East European Journal of Physics. 3. 654-658 (2026)
DOI:10.26565/2312-4334-2026-3-61 ISSN 2312-4334

INTERACTIONS BETWEEN TECHNETIUM-99m RADIOPHARMACEUTICALS AND PLASMA PROTEINS: A MOLECULAR DOCKING STUDY

V. Trusova[1]*, P. Kuznietsov[2], I. Yakymenko[2], G. Gorbenko[1]
[1]*Department of Medical Physics and Biomedical Nanotechnologies, V.N. Karazin Kharkiv National University*
4 Svobody Sq., Kharkiv, 61022, Ukraine
[2]*O.I. Akhiezer Department for Nuclear Physics and High Energy Physics, V.N. Karazin Kharkiv National University*
4 Svobody Sq., Kharkiv, 61022, Ukraine
**Corresponding Author E-Mail: valerija.trusova@karazin.ua*
Received May 16, 2026, revised July 30, 2026; accepted August 5, 2026

Technetium-99m (^{99m}Tc) is the most widespread radionuclide with physicochemical characteristics highly suitable for diagnostic nuclear medicine. The radiopharmaceuticals obtained by complexation of ^{99m}Tc with ligating agents or targeting biomolecules are increasingly used for diagnostic purposes in oncology, cardiology, nephrology, neurology and other fields of medical practice. One factor that may influence clinical efficiency of ^{99m}Tc radiotracers involves their interactions with the proteins of human blood plasma. Most studies of such kind of interactions have been focused on albumin, while much less attention was given to other protein components of blood plasma. In the present work the molecular docking technique was employed to evaluate the possibility of association between a series of ^{99m}Tc radiopharmaceuticals and plasma proteins including transthyretin, fibrinogen, alpha1-acid glycoprotein, Fc and Fab fragments of immunoglobulin G. It was found that the investigated ^{99m}Tc compounds (except pertechnetate) form the strongest complexes with alpha1-acid glycoprotein and fibrinogen. The affinities of TcMED, TcDTPA, TcMAG, TcECD, TcDIS and TcMEB for alpha1-acid glycoprotein and fibrinogen appeared to be higher than those for albumin. The structural characteristics of both plasma proteins and ^{99m}Tc radiotracers were demonstrated to determine the amino acid composition of the binding sites. The presence of peptide fragments in the structure of ^{99m}Tc compounds was assumed to markedly increase their affinity for plasma proteins. The results obtained may be helpful for gaining deeper insights into biodistribution pattern of ^{99m}Tc radiopharmaceuticals.
Keywords: *Technetium-based radiotracers; Transthyretin; Fibrinogen; Alpha1-acid glycoprotein; Immunoglobulin G; Molecular docking*

Technetium 99m (^{99m}Tc) is known as a main radionuclide currently used for obtaining a variety of diagnostic radiopharmaceuticals for nuclear medicine [1-3]. Among the advantages of ^{99m}Tc-based radiotracers are their half-life (6 h) and gamma ray energy (140 keV) resulting in a minimum dose of patient irradiation, ability to accumulate in targeting tissues or organs, rapid blood clearance, availability from ^{99}Mo/^{99m}Tc generator, relatively low cost, etc. [4-6]. Due to its unique coordination chemistry with oxidation states ranging from -1 to +7, ^{99m}Tc can form complexes with diverse ligands containing O–, C–, N–, P–, S– donor centers [7-10]. The radiopharmaceuticals with N- and S-centers appeared to be most effective in assessment of renal function, the compounds with O-centers are highly suitable for myocardial imaging, while those with S- or P-centers can be used for heart imaging and bone scintigraphy [1]. Along with these characteristics, the efficiency of radiotracers is determined by their physicochemical parameters, including size and charge, partition coefficient, stability in vitro and in vivo, pharmacokinetic behavior and plasma protein binding [11, 12]. In our previous work we employed the molecular docking technique to perform a comparative analysis of the binding affinities of ^{99m}Tc radiopharmaceuticals for albumin, the most abundant plasma protein [13]. The aim of the present study was to analyze the binding of ^{99m}Tc-based radiotracers to other plasma proteins, such as transthyretin, fibrinogen, alpha1-acid glycoprotein, Fc and Fab fragments of immunoglobulin G. A set of twelve examined ^{99m}Tc-based radiotracers included Pertechnetate [^{99m}Tc]TcO_4–(TcPER), [^{99m}Tc]Tc-Sestamibi (TcSES), [^{99m}Tc]Tc-Tetrofosmin (TcTET), [^{99m}Tc]Tc-Medronate (TcMED), [^{99m}Tc]Tc-dimercaptosuccinic acid (TcDMSA), [^{99m}Tc]Tc-diethylenetriaminepentaacetate (TcDTPA), [^{99m}Tc]Tc-mercaptoacetyltriglycine (TcMAG), [^{99m}Tc]Tc-Exametazime (TcEXA), [^{99m}Tc]Tc-diisopropyl iminodiacetic acid (TcDIS), [^{99m}Tc]Tc-ethylene cysteine dimer (TcECD), [^{99m}Tc]Tc-Mebrofenin (TcMEB), and [^{99m}Tc]Tc-hydrazinonicotinic acid conjugate-H6F (TcHYN). The plasma proteins selected for this study play significant role in many biological processes. Transthyretin is responsible for transport of the thyroid hormone thyroxine and the retinol-binding protein. Mutations in this protein lead to its misfolding and aggregation into amyloid fibrils associated with cardiomyopathy or polyneuropathy on the development of inherited transthyretin amyloidosis [14]. Fibrinogen has multiple biological functions among which are promotion of platelet adhesion and aggregation, regulation of inflammatory response, triggering of hemostasis, leukocyte activation, wound healing, etc. [15]. Alpha1-acid glycoprotein has immunomodulatory properties and affects pharmacokinetics and pharmacodynamics of drugs and endogeneous ligands [16}. Immunoglobulin G is the major serum antibody capable of binding to and neutralizing various pathogens and toxins [17].

Cite as: V. Trusova, P. Kuznietsov, I. Yakymenko, G. Gorbenko, East Eur. J. Phys. 3, 654 (2026), https://doi.org/10.26565/2312-4334-2026-3-61

METHODS

The structures of the investigated ^{99m}Tc radiopharmaceuticals [18] were built in MarvinSketch (version 18.10.0) and the geometries were further optimized in Avogadro (version 1.1.0). Five human plasma proteins such as transthyretin (TTR, PDB ID 1BMZ), fibrinogen (FIB, PDB ID 3GHG), alpha1-acid glycoprotein (AGL, PDB ID 3KQ0), Fc fragment of immunoglobulin G (IFC, PDB ID 5JII) and Fab fragment of immunoglobulin G (IFA, PDB ID 7FAB) were selected as receptors for ^{99m}Tc radiotracers. Molecular docking was conducted using the HDOCK server (https://hdock.phys.hust.edu.cn/), a hybrid docking software which combines template-based modeling and free docking [19]. The most energetically favorable docking complexes were visualized with the VMD software (version 1.14).

RESULTS AND DISCUSSION

Presented in Table 1 are the best docking scores correlating with the binding affinities of the examined ^{99m}Tc radiopharmaceuticals for plasma proteins. The analysis of the docking results revealed that TcPER has the lowest binding affinities decreasing in the order TTR > FIB > IFC ≥ AGL > IFA. Notably, the complxes of TcPER with TTR, FIB, IFC and AGL appeared to be stronger than that with albumin (the best docking score -57.77 [20]). For the other compounds under study the binding affinities were found to decrease in the rows: ***TcSES***: FIB ≥ AGL > IFA > TTR > IFC; ***TcTET***: FIB > AGL > IFA >TTR ≥ IFC; ***TcMED***: FIB ≥ AGL >IFC> TTR > IFA; ***TcDMSA***: AGL > FIB > IFC> TTR > IFA; ***TcDTPA***: AGL > FIB > TTR > IFC > IFA; ***TcMAG***: AGL > FIB > TTR > IFA ≥ IFC; ***TcEXA***: AGL > FIB ≥ TTR > IFA > IFC; ***TcDIS***: AGL > FIB > IFA > IFC ≥ TTR; ***TcECD***: AGL > FIB > TTR > IFA > IFC; ***TcHYN***: AGL > IFA > FIB > IFC > TTR; ***TcMEB:*** AGL > FIB > TTR ≥ IFA > IFC.

Table 1. Best docking scores characterizing the binding affinities of technetium-99m radiopharmaceuticals for plasma proteins

^{99m}Tc radiotracer	Transthyretin	Fibrinogen	Alpha1 acid glycoprotein	Fc fragment of immunoglobulin G	Fab fragment of immunoglobulin G
TcPER	-72.28	-67.18	-62.15	-63.11	-57.68
TcSES	-130.04	-150.47	-147.49	-126.96	-133.99
TcTET	-128.87	-143.11S	-136.31	-128.64	-132.76
TcMED	-128.69	-144.68	-142.03	-129.35	-124.69
TcDMSA	-125.36	-150.29	-159.60	-128.40	-119.23
TcDTPA	-179.19	-188.16	-209.74	-153.90	-148.29
TcMAG	-139.62	-148.47	-154.83	-114.04	-116.00
TcEXA	-137.69	-139.34	-155.74	-110.53	-119.11
TcDIS	-146.40	-193.71	-229.05	-148.80	-167.56
TcECD	-126.08	-142.34	-154.67	-110.03	-113.64
TcHYN	-185.84	-233.39	-270.04	-213.38	-251.22
TcMEB	-159.73	-195.19	-223.21	-148.14	-156.76

It appeared that the investigated ^{99m}Tc radiotracers (except TcPER) display the highest affinity for AGL and FIB, while the lowest affinities in most cases are observed for IFC and IFA. The comparison of the best binding scores presented here with those obtained in our previous work for albumin [13] indicates that some ^{99m}Tc compounds are capable of associating with plasma proteins stronger than with albumin. These systems include: TcMED – FIB / AGL, TcDTPA – AGL, TcMAG – AGL / FIB, TcECD – AGL, TcDIS – AGL / FIB, TcMEB -– AGL / FIB.

Table 2. Interface residues in the complexes of technetium-99m radiopharmaceuticals with plasma proteins

^{99m}Tc radiotracer	Transthyretin	Fibrinogen	Alpha1 acid glycoprotein	Fc fragment of immunoglobulin G	Fab fragment of immunoglobulin G
TcPER	THR_{75B} LYS_{76B} TRP_{79B} PRO_{86B} PHE_{87B} HIS_{88B} HIS_{90B} ALA_{91B} LEU_{111B} SER_{112B} PRO_{113B} TYR_{114B} SER_{115B} TYR_{116B}	TRP_{293E} LEU_{294E} GLY_{295E} ASN_{296E} ASP_{297E} ILE_{299E} SER_{300E} PHE_{329E} VAL_{331E} GLN_{332E} TYR_{338E} PHE_{75E} TRP_{403E}	PHE_{32A} TYR_{37A} HIS_{97A} PHE_{98A} PHE_{114A} ASP_{115A} ASN_{117A} ASN_{121A} TRP_{122A} GLY_{123A}	ASP_{399A} SER_{400A} PHE_{405A} ASN_{390B} TYR_{391B} LYS_{392B} LYS_{409B} LEU_{410B} THR_{411B}	VAL_{3A} ARG_{91A} VAL_{92A} PHE_{93A} LEU_{45B} GLU_{46B} TRP_{47B} ILE_{48B} ASP_{60B}
TcSES	ILE_{84A} SER_{85A} PRO_{86A} PRO_{113A} PHE_{87A} TYR_{114A} THR_{96B} ALA_{97B} ASN_{98B} ASP_{99B} SER_{100B} ARG_{103B} TYR_{105B} VAL_{122B}	ARG_{149G} TYR_{422H} TRP_{424H} HIS_{429H} GLY_{430H} THR_{431H} ASP_{432H} SER_{443H} TRP_{444H} GLY_{1S} HIS_{2S} ARG_{3S} PRO_{4S}	TYR_{27A} ALA_{29A} SER_{30A} PHE_{32A} TYR_{37A} SER_{40A} VAL_{41A} GLU_{43A} ILE_{44A} THR_{47A} LEU_{62A} GLU_{64A} GLN_{66A} ARG_{68A} LEU_{79A} ILE_{88A} ARG_{90A} TYR_{91A} VAL_{92A} GLY_{93A}	LEU_{251B} MET_{252B} ILE_{253B} HIS_{433B} ASN_{434B} HIS_{435B} TYR_{436B} THR_{437B} GLN_{438B}	PRO_{8A} GLN_{40A} LEU_{41A} PRO_{42A} GLY_{43A} THR_{44A} GLU_{78A} ALA_{79A} ASP_{80A} TYR_{82A} GLY_{95A} GLY_{96A} THR_{97A} LYS_{98A} LEU_{99A} THR_{159A} PRO_{160A} SER_{161A} LYS_{162A} TYR_{168A}

^{99m}Tc radiotracer	Transthyretin	Fibrinogen	Alpha1 acid glycoprotein	Fc fragment of immunoglobulin G	Fab fragment of immunoglobulin G
			HIS_{97A} PHE_{98A} LEU_{112A} PHE_{114A} ASN_{117A} LEU_{124A} SER_{125A} TYR_{127A}		GLN_{39B} GLY_{42B} ARG_{43B} GLY_{44B}
TcMED	LYS_{76A} LYS_{80A} SER_{85A} PRO_{86A} PHE_{87A} HIS_{88A} GLU_{89A} TYR_{114A} PHE_{95B} THR_{96B} ALA_{97B} ASN_{98B} ASP_{99B} SER_{100B} GLY_{101B} ARG_{103B} TYR_{105B} VAL_{122B}	CYS_{45G} PRO_{46G} SER_{47G} GLY_{48G} CYS_{49G} CYS_{76H} PRO_{77H} THR_{78H} GLY_{79H} CYS_{80H} LEU_{82H} CYS_{19I} PRO_{20I} THR_{21I} THR_{22I} TYR_{43J} LYS_{44J} CYS_{45J} PRO_{46J} SER_{47J} GLY_{48J} THR_{78K} GLY_{79K} CYS_{80K} CYS_{19L} PRO_{20L} THR_{21L} THR_{22L}	PHE_{32A} TYR_{37A} VAL_{41A} VAL_{92A} GLU_{96A} HIS_{97A} PHE_{98A} ALA_{99A} PHE_{114A} ASP_{115A} VAL_{116A} ASN_{117A} ASN_{121A} TRP_{122A} GLY_{123A}	PRO_{244A} PRO_{245A} LYS_{246A} PRO_{247A} THR_{250A} LEU_{251A} HIS_{310A} TRP_{313A} LEU_{314A} SER_{337A} LYS_{338A} ALA_{339A} PRO_{374A} ASP_{376A} ILE_{377A} HIS_{429A} GLU_{430A}	SER_{110A} THR_{112A} SER_{133A} ASP_{134A} GLN_{163A} ASN_{165A} ALA_{169A} ALA_{141B} GLY_{166B} VAL_{167B} HIS_{168B} PHE_{170B} VAL_{185B} VAL_{186B} THR_{187B}
TcDMSA	LYS_{76A} PRO_{86A} PHE_{87A} HIS_{88A} TYR_{114A} PHE_{95B} THR_{96B} ASN_{98B} ASP_{99B} SER_{100B} GLY_{101B} ARG_{103B} TYR_{105B} VAL_{122B} THR_{123B}	LEU_{73J} TYR_{76J} GLN_{77J} ASN_{79J} ASN_{80J} SER_{83J} HIS_{84J} THR_{87J} SER_{108K} THR_{110K} SER_{111K} SER_{114K} PHE_{115K} LEU_{47L} VAL_{50L} GLU_{51L} THR_{54L} VAL_{57L}	TYR_{27A} SER_{30A} PHE_{32A} TYR_{37A} VAL_{41A} ILE_{44A} THR_{47A} PHE_{49A} LEU_{62A} GLU_{64A} GLN_{66A} ARG_{90A} VAL_{92A} HIS_{97A} LEU_{112A} PHE_{114A} SER_{125A} TYR_{127A}	PRO_{244A} PRO_{245A} LYS_{246A} PRO_{247A} LYS_{248A} THR_{250A} LEU_{251A} TRP_{313A} LEU_{314A} ILE_{336A} SER_{337A} LYS_{338A} ALA_{339A} PRO_{374A} ASP_{376A} ILE_{377A} MET_{428A} HIS_{429A} GLU_{430A}	GLN_{40A} LEU_{41A} PRO_{42A} GLY_{43A} THR_{44A} ALA_{79A} ASP_{80A} TYR_{82A} LYS_{98A} GLN_{39B} PRO_{40B} PRO_{41B} GLY_{42B} ARG_{43B} VAL_{92B} TYR_{94B}
TcDTPA	PHE_{95A} THR_{96A} ALA_{97A} ASN_{98A} ASP_{99A} SER_{100A} GLY_{101A} ARG_{103A} TYR_{105A} VAL_{122A} THR_{123A} LYS_{76B} SER_{85B} PRO_{86B} PHE_{87B} HIS_{88B} GLU_{89B} TYR_{114B}	PRO_{204K} VAL_{205K} VAL_{206K} GLY_{218K} GLY_{219K} GLU_{220K} THR_{221K} SER_{222K} GLU_{223K} TYR_{225K} ASN_{284K} TYR_{285K} SER_{201L} VAL_{202L} ASP_{203L} LYS_{206L} GLN_{210L} GLY_{214L} PHE_{215L} GLY_{216L} HIS_{217L}	TYR_{27A} VAL_{41A} ILE_{44A} THR_{47A} PHE_{49A} PHE_{51A} LEU_{62A} GLU_{64A} GLN_{66A} LEU_{79A} ILE_{88A} ARG_{90A} TYR_{110A} LEU_{112A} PHE_{114A} SER_{125A} TYR_{127A}	VAL_{273A} LYS_{274A} PHE_{275A} ASN_{276A} TRP_{277A} GLU_{283A} VAL_{284A} HIS_{285A} ASN_{286A} ALA_{287A} LYS_{288A} THR_{289A} SER_{304A} LEU_{306A}	SER_{110A} VAL_{111A} THR_{112A} LEU_{131A} ILE_{132A} SER_{133A} ASP_{134A} GLN_{163A} ASN_{165A} GLY_{166B} VAL_{167B} HIS_{168B} PHE_{170B} VAL_{185B} VAL_{186B} THR_{187B}
TcMAG	LYS_{76A} SER_{85A} PRO_{86A} PHE_{87A} HIS_{88A} GLU_{89A} TYR_{114A} PHE_{95B} THR_{96B} ALA_{97B} ASN_{98B} ASP_{99B} SER_{100B} GLY_{101B} ARG_{103B} TYR_{105B} VAL_{122B}	ASN_{79A} ASN_{80A} SER_{83A} HIS_{84A} THR_{87A} SER_{111B} SER_{112B} SER_{114B} PHE_{115B} GLN_{116B} TYR_{117B} MET_{118B} THR_{54C} SER_{55C} VAL_{57C} LYS_{58C} ILE_{61C}	TYR_{27A} SER_{30A} THR_{47A} PHE_{49A} PHE_{51A} LEU_{62A} GLU_{64A} LEU_{79A} ILE_{88A} ARG_{90A} TYR_{110A} LEU_{112A} PHE_{114A} SER_{125A} TYR_{127A}	VAL_{273B} LYS_{274B} PHE_{275B} ASN_{276B} TRP_{277B} GLU_{283B} VAL_{284B} HIS_{285B} ALA_{287B} THR_{289B} SER_{304B}	GLN_{40A} LEU_{41A} PRO_{42A} GLY_{43A} THR_{44A} ASP_{80A} TYR_{82A} GLN_{39B} PRO_{40B} PRO_{41B} GLY_{42B} ARG_{43B} GLY_{44B} VAL_{92B} TYR_{94B}
TcEXA	TRP_{41A} LYS_{70A} GLU_{72A} HIS_{90A} GLU_{92A} VAL_{94A} TRP_{41B} LYS_{70B} GLU_{2B} HIS_{90B} GLU_{92B}	TYR_{76A} ASN_{79A} ASN_{80A} SER_{83A} HIS_{84A} THR_{87A} THR_{110B} SER_{111B} SER_{114B} PHE_{115B} TYR_{117B} $ET_{118}B$ LYS_{53C} THR_{54C} VAL_{57C} LYS_{58C} ILE_{61C}	TYR_{27A} SER_{30A} PHE_{32A} VAL_{41A} ILE_{44A} THR_{47A} PHE_{49A} PHE_{51A} LEU_{62A} GLU_{64A} GLN_{66A} LEU_{79A} ARG_{90A} TYR_{110A} LEU_{112A} PHE_{114A} SER_{125A} TYR_{127A}	VAL_{273A} LYS_{274A} PHE_{275A} ASN_{276A} TRP_{277A} GLU_{283A} VAL_{284A} HIS_{285A} ASN_{286A} ALA_{287A} THR_{289A} SER_{304A} LEU_{306A}	GLY_{32A} HIS_{33A} ASN_{34A} LYS_{36A} TYR_{86A} ARG_{88A} SER_{89A} ARG_{91A} ILE_{100B} ALA_{101B} GLY_{102B} GLY_{103B}
TcECD	LYS_{76A} LYS_{80A} SER_{85A} PRO_{86A} PHE_{87A} HIS_{88A} GLU_{89A} TYR_{114A} PHE_{95B} THR_{96B} ALA_{97B} ASN_{98B}	TYR_{76J} ASN_{79J} ASN_{80J} SER_{83J} HIS_{84J} LEU_{86J} THR_{87J} SER_{111K} SER_{114K} PHE_{115K} TYR_{117K} LYS_{53L}	TYR_{27A} SER_{30A} PHE_{32A} VAL_{41A} ILE_{44A} THR_{47A} PHE_{49A} PHE_{51A} LEU_{62A} GLU_{64A} GLN_{66A} LEU_{79A}	PRO_{244A} PRO_{245A} LYS_{246A} PRO_{247A} THR_{250A} LEU_{251A} TRP_{313A} LEU_{314A} SER_{337A} LYS_{338A} ALA_{339A} PRO_{374A}	THR_{112A} LEU_{131A} SER_{133A} ASP_{134A} GLN_{163A} SER_{164A} ASN_{165A} HIS_{168B} THR_{169B} PHE_{170B} VAL_{185B} THR_{187B}

^{99m}Tc radiotracer	Transthyretin	Fibrinogen	Alpha1 acid glycoprotein	Fc fragment of immunoglobulin G	Fab fragment of immunoglobulin G
	ASP_{99B} ARG_{103B} TYR_{105B} VAL_{122B}	THR_{54L} SER_{55L} VAL_{57L} LYS_{58L} ILE_{61L}	ILE_{88A} ARG_{90A} TYR_{110A} LEU_{112A} PHE_{114A} SER_{125A} TYR_{127A}	ASP_{376A} ILE_{377A} HIS_{429A} GLU_{430A}	
TcMEB	THR_{96A} ALA_{97A} ASN_{98A} ASP_{99A} SER_{100A} GLY_{101A} ARG_{103A} TYR_{105A} VAL_{122A} LYS_{76B} LYS_{80B} PRO_{86B} PHE_{87B} TYR_{114B}	SER_{222K} TYR_{239K} ASP_{241K} ASN_{243K} THR_{244K} VAL_{251K} GLN_{253K} ASN_{254K} ARG_{255K} GLN_{256K} GLY_{287K} LEU_{288K} PRO_{289K} GLU_{313K} MET_{314K} GLU_{315K} LYS_{321K} LYS_{449K} MET_{450K} SER_{451K} MET_{452K} LYS_{453K}	TYR_{27A} SER_{30A} PHE_{32A} TYR_{37A} SER_{40A} VAL_{41A} ILE_{44A} THR_{47A} LEU_{62A} GLU_{64A} GLN_{66A} ARG_{68A} ARG_{90A} VAL_{92A} GLY_{93A} HIS_{97A} PHE_{114A} SER_{125A} TYR_{127A}	SER_{354A} ARG_{355A} ASP_{356A} TYR_{349B} THR_{350B} LEU_{351B} PRO_{352B} TRP_{417B} LYS_{439B} SER_{440B} LEU_{441B} SER_{442B} LEU_{443B} SER_{444B}	SER_{110A} VAL_{111A} THR_{112A} SER_{133A} ASP_{134A} GLN_{163A} THR_{139B} ALA_{141B} GLY_{166B} VAL_{167B} HIS_{168B} PHE_{170B} VAL_{185B} VAL_{186B} THR_{187B}

The analysis of interfacial amino acid residues showed that TcSES, TcMED, TcDMSA, TcDTPA, TcMAG, TcECD and TcMEB associate with essentially similar binding sites located at the interface between identical A and B chains of homotetrameric transthyretin molecule, while TcPER and TcEXA occupy distinct sites (Table 2). In contrast to transthyretin, for fibrinogen the similarity between the amino acids constituting the binding sites was observed only for TcMAG, TcEXA and TcECD, while the other compounds interacted with completely different sets of amino acid residues. In the case of AGL the binding motif common for TcSES, TcDMSA, TcDTPA, TcMAG, TcEXA, TcECD and TcMEB involves the residues TYR_{27A} VAL_{41A} ILE_{44A} THR_{47A} PHE_{49A} LEU_{62A} GLU_{64A} GLN_{66A} ARG_{90A} LEU_{112A} PHE_{114A} SER_{125A} TYR_{127A}, while the binding sites for TcPER and TcMED contain the only residue (PHE_{114A}) from the above binding motif. The Fc fragment of immunoglobulin G has essentially similar binding sites for TcMED, TcDMSA and TcECD, all containing the residues PRO_{244A} PRO_{245A} LYS_{246A} PRO_{247A} THR_{250A} LEU_{251A} TRP_{313A} LEU_{314A} SER_{337A} LYS_{338A} ALA_{339A} PRO_{374A} ASP_{376A} ILE_{377A} HIS_{429A} GLU_{430A}. Analogously, the sites for TcDTPA, TcMAG and TcEXA include similar residues such as VAL_{273B} LYS_{274B} PHE_{275B} ASN_{276B} TRP_{277B} GLU_{283B} VAL_{284B} HIS_{285B} ALA_{287B} THR_{289B} SER_{304B}. For the Fab fragment of immunoglobulin G similar binding modes were revealed for TcMED, TcDTPA and TcMEB, as well as for TcDMSA and TcMAG.

Overall, the above findings indicate that structural peculiarities of both ^{99m}Tc radiopharmaceutical and plasma protein determine the mode and strength of their complexation. For instance, the highest binding affinities observed for TcHYN for all examined proteins seem to arise from the presence of specific peptide (YLFFVFER) in its structure, in contrast to the other ^{99m}Tc compounds.

CONCLUSIONS

In summary, the molecular docking study of the interactions between twelve structurally different ^{99m}Tc radiopharmaceuticals and five functionally important proteins of human blood plasma revealed that: (i) the explored ^{99m}Tc compounds (except pertechnetate) showed the highest affinity for alpha1-acid glycoprotein and fibrinogen, while the lowest affinities were observed for Fc and Fab fragments of immunoglobulin G; (ii) the affinities of TcMED, TcDTPA, TcMAG, TcECD, TcDIS, TcMEB for alpha1-acid glycoprotein, and the affinities of TcMED, TcMAG, TcDIS, TcMEB for fibrinogen are higher than the corresponding parameters for albumin; (iii) among the ^{99m}Tc compounds under study TcHYN forms the strongest complexes with plasma proteins; iv) the amino acid composition of the binding sites shows both similarities and differences depending on the structural features of ^{99m}Tc radiotracers and plasma proteins. These findings suggest that pharmacokinetics and pharmacodynamics of ^{99m}Tc radiopharmaceuticals can be affected by their complexation with functional proteins of human blood plasma that have to be taken into account while using these compounds in clinical practice.

Acknowledgements

This work was supported by the Ministry of Education and Science of Ukraine (the project № Д3/174-2025).

ORCID IDs

Valeriya Trusova, https://orcid.org/0000-0002-7087-071X; **Galyna Gorbenko,** https://orcid.org/0000-0002-0954-5053
Pylyp Kuznietsov, https://orcid.org/0000-0001-8477-1395, **Ivan Yakymenko,** https://orcid.org/0000-0002-0194-8376

REFERENCES

[1] M.U. Akbar, M.R. Ahmad, A. Shaheen, and S. Mushtaq, J. Radioanal. Nucl. Chem. **310**, 477–493 (2016). https://doi.org/10.1007/s10967-016-5019-7
[2] T. J. Ruth, Annu. Rev. Nucl. Part. Sci. **70**, 77–94 (2020). https://doi.org/10.1146/annurev-nucl-032020-021829
[3] M. T. Ma, Front. Chem. Biol. **4**, 1729615 (2026). https://doi.org/10.3389/fchbi.2025.1729615
[4] G. M. Currie, and E. M. Rohren, Semin. Nucl. Med. **55**, 829-840 (2025). https://doi.org/10.1053/j.semnuclmed.2025.01.005

[5] E. Strub, D. Badea, J. Bruns, A. Frontera, N. Mayordomo, A. Sakhonenkova, M. R. Jungfer, M. Wickleder, C.Yong, and M. Zegke, Eur. J. Inorg. Chem. **28**, e202400780 (2025). https://doi.org/10.1002/ejic.202400780
[6] N. Ahmed, and M. Zia, J. Acad. Radiol. **6**, 143–159 (2023). https://doi.org/10.1007/s42058-023-00128-7
[7] A. Maruk, A. Bruskin, and G. Kodina, Radiochemistry **53**, 341–353 (2011). https://doi.org/10.1134/S1066362211040011
[8] I. Ibrahim, J. Radioanal. Nucl. Chem, **281**, 669–674 (2009). https://doi.org/10.1007/s10967-009-0040-8
[9] M. Sanad, Radiochemistry **55**, 539–544 (2013). https://doi.org/10.1134/S1066362213050159
[10] E. von Guggenberg, H. Dietrich, I. Skvortsova, M. Gabriel, I. Virgolini, and C. Decristoforo, Eur. J. Nucl. Med. Mol. Imaging **34**, 1209–1218 (2007). https://doi.org/10.1007/s00259-006-0348-3
[11] Y. Arano, Ann. Nucl. Med. **16**, 79–93 (2002). https://doi.org/10.1007/BF02993710
[12] A. S. Dzik-Jurasz, Br. J. Radiol. **76**, 98–109 (2003). https://doi.org/10.1259/bjr/25833499
[13] V. Trusova, U. Malovytsia, P. Kuznietsov, I. Yakymenko, and G. Gorbenko, East Eur. J. Phys. **2**, 405-411 (2025). https://doi.org/10.26565/2312-4334-2025-2-49
[14] M. A. Liz, T. Coelho, V. Bellotti M. I. Fernandez-Arias, P. Mallaina, and L. Obici, Neurol. Ther. **9**, 395–402 (2020). https://doi.org/10.1007/s40120-020-00217-0
[15] A. S. Wolberg, J. Thromb. Haemost. **21**, 3005-3015 (2023). https://doi.org/10.1016/j.jtha.2023.08.014
[16] T. Fournier, N. Medjoubi, and D. Porquet, Biochim. Biophys. Acta Protein Struct. Mol. Enzymol. **1482**, 157–171 (2000). https://doi.org/10.1016/S0167-4838(00)00153-9
[17] S. Yanaka, R. Yogo,and K. Kato, Biophys. Rev. **12**, 637–645 (2020). https://doi.org/10.1007/s12551-020-00698-1
[18] S. Rathmann, Z. Ahmad, S. Slikboer, H. Bilton, D. Snider, and J. Valliant, In: J. Lewis, A. Windhorst, B. Zeglis (eds) Radiopharmaceutical Chemistry. Springer, Cham. (2019). https://doi.org/10.1007/978-3-319-98947-1_18
[19] Y. Yan, H. Tao, J. He, and S-Y. Huang, Nat. Protoc. **15**, 1829–1852 (2020). https://doi.org/10.1038/s41596-020-0312-x
[20] V. Trusova, P. Kuznietsov, I. Yakymenko, and G. Gorbenko, East Eur. J. Phys. **1**, 520-524 (2026). https://doi.org/10.26565/2312-4334-2026-1-59

ВЗАЄМОДІЇ МІЖ РАДІОФАРМПРЕПАРАТАМИ ТЕХНЕЦІЮ 99m ТА БІЛКАМИ ПЛАЗМИ: ДОСЛІДЖЕННЯ МЕТОДОМ МОЛЕКУЛЯРНОГО ДОКІНГУ

Валерія Трусова[1], Пилип Кузнєцов[2], Іван Якименко[2], Галина Горбенко[1]

[1]Кафедра медичної фізики та біомедичних нанотехнологій, Харківський національний університет імені В.Н. Каразіна м. Свободи 4, Харків, 61022, Україна

[2]Кафедра фізики ядра та високих енергій імені О.І. Ахієзера, Харківський національний університет імені В.Н. Каразіна м. Свободи 4, Харків, 61022, Україна

Технецій-99m (^{99m}Tc) є найбільш розповсюдженим радіонуклідом з фізико-хімічними характеристиками, необхідними для діагностичної ядерної медицини. Радіофармпрепарати, отримані шляхом комплексоутворення між ^{99m}Tc та лігандами чи таргетними біомолекулами все ширше застосовуються для діагностичних цілей в онкології, кардіології, нефрології, неврології та інших сферах клінічної практики. Одним із чинників, що можуть впливати на клінічну ефективність сполук ^{99m}Tc, є їхні взаємодії з білками плазми крові людини. Переважна більшість досліджень такого типу взаємодій були сфокусовані на альбуміні, тоді як значно менше уваги приділялось іншим білковим компонентам плазми крові. У даній роботі метод молекулярного докінгу був застосований для оцінки можливості асоціації між серією ^{99m}Tc радіофармпрепаратів та білками плазми включаючи транстиретин, фібриноген, альфа1 кислий глікопротеїн, Fc та Fab фрагменти імуноглобуліну G. Було показано, що досліджувані сполуки технецію 99m (окрім пертехнетату) утворюють найміцніші комплекси з альфа1 кислим глікопротеїном та фібриногеном. Спорідненість TcMED, TcDTPA, TcMAG, TcECD, TcDIS та TcMEB до альфа1 кислого глікопротеїну та фібриногену виявилась вищою, ніж спорідненість цих сполук до альбуміну. Було продемонстровано, що структурні характеристики як білків плазми, так і комплексів технецію 99m визначають амінокислотний склад сайтів зв'язування. Висловлено припущення, що наявність пептидного фрагменту в структурі ^{99m}Tc сполук значно підвищує їхню спорідненість до білків плазми. Отримані результати можуть бути корисними для більш глибокого розуміння розподілу ^{99m}Tc радіофармпрепаратів в організмі.

Ключові слова: *радіофармпрепарати на основі технецію 99m, транстиретин, фібриноген, альфа1 кислий глікопротеїн, імуноглобулін G, молекулярний докінг*