This shows that ^{209}Bi have greater potential of been the target material that can produce high yield since it is capable of producing high cross-sections with both light and heavy ion beams. For the production of $^{225}Ac/^{213}Bi$, bombarding ^{226}Ra target with proton beam is most promising as it produced high cross-section at low energy. Though ^{232}Th is a good candidate material, it requires high energy projectile beam. Exploring ^{232}Th can produce good result.

Generally, most of the cross-section data were cumulative. Virtually all the cross-section data of the heavy ion induced reactions recorded were cumulative as a result there is no certainty of which particular routes contributed most in the production cross-section hence the data needs model calculations and evaluation to ascertain the direct production routes for the purpose of maximizing the production yield.

The review shows that most of the measurements were done long ago and there are wide energy gaps in the projectile beam energy used in the measurements especially in the measurement of the cross section of heavy ion induced reactions for the production of ^{211}At, where in some cases only low energy projectiles were used and, in some cases, only the high energy projectiles were used. Most of the reactions were measured once, and some at only one or two energy points. This calls for update especially with the development in the facilities in the nuclear field. There is need for intense study with interpolation and extrapolation of the reactions cross-section data to cover the energy gaps. The overview of the models for the calculation and evaluation of the cross-section data revealed the need to use modular codes to calculate and evaluate the data.

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