^{117m}Sn — THE PROMISING RADIOISOTOPE FOR USE IN NUCLEAR MEDICINE*

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This review paper is dedicated to ways of production and medical applications of the tin isomer ^{117m}Sn in the context of its wider use in nuclear medicine, particularly, in diagnostics. Until now, ^{117m}Sn has been used as an effective agent for the palliation of pain from bone metastases. However, the energy of gamma-rays emitted by ^{117m}Sn is optimal for scintigraphy and, moreover, this tin isomer can also be connected to many different ligands. Tin-117m can be effectively produced in many nuclear reactions without the use of research reactors, which is a very big advantage particularly in the light of the perceptible crisis in the production of technetium-99m.

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1. Introduction

1.1. Nuclear medicine

Nuclear medicine is one of the specialties of medicine consisting in giving patients radiopharmaceuticals *i.e.* substances with radioactive isotopes emitting ionizing radiation (photons, electrons and positrons) for the diagnosis and treatment of disease. In the diagnostics, two techniques of imaging are applied. The first one is scintigraphy known also as a gamma scan based on radioisotopes emitting gamma rays with an energy of a hundred keV up to several hundred keV. The radioisotopes commonly used in scintigraphic imaging are ^{99m}Tc, ^{123}J and ^{81m}Kr [1–3]. Positron emission tomography (PET) is the second main diagnostics technique. It uses the β^+ emitters such as ^{18}F, ^{68}Ga and many others [1, 4–9]. A good example of a radionuclide used in radiopharmaceutical therapy is ^{131}J [1, 10]. This iodine radioisotope is applied for destruction of thyroid tissue in treatment of hyperthyroidism and cancers. Recently, nuclear medicine has been strongly supporting the advanced investigations in immunology. This branch of nuclear medicine is

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called radioimmunoassay [11]. An example of such studies can be *in vitro* diagnostics determining amount of various substances such as drugs, hormones and antibodies in blood [12–14]. The *in vitro* diagnostics is based on radioisotopes of ^{125}J, ^{14}C and ^{3}H [15].

1.2. Production of medical radioisotopes

Due to the rapid development of nuclear medicine, the demand for radioactive isotopes used in the diagnostics and the therapy is growing [16]. Currently, most medical radionuclides are produced by irradiation of uranium disks (fission reactions) or targets enriched in the parent isotope (simple capture reactions $(n.\gamma)$ called also radiative neutron capture) in research reactors [16, 17]. The main suppliers of reactor-produced radioisotopes are Belgium, Canada, The Netherlands, France, Poland and South Africa [16]. The radioisotopes with excessive neutrons (β^- emitters) are mainly produced in research reactors, whereas those with excessive protons are produced in cyclotrons [18] in various reactions — (p,n), $(p,p'n)$, (d,n) and (γ,n). Nuclei with an excess of protons disintegrate by β^+ decay. Therefore, most of cyclotron radionuclides are suitable for application in the positron emission tomography.

1.3. Technetium-99m

As already mentioned, technetium-99m is the basic radioisotope used in nuclear medicine. This radionuclide has a relatively short half-life $T_{1/2}$ = 6 hours which makes it impossible to use in medical centers far away from research reactors. Therefore, the ^{99}Mo/^{99m}Tc generators supplied from fission production are applied (^{99}Mo, $T_{1/2}$ = 65.94 hours [19]). 85% of all nuclear medicine examinations use the ^{99}Mo/^{99m}Tc generators for diagnostics of liver, lungs, bones [20]. The shortage of ^{99m}Tc caused by the unexpected prolonged shutdown of the Chalk River (Canada) and Petten (The Netherlands) reactors, and the permanent cessation of ^{99}Mo production at The Chalk River in 2016 contributed to the exploration of alternative methods of producing ^{99m}Tc [21–23]. The non-reactor technetium-99m can be produced in a cyclotron by bombarding a ^{100}Mo target with a 18 MeV proton beam (in the $(p,2n)$ reaction) to produce ^{99m}Tc directly [21], or in a linear accelerator to generate ^{99}Mo in the photonuclear reaction ^{100}Mo$(\gamma,n)^{99}$Mo induced by high-energy X-rays [21, 22]. IAEA recommends using medical cyclotrons for the production of ^{99m}Tc [24]. A search for new radioisotopes which could be an alternative to technetium-99m has also attracted significant interest. The good candidate is the tin isomer — ^{117m}Sn. The purpose of this paper is to review applications of ^{117m}Sn and ways of its production in the context of replacing technetium-99m with tin-117m.

2. Characteristic of tin-117m

^{117m}Sn is a nuclear isomer at the second exited state of tin. This state is characterized by spin of 11/2, negative parity, excitation energy of 314.6 keV, and a half-life $T_{1/2} = 13.6$ d [19, 24]. It disintegrates by a cascade gamma-decay and internal conversion. The de-exciting transition energies of all decay products of ^{117m}Sn are presented in Table I.

TABLE I

Characteristic of the ^{117m}Sn decay [17].

Product	Energy [keV]	Emission intensity (Transition probability) in [%]
Gamma-rays	158.6	86.4
	156.0	2.1
Electrons	126.8	64.9
	151.6	26.2
	129.4	11.7

3. Production of tin-117m

This tin isomer can be produced in a research reactor by two reactions: the radiative neutron capture (n, γ) of enriched tin-116 (abundance of 14.54%) and the neutron inelastic reaction (n, n') on enriched tin-117 (7.68%). This second reaction is the most effective in higher flux reactors since specific activity values of about two times higher than the radiative

TABLE II

The list of nuclear reactions leading to the formation of ^{117m}Sn.

Reaction	Cross section	Ref.
$^{115}\mathrm{In}(\alpha, pn)$	16 mb at 31.5–35.4 MeV	[26]
$^{117}\mathrm{S}(p, p'\gamma)$	0.37 mb at 23.6 MeV	[27]
$^{114}\mathrm{Cd}(\alpha, n)$	480 mb at 20 MeV	[28]
$^{116}\mathrm{Cd}(\alpha, 3n)$	1.2 b at 36 MeV	[29]
$^{121}\mathrm{Sb}(p, \alpha)$	several hundred mb at 30–42 MeV	[27]
$^{118}\mathrm{Sn}(\gamma, n)$	290 mb at 15 MeV	[29]
$^{116}\mathrm{Sn}(n, \gamma)$	6 mb at thermal energies	[30]
$^{118}\mathrm{Sn}(n, n')$	over 317.2 keV	[30]

capture reaction can be achieved [25]. Production using uranium disks is ineffective because of very small amounts of tin-117m in the fission products. However, ^{117m}Sn can be produced in cyclotrons and linear accelerators. The characteristics of nuclear reactions leading to the formation of tin-117m are shown in Table II.

4. Discussion of applications of tin-117m

Until now, ^{117m}Sn has been used as an effective agent for the palliation of pain from bone metastases [31–33]. Such a radionuclide therapy leads to the significant improvement of the quality of patients life. This application results from the desired half-life of tin-117m, the energy of the emitted electrons and the emission intensities of the internal conversions. Until now, tin-117m has not been widely used in radiopharmaceuticals. At present, the only radiopharmaceutical is tin(IV)-117m-DTPA (pentitic acid) [32] used for the bone pain palliation. The main impediment for wider use of this radioisotope is the low specific activity of tin-117m produced in research reactors. Tin-117m can also be connected to other ligands as PyP (pyrophosphate), EHDP (ethylidenehydroxy disodiumphosphonate) and MDP (methylene diphosphonate) [32]. ^{117m}Sn is also a diagnostically promising radioisotope, because it emits gamma rays of 158.6 keV, which is close to the energy of ^{99m}Tc. This allows to use existing standard gamma camera imaging, for example, to use the same collimator system as for technetium-99m. Thus, the energy of gamma rays emitted by ^{117m}Sn is optimal for scintigraphy. Higher energies cause loss of resolution of the scintigraphic images, whereas lower energies cause the increase of a dose delivered to patients during examination. The relatively long half-life makes it possible to use tin-117m without a generator. In consequence, the problem of the contamination of radiopharmaceuticals with a parent radioisotope disappears. In diagnostics, the contaminated radiopharmaceuticals are a source of an additional dose to patients [34, 35].

5. Summary

Tin-117m is one of few medical radioisotopes that can be used in radiopharmaceutical therapy as well as in diagnostics. This tin isomer does not require to apply a radionuclide generator because of its relatively long half-life. Tin-117m can be effectively produced in many nuclear reactions without the use of research reactors, which is a very big advantage particularly in the light of the perceptible crisis in the production of technetium-99m.

REFERENCES

[1] A.K. Mitra, «Emerging Nanotechnologies for Diagnostics, Drug Delivery and Medical Devices», *Elsevier Science*, 2017.

[2] J.H. Lawrence, B. Manowitz, B.S. Loeb, «Radioisotopes and Radiation», *McGraw-Hill Book Company*, New York 1964.

[3] P. Siostrzonek *et al.*, *J. Vascular Dis.* **16**, 140 (1987).

[4] R. de Laroche *et al.*, *Med. Nucl.* **41**, 55 (2017).

[5] C.D. Baker, J.C. Fowler, *Eur. J. Nucl. Med. Mol. Imaging* **40**, S410 (2013).

[6] A. Shields *et al.*, *Nat. Med.* **4**, 1334 (1998).

[7] H. Vesselle *et al.*, *Clin. Cancer Res.* **6**, 3837 (2000).

[8] J. Eary *et al.*, *Clin. Cancer Res.* **4**, 1215 (1998).

[9] T. Ul *et al.*, *Bioorg. Med. Chem.* **28**, 115189 (2020).

[10] Z. Petrovski, J. Gjorgievski, *Eur. J. Nucl. Med. Mol. Imaging* **34**, S374 (2007).

[11] D. Wild, «The Immunoassay Handbook», *Elsevier Science*, 2013, 4^{th} edition.

[12] P. Diamandis, K. Theodore, «Immunoassay», *Academic Press*, 1996.

[13] R. Lequin, *Clin. Chem.* **51**, 2415 (2005).

[14] E.I. Gofflot, *J. Immunoassay Immunochem.* **25**, 241 (2004).

[15] T. Das, M.R.A. Pillai, *Nucl. Med. Biol.* **40**, 23 (2013).

[16] European Commission, Preliminary Report on Supply of Radioisotopes for Medical use and Current Developments in Nuclear Medicine, SANCO/C/HWD 2009.

[17] IAEA-TECDOC-1340, Manual for reactor produced radioisotopes, Vienna, 2003.

[18] IAEA Technical Report Ser. No. 468, Cyclotron Produced Radionuclides: Physical Characteristics and Production Methods; Vienna, 2009.

[19] R.B. Firestone, «Table of Isotopes», *University of California: Lawrence Berkeley National Laboratory*, 1996, 8^{th} edition.

[20] A. Waltar, «Radiation and Modern Life: Fulfilling Marie Curie's Dream», *Prometheus Books*, 2005.

[21] K. Gagnon *et al.*, *Nucl. Med. Biol.* **38**, 907 (2011).

[22] V.N. Starovoitova *et al.*, *Appl. Radiat. Isot.* **85**, 39 (2014).

[23] IAEA Radioisotopes and Radiopharmaceuticals Reports No. 2, Cyclotron Produced Radionuclides; Vienna, 2017.

[24] E. Bodenstedt, *Z. Phys. A* **325**, 281 (1986).

[25] S. Mirzadeh *et al.*, *Appl. Radiat. Isot.* **48**, 441 (1997).

[26] S. Fukushima, *Bull. Chem. Soc. Jp.* **36**, 1225 (1963).

[27] E. Betak *et al.*, *Nukleonika* **52**, 17 (2007).

[28] M.N. Aslam *et al.*, *Appl. Radiat. Isot.* **132**, 181 (2018).
[29] S.S. Dietrich, B.L. Berman, *Atomic Data Nucl. Data Tables* **38**, 199 (1988).
[30] Manual for reactor produced radioisotopes, IAEA-TECDOC-1340, 2003.
[31] B. Ponsard *et al.*, *Appl. Radiat. Isot.* **67**, 1158 (2009).
[32] J. Vucina *et al.*, Yugoslav Nuclear Society Conference, YUNSC, 325, 2014.
[33] I. Martinez-Rovira, Y. Prezado, *Med. Phys.* **42**, 6703 (2015).
[34] D.R. Shearer *et al.*, *J. Nucl. Med.* **29**, 695 (1988).
[35] B.M. Dantas *et al.*, *Braz. Arch. Biol. Technol.* **48**, 2015 (2008).